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RODERICK DUNCAN MACLEOD
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Textbook of Palliative Care

Springer

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With 194 Figures and 184 Tables

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ISBN 978-3-319-77738-2 ISBN 978-3-319-77740-5 (eBook)
ISBN 978-3-319-77739-9 (print and electronic bundle)
https://doi.org/10.1007/978-3-319-77740-5

Library of Congress Control Number: 2019932976

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Foreword by Luc Deliens

We recently commemorated the 100th birth anniversary of Cicely Saunders, born in 1918. She began her education by studying philosophy, politics, and economics at the University of Oxford and then qualified as a nurse during the Second World War in the Nightingale Home and Training School in London; as a medical social worker, again at Oxford; and then as a medical doctor in the 1950s at King's College London. Her multidisciplinary educational background, combined with her personal experience (she twice fell in love with dying patients, both Polish refugees) which included a period of what she called "pathological grieving" after a series of bereavements, will have had an impact on her thinking and the development of the concept of palliative care, but also on her activism and her decades-long campaign against the terminal neglect of those who are dying and the medicalization of death. She wrote her first medical paper on care for dying people in 1957, and by the summer of 1967, she had initiated palliative care as an interdisciplinary concept at St. Christopher's Hospice in London, in the establishment of which she was involved. She is now acknowledged worldwide as one of the founders of the palliative care and hospice movement. Ever since, the field of palliative care has grown rapidly across the world, and the scientific evidence for its effectiveness is steadily growing, as is the list of countries with a national palliative care policy. The number of scientific journals covering death, dying, supportive care, palliative care, and end-of-life care is also rapidly growing, and about 20 of these have an impact factor indexed by the Web of Science, with around 5 being classified in the upper quartile of their domain. Hence, this textbook is timely and one of the indicators that palliative care as a clinical as well as a scientific domain has come to full growth.

"Palliative care" can be understood in several ways. It can be understood as a clinical specialism for medical doctors, as it is now recognized by the Royal College of Physicians as a specialty within the UK; it can also be understood as a specialist palliative care service, e.g., an inpatient hospice or palliative care unit, in which a multidisciplinary team delivers the care of people with serious illnesses, or, as a concept of care, a holistic philosophy of care taking into account more than just medical problems such as the burden of physical symptoms. This is reflected in the holistic definition of palliative care by the World Health Organization in which (apart from the medical aspects), nursing, social, psychological, and existential aspects are covered, or ideally should be covered. The latter suggests that there is a difference between what palliative

care is in the real world and what it should be in the reality of our health-care systems; in most countries, the quality of palliative care in most care settings or contexts is suboptimal or can potentially be improved and further developed. This textbook can help clinicians, students, health-care providers, managers, researchers, and also policy-makers to improve their knowledge and skill in palliative care.

This textbook presents 101 chapters in 11 different parts: Palliative Care: Definitions, Development, Policies; Symptom Assessment and Management; Palliative Care Professionals and Provision; Organization of Palliative Care in Different Settings; Palliative Care in Specific Disease Groups; Palliative Care in Specific Populations; Palliative Care Emergencies; Ethics of Palliative Care and End-of-Life Decision-Making; Research in Palliative Care; Public Health Approach in Palliative and End-of-Life Care; and Financial Aspects and Cost-Effectiveness in Palliative Care. It offers a synthesis of the practice and knowledge base that has grown over the last 50 years. Since Cicely Saunders developed the concept of palliative care, focusing on preventing harm to people who are dying and promoting their quality of life, the field has evolved professionally and now covers a complex and wide range of aspects of care for all people with a serious illness, involving informal or family carers and volunteers as well as health-care professionals. Palliative care promotes life until death and should be understood as different from the narrow concept of terminal care. In order to challenge this narrow understanding, palliative care should also embrace the knowledge and skills of the disciplines of health promotion and public health, the latest developments of which are well covered in this textbook.

Cicely Saunders' multidisciplinary background is well reflected by the contents of the *Textbook of Palliative Care* and by its editors, a palliative care doctor, Professor Rod MacLeod from New Zealand, and a social scientist and clinical psychologist, Professor Lieve Van den Block from Belgium. The textbook, with over 100 chapters, covers the breadth of the domain, including clinical, health services, and public health-related aspects of palliative care. The editors should be congratulated on this impressive academic achievement and, more specifically because they have consulted a wide range of clinicians, far more social scientists, and public health experts than any other textbook on palliative care. I hope that this book, available online as well as in print, soon finds its way into the classrooms, universities, and vocational schools of all involved in the care of those who are dying or those with serious illness.

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Luc Deliens

Foreword by Sheila Payne

Palliative care has come of age. No longer can we claim, or make excuses, that palliative care is a young or novice discipline. This impressive *Textbook of Palliative Care* with over 100 chapters offers convincing evidence that palliative care is now a mature discipline. The textbook provides a comprehensive overview of numerous topics that form the core and substance of the discipline. The global reach of the chapter contributors and the distinguished section editors and the overall guidance from two remarkable editors have produced an outstanding testament to not only palliative care's place within medicine but also, importantly, within society.

However, let me caution you from any feelings of complacency and premature celebration. There are still many challenges ahead. We know from the work of the Lancet Commission on pain relief and palliative care that on a global scale, there remain very poor access to palliative care and woefully insufficient affordable and accessible pain relief (Knaul et al. 2017). According to the authors, in 20 health conditions where there were identifiable palliative care needs, 84% account for deaths in adults and 60% in children. Global projections indicate that between 40 and 80 million patients with advanced disease need access to palliative care, with 78–95% of them living in low- and middle-income countries (Knaul et al. 2017). Shockingly, infants and children have even less access to pain relief and palliative care than adults (Knaul et al. 2017).

One way forward is to ensure that the key principles of palliative care are taught as a fundamental part of all basic and post-basic health and social care education programmes. Let me draw a comparison here with the recognition of communication skills as a core element of all courses. When I trained as a nurse in the early 1970s in a well-respected London teaching hospital, my only communication skills education was the well-worn advice for nurses working in hospital wards, which was to *draw the curtains and reassure the patient*. Quite how I might provide that 'reassurance', when the poor patient was likely to be facing an uncomfortable, painful and/or embarrassing procedure, was never revealed. Fortunately, communication skills education is now a core topic in virtually all medical, nursing and other health professional programmes. In some countries, it is even mandatory. In my view, likewise, palliative care core competencies also need to be embedded in all health and social care programmes as essential aspects of professional education (Gamondi et al. 2013).

So what will be the future challenges facing palliative care? We need to be prepared to 'give it away' so that basic palliative care practices and knowledge move beyond the restricted domains of certain places such as specialist palliative care units, or disease groups such as those with cancer, or age groups, or professional disciplinary boundaries. I am not arguing that there is no future for specialist palliative care, as the people working in these settings, and with this expertise, are essential to drive the education of others; improve the quality of care, through research and reflective practice; and provide leadership. However, to ensure universal coverage and access to basic palliative care, more energy, resource and leadership need to be devoted to spreading the political and policy message that palliative care is not a luxury for the few but a fundamental human right.

Universal access to high-quality palliative care may not be quite within our grasp yet but should be a goal for everyone. Suffering, especially avoidable suffering, blights the lives of millions of people, creating a lasting impact on their families in terms of financial burden and emotional distress. Addressing the challenges of responding compassionately, while drawing on the best scientific evidence, to ameliorate suffering for those with complex, advanced and life-limiting conditions lies at the heart of palliative care. This textbook is a good example of this commitment to improve care for all in need.

This textbook is truly outstanding. I am not going to highlight specific chapters, as I am sure that all contributors will have fulfilled their brief under the guidance of the editorial team. It is a textbook to dip into, relishing the quality of the information contained in these pages. You, dear reader, will make your choices, but let me urge you to venture into new areas, perhaps reading those chapters that are outside your normal interest zone. Become a critical consumer of the material and resources presented in this textbook. How does it compare to your practice? What does it challenge you to think about in a new and different way? What do you agree with? This textbook, developed by an international team of experts, offers guidance on the development and establishment of all aspects of palliative care services, and it wonderfully captures the flourishing of a mature discipline.

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Preface

Nothing in life is to be feared, it is only to be understood.

Attributed to Marie Curie. *On ne doit rien craindre dans la vie—il suffit de comprendre* in Université Laval, Faculté de médecine, Société medicale des hôpitaux universitaires de Québec, Laval médical (1951), 16, 569

Palliative care has been identified as a discrete part of healthcare for over 50 years, and yet we still find ourselves having to explain the nature and practice of palliative care to many of our professional colleagues and to the public in general. Healthcare education and training has been slow to recognize the vital importance of ensuring that *all* practitioners have a good understanding of what is involved in the care of people with serious or advanced illnesses and their families. Because of this limited exposure, many laypeople and professionals still have understandable fear and anxiety about death and dying.

However, the science of palliative care is advancing, and our understanding of the evidence concerning many aspects of palliative care is developing rapidly. There are now excellent research teams and facilities around the world exploring different characteristics of this essential aspect of healthcare from a wide range of disciplines.

There have been many authoritative books on various facets of palliative care produced over the last years. In planning this *Textbook of Palliative Care,* we hoped to produce a comprehensive, clinically relevant, and state-of-the-art book, aimed at advancing palliative care, as a science, a clinical practice, and an art.

For this major reference work, we have been able to draw on our own collective experience and the goodwill of many fine people from around the world. We have endeavored to produce a *Textbook* that showcases the multi- and interdisciplinarity of palliative care and is unique in bringing together authors from all fields of palliative care – physical, psychological, social, and existential or spiritual. The majority of them are internationally recognized experts in their chosen discipline. We have been helped by dozens of authors and the committed section editors, who have given their time, expertise, and wisdom to ensure that this work can be disseminated around the globe to assist in the understanding of all aspects of illness and disease near the end of life as

well as death, dying, and into bereavement. Our authors have drawn not only on the evidence available but also on their own phronesis or practical wisdom. They have summarized and extended the state of the art in their field and challenge the reader with new insights, challenges, opportunities, and potential future evolutions. We are deeply indebted to all those who have been involved in the preparation, writing, and editing of this work. They all undertook their work with enthusiasm and commitment.

We expect this *textbook* will be of value to practitioners in all disciplines and professions where the care of people approaching death is important, specialists as well as nonspecialists, in any setting where people with serious advanced illnesses reside. It can also be an important resource for researchers, policy-makers, and decision-makers – national or regional – as well as for laypersons, patients, and/or families, seeking to learn more about palliative care. Neither the science nor the art of palliative care will stand still, so we hope to be able to keep this *textbook* updated as the authors find new evidence and approaches to care.

Our special appreciation goes to Vasowati Shome and Tina Shelton of Springer who have guided us expertly through the process of creating this reference work – we are deeply indebted to them.

March 2019

Roderick Duncan MacLeod
Lieve Van den Block

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About the Editors

Roderick Duncan MacLeod is a Palliative Medicine Specialist at Harbour Hospice in Auckland, New Zealand, and Consultant to HammondCare in Sydney where he is also Honorary Professor in the University of Sydney School of Medicine.

He gained his primary medical degrees from the University of Dundee in 1976 and went on to train for general practice. He was a Principal in general practice for almost 10 years before moving to the discipline of palliative care. He was first appointed as Medical Director of the Dorothy House Foundation in Bath, England, in 1989 after having completed a period of prolonged study leave exploring palliative care in the community. In 1994, he was appointed Medical Director and subsequently Director of Palliative Care at the Mary Potter Hospice in Wellington, New Zealand. He was made a Fellow of the Royal College of General Practitioners (UK) in 1999. He was a Foundation Fellow of the Royal Australasian College of Physicians, Australasian Chapter of Palliative Medicine, in 2000. He received his Ph.D. in 2001 from the University of Glamorgan (Prifysgol De Cymru) for his work and publications on "Changing the Way that Doctors Learn to Care for People Who Are Dying."

In 2003, he was appointed to New Zealand's first Chair in Palliative Care as the inaugural South Link Health Professor in Palliative Care at the University of Otago Dunedin School of Medicine and in 2013 was appointed Conjoint Professor in Palliative Care at the University of Sydney and worked clinically as Senior Staff Specialist in Palliative Care for HammondCare in Sydney. He has been a Member of the Australasian Chapter of Palliative Medicine

Education Committee, the NZ National Health Committee – Working Party on Care of People Who Are Dying, the NZ Palliative Care Expert Working Group, and the Council of the Asia Pacific Hospice Network. He was appointed to the Expert Advisory Group (Physician Education) and the Chapter of Palliative Medicine Committee of the Royal Australasian College of Physicians and the NZ Ministry of Health Palliative Care Advisory Group. He has also held a number of roles within Hospice NZ.

He has published over 130 peer-reviewed articles in the field of palliative care in national and international journals and has written over 20 chapters for palliative care texts. In addition, he has been on editorial boards of international peer-reviewed journals in the field of palliative care and has reviewed manuscripts for over 25 different academic journals. He has also published two anthologies of poetry, exploring what it might be like to approach death and experience bereavement and loss.

He is one of the authors of *The Palliative Care Handbook*, which has become a freely available standard text for healthcare professionals in New Zealand and parts of Australia.

He was appointed a Member of the New Zealand Order of Merit by Her Majesty Queen Elizabeth II in the Queen's birthday honors in 2015.

Lieve Van den Block is Professor of Ageing and Palliative Care at the Vrije Universiteit Brussel (VUB) and Chair of the Ageing and Palliative Care Research Programme at the End-of-Life Care Research Group of the VUB and Ghent University in Belgium. She holds a Ph.D. in Medical Social Sciences and a master's in Clinical Psychology. Professor Van den Block has been involved in palliative care research for over 15 years, focusing on national and international public health and interventional research aimed at monitoring and improving palliative and end-of-life care. She has received several scientific awards for her work, including the 2014 Early Researcher Award of the European Association for Palliative Care. She has published over 100 peer-reviewed articles on palliative care and is editor and author of several books and chapters. Her work has been supported by grants from the European Commission, national fundamental and applied research foundations, and leading medical and health charities.

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Part I

Palliative Care: Definitions, Development, Policies

Approach and Nature of Palliative Care

1

Roderick D. MacLeod

Contents

Abstract

Caring for people who are near the end of life has a relatively short timeframe as a specialist health care activity. In this chapter, the history of palliative care is briefly outlined along with a description of who might provide such care. An introduction to aspects of learning in palliative care is followed by an emphasis on the importance of psychosocial-spiritual assessment and care; some of the universal needs of people who are dying is outlined. It is important to recognize the significance of understanding the social, emotional, psychological, cultural, sexual, and spiritual context of each

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_3

clinical situation and to view these within our own and our institution's and perhaps our society's ethical framework. By doing so, we can begin to understand how best to understand the nature of palliative care and how best we might approach this most significant aspect of care in people's lives.

Caring for people who are dying is clearly not new but has been seen as a special form of care for centuries. In the first millennium, the Christian church was closely involved with this activity, and the original hospices were set up as resting places for travelers. Religious orders advanced the notion of care for people who were dying in the nineteenth century, and perhaps the first of its kind, St Joseph's Hospice, was founded in London in 1905. It was however as a response to the perceived inadequacies of medical care that what has become known as the modern hospice movement was born (Clark 2002). The pioneering work of hospices such as St Christopher's Hospice, which opened in Sydenham, London, in 1967, demonstrated that the principles of hospice care (good clinical practice, whatever the patient's illness, wherever the patient is under care, whatever his/her social status, creed, culture or education, http://hospicecare.com/about-iahpc/publications/manuals-guidelines-books/getting-started/6-principles-of-palliative-care) could be applied in a variety of settings.

Dame Cicely Saunders introduced the concept of whole person care in that institution and developed the model of "total pain" which highlighted not only the physical aspects of a person's pain but also psychological, social, and spiritual dimensions of their distress (Saunders and Sykes 1993). The term "palliative care" was coined in Canada in 1974 by Balfour Mount, a pioneering surgeon who had worked in London with Saunders and wanted to take the concept back to Canada where there could have been confusion among the French-speaking population about the term hospice. Using the term palliation to reflect the non-curative nature of care was not new – it had been used in the seventeenth century. This terminology was subsequently adopted in many countries, and a new medical specialty was proposed – that of palliative medicine. The discipline received recognition by the Royal College of Physicians, London, in 1987 as a specialty within medicine in the United Kingdom (UK). Since that time other countries have adopted that approach, and palliative medicine and palliative care are practiced around the world in over 100 countries. A universally agreed definition of palliative care was disseminated by the World Health Organization (WHO) in 1986, followed by a revision in 1990. A revised and updated definition of palliative care was accepted by the WHO in 2002 (Sepúlveda et al. 2002).

Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual.

Palliative care:

- Provides relief from pain and other distressing symptoms
- Affirms life and regards dying as a normal process
- Intends neither to hasten or postpone death
- Integrates the psychological and spiritual aspects of patient care
- Offers a support system to help patients live as actively as possible until death
- Offers a support system to help the family cope during the patient's illness and in their own bereavement
- Uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated
- Will enhance quality of life and may also positively influence the course of illness
- Is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications

Definitions are helpful in gaining consensus about the limits of a specialty, but what does it mean in practice? Generally speaking, people

with advancing disease need to be supported and cared for by clinicians with excellent skills.

1 Who Provides Palliative Care?

Palliative care is provided by two distinct categories of health and social care professionals:

- Generalist palliative care is provided by those working to provide day-to-day care to patients, families, and carers in their homes and in hospitals:
  - They should be able to assess the care needs of each patient and their families across the domains of physical, psychological, social, and spiritual needs.
  - Meet those needs within the limits of their knowledge, skills, and competence in palliative care, and know when to seek advice from or refer to specialist palliative care services.
- Specialist palliative care is provided by professionals with additional training in the discipline and who only work in palliative care (e.g., consultants in palliative medicine and clinical nurse specialists in palliative care).

2 Specialist Palliative Care Services

These services are provided by specialist interdisciplinary teams and include:

- Assessment, advice, and care for patients and families in any or all care settings, including hospitals and care homes, also known as palliative care consultation
- Specialist inpatient facilities (in hospices or hospitals) for patients and families who benefit from the continuous support and care of those specialist teams
- Intensive coordinated home support for patients with complex needs who wish to stay at home (this may involve the specialist palliative care service working with the patient's own doctor and community nurse to enable someone to stay in their own home).
  - Many teams also now provide extended specialist palliative nursing, medical, social, and emotional support and care in the patient's home, often known as "hospice at home."
- Outpatient clinic appointments and day-care facilities that offer a range of opportunities for assessment and review of patients' needs and enable the provision of physical, psychological, and social interventions within a context of social interaction, support, and friendship. Many also offer creative and complementary therapies.
- Advice and support to all the people involved in a patient's care.
- Bereavement support services which provide support for the people involved in a patient's care before and following the patient's death.
- Education and training (and for many, research) in palliative care.

The specialist teams should include palliative medicine and palliative care nurse specialists together with a range of expertise provided by physiotherapists, occupational therapists, art and music therapists, dieticians, pharmacists, social workers, and those able to give spiritual and psychological support.

3 Who Should Receive Palliative Care?

Anyone with a life-limiting disease should be able to have access to palliative care services. Historically modern palliative care services were primarily involved with providing care for people with cancer and some neurological disorders such as motor neuron disease or other degenerative disorders of the nervous system.

The other major group of people who should receive palliative care are those with failure of one of the major organs of the body such as the lungs, heart, kidneys, liver, or brain. In these situations, people often have a prolonged period of time to adjust to the understanding that the body is failing. One problem though can be that medical science has become so adept at propping up failing bodies that the realization that death is approaching may not be so apparent. This can produce problems for families and carers as death approaches.

It has been suggested that the clinical course of people who do not die suddenly tends to follow one of three trajectories (Dy and Lynn 2007). The first is the maintenance of relatively good function until a predicted decline a few weeks or short months before death. The second is the course of chronic organ failure which shows a slow decline with exacerbations that may end in sudden death. The third trajectory is one where there is poor functional status over a long time with a slow but relentless decline; frail elderly people with many comorbidities fit into this group. It is important therefore that services are developed for people who are dying in any of these ways. There are a number of models available – for example, the Gold Standards Framework in the UK which incorporates resources and end-of-life tools into primary care, hoping to enable people to have real choice about where they wish to die (Thomas 2003; King et al. 2007).

Of course, the majority of people who are dying would prefer to do so at home being cared for by their primary healthcare professionals. Primary care shares common values with specialist palliative care – holistic, patient centered, and delivered in the context of their families – but too often it becomes difficult for a number of reasons for people to be cared for in their own homes (Murray et al. 2004). Developing primary palliative care is essential if people are to exercise their right to die in the bed of their choice.

Twenty years ago, David Field, an expert in the sociology of death and dying, identified two important differences between patients with cancer and those with nonmalignant conditions (Field 1998). Perhaps not much has changed over those 20 years? First, differences in disease progression mean there is a continuing benefit from curative/restorative interventions and treatments for the latter category. Second, there was greater uncertainty about the fact and likely time of death with non-cancer patients. Field identifies the latter as appearing to be the key obstruction to extending specialist palliative care services to non-cancer patients. This is because they will not be seen as suitable candidates for palliative care until they have been defined as terminally ill. One of the reasons that this may occur is because of the difficulty many clinicians have in dealing with uncertainty in general. In medicine, and possibly in other disciplines as well, uncertainty stimulates and propels activity (Hall 2002) – doctors have a "propensity to resolve uncertainty and ambiguity by action rather than inaction" (Katz 1984). Increasing diagnostic uncertainty leads to a reluctance to withdraw from "active" interventions, leaving patients and families in a similar situation of ambiguity and doubt about the future (Christakis and Asch 1993). This relates to a tendency for the continuation of what might be deemed futile treatment in the face of relentlessly advancing disease. Taken out of context (i.e., without considering the person as a whole), almost any disease may be deemed "treatable" – such are the advances in medical science and technology. This confidence in the advancement of medical science is relayed not only to the medical and nursing professions but to the lay public as well, with a consequent sense of expectation that is unfortunately not wholly realized. This situation is compounded with the advancing age of people being treated. Many elderly patients have multiple clinical diagnoses involving multi-system pathology, and the diagnosis of dying is often made only by exclusion. Communication may be more difficult due to a combination of a higher incidence of confusion in elderly patients with nonmalignant disease than in younger people with cancer, and reduced social networks in the elderly may potentially lead to reduced care and support from family and friends. The incidence, duration, intensity, and type of symptoms follow a different pattern in cancer compared to other illnesses. People with nonmalignant disease also tend to be older. People aged 75 and over who do not die from cancer are more likely to have outlived their spouses, brothers and sisters, and even their children. They are predominantly women, and many live alone or in residential care and therefore present differing challenges for the provision of social support.

The scope of palliative care therefore extends beyond people with a diagnosis of cancer to include patients with other chronic life-threatening diseases.

Perhaps one of the greatest challenges for palliative care services is the provision of care for people with dementia – an area which until recently modern palliative care avoided (https://www.nhpco.org/hospice-statistics-research-pressroom/facts-hospice-and-palliative-care). The annual incidence of dementia in North Americans, for example, doubles nearly every 5 years from 7 in 1000 (65–69 years of age) to 118 in 1000 (86–89 years of age) (Hanrahan et al. 2001). The European Association for Palliative Care (EAPC) published a white paper which helpfully defines optimum palliative care for people with dementia and provides a set of 57 recommendations for practice, policy, and research (van der Steen et al. 2014). Further, the white paper provides a model of dementia progression and suggested prioritizing of care goals and a recommendation of further research into how to give shape to palliative care in dementia across dementia stages.

4 How Should Learning in Palliative Care Be Approached?

Clearly much of what is taught and what is learned is of a technical and knowledge-based nature. This is fundamental in any healthcare practice and particularly relevant in a specialty where so many patients have such a wide range of clinical problems. It would be seductive to imagine that the essence of palliative care lies within these technical and knowledge-based areas, but it is essential that those responsible for teaching and learning in this area maintain a focus on those aspects of the discipline that are less easily quantified and identified. In any domain of professional practice, it is important to identify the true nature of that practice. Professional practice involves not only professional content but also professional process, and it is in the untangling of these two elements that we can discern something of the difficulty facing those responsible for the training of palliative care clinicians for the future. Palliative care cannot be seen solely in terms of skills and knowledge – it must include those processes that can be identified as metacognitive and reflective as well (MacLeod 2000).

The care of seriously ill and dying people necessitates a philosophical and ethical basis. Palliative care must be based on a philosophy that acknowledges the inherent worth and dignity of each person. The ethic of care must include respect for autonomy, justice, non-maleficence, and beneficence. The context of death exerts a powerful influence over what is said, received, and interpreted, and professionals must relinquish control, share decision-making, and treat patients and families as partners.

Caring can be thought of in terms of behavior or as a motivation. As behavior, it is often thought to mean "looking after people and seeing to their needs." As a motivation it can refer to being fond of someone, feeling sympathy or empathy for that person, being concerned for their well-being, or having a professional commitment to them. It could be argued that the best caring professionals show both of these aspects of care. If we care about anything or if we care for someone, it is because deep caring is part of the very nature of our being (van Hooft 1996).

Empathy is an essential component of the way that care is provided and can be an elusive concept in medicine. Empathy helps us to know who we are and what we feel. Empathy requires living and knowing – it requires the ability to put oneself imaginatively in the place of another. The aspect of empathy that is crucial for clinical practice is that of genuine attention to the individual's concerns and the acceptance of those concerns. Empathy can be thought of as a mode of caring. Specifically, it involves caring for the fate of another human being – the concept of empathy is relevant to the care of people who are dying because more than anything they are people in need. Empathy is an understanding of how a disease or its treatment is likely to affect how patients actually live and hope to live their lives. It is an openness to, and respect for, the individuality of another human being.

Francis Peabody (1927) emphasized the importance of getting to know the patient as a major part of the art of medicine. By writing that the art of medicine and the science of medicine were not antagonistic but supplementary to one another, he was essentially saying that empathy is

a prerequisite for the effective care of any patient. It was perhaps particularly poignant that Peabody was terminally ill when he wrote the article.

Sir William Osler (1904) wrote "it is a safe rule… to have no teaching without a patient for text and the best teaching is taught by the patient himself." This was written in 1904 in an attempt to encourage students to learn at the bedside rather than through books alone. This assertion encourages students to pay heed to the patients' stories and the themes that flow from them. Empathic listening is a most powerful means of understanding a person and the things in their life that are of significance for them at that time. Until the start of the nineteenth century, the science of medicine was taught as an apprenticeship – not based on scientific principles but on clinical observation and narrative. Such stories were once the primary source of medical knowledge and the science of medicine developed through the collection of anecdotes. The case presentation is the narrative center of medicine as a discipline – the care of the patient begins with such a story, and the clinician translates those stories in a way that helps the patient understand their ill-health. Without the experience of such stories, the education of healthcare practitioners is incomplete. It is also possible though to encounter stories in other forms; literature, poetry, art, film, and music can all give indications of the human condition and can help us better understand the meaning of care.

Over the last 50 years, since the birth of the modern hospice movement, great progress has been made toward the alleviation of many symptoms that accompany the end of life – particularly in those who have malignant disease, so enabling the maintenance of the highest possible quality of life. Such progress has been made in clinical practice that in many minds the "mainstreaming" of palliative medicine into all healthcare is a given. Alongside this mainstreaming is a desire to see palliative care practiced with the same evidence-based approach that other specialties and subspecialties are adopting. This is clearly a laudable sentiment. However, there is a danger that in adopting such an approach much of what is unique about care at the end of life may be lost. If we are to focus on purely practicing from an evidence base, we will surely lose aspects of the art of clinical care as we become more and more seduced by the science of what we have been led to believe is predominantly a scientific discipline. For example, the doctor's role as technician, guided by standard empiricism, does not exclude their adopting other roles as a consoler, healer, or even friend. The evidence that is built from the "gold standard" double-blind, randomized, controlled clinical trial has been a powerful instrument in furthering medical knowledge, but it is often not enough in recommending a form of management or treatment for a particular individual. Medicine is an art that is especially concerned with human beings as individual and unique creations, but it provides us with a context that shows us that our bodies are fragile and that ultimately they will fail us. The good that medicine in particular and healthcare in general is purported to achieve is not just the maintenance of organic functioning. It is also to maintain a spiritual, emotional, and social well-being that enables each individual to function to some degree within the society in which we live. If we focus too strongly on the achievement of biomedical good, there is a danger that the shortcomings of modern healthcare will be exposed. Evidence-based practice and the strong beliefs of standard empiricism offer a structure for analyzing clinical decision-making but are not sufficient to describe the more tacit processes of expert clinical judgment. It is not possible to find or provide evidence for all aspects of clinical competence. There is a generally widely held belief that medicine has become so powerful that it enables us to overcome not only the bodily ills that we may all experience but also some of life's other misfortunes, not only physical pain but human suffering as well. Part of the difficulty with developments in the academic aspects of medical and nursing sciences is that they tend to have a narrow focus on what constitutes knowledge (and therefore the "evidence base"). It is the application of the knowledge base that becomes problematic in health sciences. It is not sufficient to address only the technical approaches to disease management; there must also be a realistic context for social definition. Those who work with people at the end of life

soon realize that we often face the limits of medicine and the temporal and physical limits of being human. When we acknowledge that all our efforts are for the "good of the patient," we also are confronted with the limits of our clinical expertise and face the reality that ultimately what we offer people is not our role as doctor or nurse but as human being. The challenge for clinicians is to identify not only the evidence base for the practice of palliative care but also the features of sound clinical judgment and the character of those clinicians who make those judgments. It is in this aspect that we must identify the role of wisdom in palliative care. Professional practices are refined by science and corrected by wisdom (Cogan 1953). Wisdom is a form of understanding that combines the practicalities of knowledge with a reflective approach to the utilization of that knowledge over time. There are certain aspects of wisdom that can be readily identified. Practical wisdom is that habit of mind that enables one to choose well, not only with respect to a particular domain of human action but in the whole of one's life. It is the "intellectual virtue that orders human practice in order to attain truth for the sake of action as opposed to truth for its own sake" (Pellegrino and Thomasma 1993).

So, understanding the nature of care, the importance of empathy, and the utilization of wisdom are all essential in our approach to the care of people who are dying. There are some specific dimensions of care that we need to address, and these are identified below.

5 Psychosocial Care

Psychosocial care (a better term might be psychosociospiritual care) has been defined as that which is "concerned with the psychological and emotional well-being of the patient and their family/carers, including issues of self-esteem, insight into an adaptation to the illness and its consequences, communication, social functioning and relationships" (National Council for Hospice and Specialist Palliative Care Services 1997).

Psychosocial care addresses the psychological experiences of loss and facing death for the patient and their impact on those close to them. It involves the spiritual beliefs, culture, and values of those concerned and the social factors, which influence the experience. Psychosocial care includes the practical aspects of care such as financial, housing, and aids to daily living and overlaps with spiritual care. Spiritual care is less easy to define and is often subjective, arbitrary, and personal. It is generally assumed to include an individual's beliefs, values, sense of meaning and purpose, identity, and for some people religion. It may also encompass the emotional benefits of informal support from relatives, friends, religious groups, and more formal pastoral care. For many, existential questions about the human condition can be ignored during many phases of life but are brought into acuity at the end of life (Williams 2006).

Psychosocial care also includes the professional carers who are inevitably affected by their experiences and who thus require support.

Thus, psychosocial care encompasses psychological approaches, which are concerned with enabling patients and those close to them to express thoughts feelings and concerns relating to illness. It also incorporates interventions to improve the psychological and emotional well-being of the patient and their family/carers.

In the past there has been a greater emphasis on psychological needs than social needs – the National Council for Hospice and Specialist Palliative Care Services (NCHSPCS 1997) have emphasized the importance of social care to patients:

> The social fabric of their lives is central to how they make sense of their illness experiences, the meanings they draw upon to understand these and the range of resources they can call upon to help them manage them.

In practice, the social aspects of palliative care are often limited to a focus upon the patient's family, ignoring community influences.

6 Psychosocial Assessment

Patients and families face a range of issues which are not only related to illness and approaching death. Healthcare professionals need to assess

individual strengths and coping styles, experience, and stress and attend to previous losses.

The initial assessment of a patient is carried out by a member of the specialist palliative care team and will include a detailed assessment of the patient's and family's/carers' needs. The time invested in this initial assessment is essential in creating a framework for the provision of future care, a partnership between patient and professionals. The initial assessment may indicate the need for more formal psychological, social, or spiritual assessment. This will for many include the need to maintain autonomy which includes respect for dignity and the opportunity to exercise choice.

In order to identify caregivers at risk of poor psychosocial functioning, self-reported anxiety and competence rating is suggested as an aid to care provision (Hudson et al. 2006). A small group of caregivers (35) was studied. Using a screening tool, these researchers identified the possibility of low-level psychosocial functioning as a potential determinant for family caregivers at risk of psychosocial distress.

There are however a multitude of assessment tools and techniques that will illuminate elements of psychosocial well-being and identify psychological and social needs of patients and caregivers.

The psychosocial aspects of care of the dying person whatever their diagnosis include the need for:

- Understanding – of symptoms and the nature of disease and of the process of dying
- Acceptance – regardless of mood, sociability, and appearance
- Self-esteem – involvement in decision-making
- Safety – a feeling of security
- Belonging – a wish to feel needed and not to feel a burden
- Love – expressions of affection and human contact (touch)
- Spirituality – an explanation of meaning and purpose, both religious and nonreligious
- Hope – for an improvement in any aspect of their life or of their living

In the provision of psychosocial care for people at the end of life, each of these needs must be identified and addressed.

7 Social Context

Social elements of care are often influenced by the disease that is ending a life. Dying from a nonmalignant disease, in many ways, creates a different social structure or standing than dying from cancer. The language that we use is quite different – for example, people who die from cancer are often referred to as "brave" in their "battle" with cancer. They often talk of "beating" the disease or "fighting" it. Nonmalignant disease does not seem to have that same social cachet. Death from end-organ failure is often silent and slow – in many ways relentless in its nature. Without heroic medical interventions to replace organs or use artificial means to support ailing bodies, many of these people would die earlier and perhaps more suddenly. In identifying social or psychological care for these people, it is important to recognize this significant difference in perception of disease that is possible to have originated both from the individual and from society.

For many people with cancer, there are well-recognized social networks or programs that may provide both psychological and social support. Social supports for people with nonmalignant diseases should emerge from people in similar situations, family, and friends and from the wider community. With the exception of some of the neuromuscular degenerative diseases, many of the current support systems for people with nonmalignant disease are focused on raising awareness and funding for curative interventions rather than supporting people in the last stages of their disease. The professions, while openly supporting cancer networks and programs, have been slower to acknowledge the need for similar systems for people with incurable nonmalignant disease.

8 Emotional Context

Some feelings and emotions are almost universally experienced near the end of life.

- Fear of being left alone or having to leave loved ones, of breaking down or losing control

– of the situation they are currently in, getting worse.
- A sense of helplessness in which physical and psychological crises show up human powerlessness. Alongside this is the knowledge of physical and emotional strength gradually deteriorating – loss of physical ability bringing with it attendant psychological and social helplessness.
- Feelings of sadness for what is not to be and for the loss to come.
- A sense of longing for all that has gone before and all that is not going to be, in the future.
- Feelings of guilt for being better off than others or regret for things that have been done or not done.
- A sense of shame for having been exposed as helpless, emotional, and of needing others or for not having reacted, as one would have wished.
- Anger at what has happened, at whatever caused it or allowed it to happen, that the treatment hasn't worked, at the injustice and senselessness of it all and the shame and indignity and at the lack of proper understanding by others.

These feelings and emotions may also be influenced by memories of feelings or loss or of love for other people in their lives who have been injured or died, perhaps let down by doctors, by the system or society, or by the family.

9 Psychological Context

The fundamental clinical skill of medicine is acquiring the history of the illness from the patient, and providing the patient with the opportunity to identify their concerns is mandatory. Specific questions need to be asked to elucidate psychological distress; in particular, they should include questions concerning fatigue, hallucinations, and suicide risk (Macleod 2011).

Examples of psychological interventions include psychosocial support and psychotherapy, behavioral-cognitive therapies, and educational therapies.

Initially it is helpful to look for indicators of pathological levels of psychological disturbance such as clinical depression or other mood disturbance or personality disorder. These lend themselves well to specific psychological interventions. Variables suggesting that the patient or family is at serious risk of psychological disorder or distress may be identified (e.g., social isolation or a history of psychiatric hospitalizations). All members of the healthcare team may observe and subjectively report distress that they feel is psychological in nature (fear or anger) or psychologically mediated (pain or breathlessness) but may not meet the criteria of a discrete psychological disorder. The team should also look for the potential for preventative interventions that may forestall, minimize, or bolster resources for predictable areas or times of vulnerability and hardship (similar patterns of ill-health, pre-bereavement work, or anniversary calls to the bereaved).

Specific psychoeducational interventions that may enhance coping skills, psychological insights, and quality of life should be employed, regardless of the presence or absence of clinical levels of psychological distress. (For an extensive review of psychiatric syndromes and interventions, see Macleod (2011).)

People with neuromuscular degenerative disorders such as motor neuron disease, multiple sclerosis, muscular dystrophies, and less frequently seen disorders like Creutzfeldt-Jakob disease may have particular psychological needs associated with their care. Such disorders bring with them potentially challenging communication issues. For example, some patients may not be able to communicate verbally but retain effective cognitive functioning. It is important to help families to differentiate between behavioral disturbances associated with cognitive impairment from other communication difficulties. Cognitive impairment, depressive symptoms, emotional incontinence, or lability all need expert assessment and careful explanation and management. All or any of these may significantly impact on coping ability, psychological adjustment, and communication both of the patient and family (Macleod 2001).

10 Cultural Context

In palliative care, the cornerstone of practice is the holistic approach to care that is exemplified by the management of "total" pain. As stated earlier, this

classically includes physical, psychological, social, and spiritual pain. Cultural pain or distress can be expressed through any of these dimensions. Often closely allied to culture is spiritual and religious beliefs that have a bearing on how people approach and understand their disease. In many societies people define themselves by their religious, cultural, or tribal grouping, even when their faith or immersion in religion or culture is limited. There are wide variations between people of differing faiths, ethnic backgrounds and national origins, and their approach to the end of life. Although documented evidence is sparse, there is anecdotal evidence to suggest that there is a difference in approach to dealing with malignant and non-malignant disease. In order to understand these differences, it is important to understand the culture from the perspective of the patient and family.

In caring from people of a different culture to our own, it is imperative that we understand the expectations of that culture in order that we act appropriately. For example, the notion of individual autonomy is essentially a western one – many peoples live together and make decisions together in extended families. Many people in China, Japan, and the Pacific Islands as well as many Māori in New Zealand, for example, consider the family as the fundamental unit of society and will expect the family to make medical decisions. Without the accurate and honest provision of information in the right form, at the right time, and in the right place, there can be little hope of an understanding being reached about the situation the patient and family is facing and the goals of care that are being formulated. Without asking, we cannot know what individuals need to make a difference to the end of their life. That asking must include an acknowledgment of difference – difference in culture, in religious beliefs, in understanding of the nature of disease, in expectations in a particular situation, and in perceptions for hope at the end of life.

11 Sexual Context

Sexuality is an element of being that is often easily sidelined or overlooked when caring for people at the end of life, particularly if those people are elderly. It is too often assumed that because people approaching death are weak and tired that their sexual identity or needs are minimized, this fails to recognize the many ways in which human beings can express their sexuality. Staff often view people's sexual interests as "behavioral problems" rather than natural occurrences or expressions of needs for loving contact (Steinke 1997; McPherson et al. 2001). Many people approaching the end of life with a non-malignant disease have had a relentless decrease in their physical being for some time. Much of their time may have been spent in repeated hospital admissions and the physical isolation that encourages. Many treatments, as well as the diseases themselves, can affect sexual function, and of course sexual activity will most often not be at the forefront of people's minds as they approach death. Acknowledging that all people are sexual beings is a starting point in helping people address their sexual needs and wishes – it is in no way different to acknowledging that they are physical or emotional beings as well. This is one aspect of their functional health that can contribute to their sense of self-worth or self-esteem. Changes in physical appearance, size, skin color, and texture as well as increasing fatigue often decrease an individual's sense of self-worth or attractiveness. Identifying psychological elements of their functional health may help to reverse this decrease. Providing information and advice on ways of expressing sexuality other than through sexual intercourse may help to restore an individual's sense of worth in this aspect of themselves.

12 Spiritual Needs

Understanding spiritual needs is essential in the care of people who are dying as these needs are intertwined with an individual's meaning of life, hope, transcendence, and beliefs as they arise from social relationships. Near the end of life, for example, pain can present that defies the efforts of clinicians to manage it. Increasingly clinicians, researchers, and educators have acknowledged the importance of spirituality in the end of life. The

presence of spiritual pain, especially in people who are dying, can be recognized in terminal agitation or restlessness in the absence of other obvious factors. This can manifest as a pre-death event that indicates physical, psychological, and/or spiritual discomfort or distress.

A particularly helpful definition of spirituality that has been articulated by Puchalski et al. (2009) was arrived at by consensus in a conference of invited expert practitioners. This definition states: "Spirituality is the aspect of humanity that refers to the way individuals seek and express meaning and purpose and the way they experience their connectedness to the moment, to self, to others, to nature, and to the significant or sacred."

Meaning as related to life purpose is aptly described as "having a sense that one's life has meaning, or involves the conviction that one is fulfilling a unique role and purpose in a life that is a gift" according to Frankl (cited in Chochinov and Cann 2005, pS107). Palliative care aims to recognize and facilitate resolution of spiritual, social, emotional, and physical issues to enable dying well. Clinicians need to be able help people to identify any sources of spiritual unrest and to contemplate their contextual meaning and importance so assisting in the alleviation of spiritual suffering at the end of life.

13 Ethical Context

In all of our care for people near the end of life, one of our goals is to help people to do what they want in the way that they want. In many ways that is what has become known as autonomy. People's choices at the end of life are often different to those they may make earlier in their life. Patients' authority to choose what interventions they have and even to refuse interventions is seen as one way of protecting dignity and autonomy. Being in charge is better than having control taken away (Carter et al. 2004). That idea of being in charge though will be different for people from different ethnic groups. Professional carers need to ensure that they understand the nature of communication and decision-making that is the norm for each person and family they encounter. Assessment of family dynamics from a different culture may help ensure that their ethical constructs are not overridden.

The ethics of the provision of palliative care are really no different to those required for any form of healthcare; however, in providing care for the most vulnerable, there are particular issues to address. Palliative care must be based on a philosophy that acknowledges the inherent worth and dignity of each person and in order to understand that worth and dignity every facet of their being should be explored – not just the physical. This philosophy must be based on an ethical framework – this is most commonly represented by the "four principles" postulated by Tom Beauchamp and James Childress in their textbook *Principles of biomedical ethics* – autonomy, beneficence, non-maleficence, and justice (Gillon 1994). These principles encourage a sharing of decision-making between carer and cared for but also create the right environment for promoting patient well-being. In addition to this framework, virtue-based ethics may give some indicators for the way in which we could practice our professions. Virtues are often thought to be "old-fashioned," but they are particularly relevant to end-of-life care.

Integrity and trust are perhaps the cornerstones of the caring relationship. Development of these can be gained by attending to the psychosocial and spiritual as well as the physical wants and needs of individuals and families. Trust is essential in any human relationship but in one where one party is so vulnerable then perhaps it is even more important. In all of our dealings with patients and their families, we must be truthful and honest. People who are dying have lost so many elements of their being that it is essential that they can maintain trust in their professional attendants.

Compassion, a further virtue required in all our dealings with patients and their families, could be described as suffering together *with* another or participation *in* suffering. Suffering is clearly not only related to the physical elements of our being, and in order to understand suffering in its broadest sense, we must address social, psychological, and spiritual elements as well.

Phronesis is a virtue rarely mentioned in modern practice, but it is essentially prudent. Nowadays this can be regarded as timidity, undue self-interest, or unwillingness to take risks, but it might also be considered to be discretion or common sense. In history, phronesis was thought to be practical wisdom – the link between the intellectual and moral life. Phronesis urges us to look for the right way of acting.

In modern healthcare practice, working from an effective evidence base, where randomized controlled trials are sought for as many interventions as possible to guide us, it is often forgotten that practical wisdom, phronesis, can guide us where there is no concrete evidence to do so.

The virtue of justice or fairness requires that people are not put down or labelled in any way. Such labels can determine how people are cared for in the future, and they may often have arisen from isolated encounters. So often, labels can imply intolerance – this in turn can lead to an expectation that there is a particular "right" way to live or a right way to die.

Integrity defines the nature of the individual, and it also integrates all the virtues.

A person with integrity is someone who can judge the relative importance in each situation of principles, rules, guidelines, and other virtues in reaching a decision. It implies honesty and righteousness. The integrity of a person is shown in the right ordering of the parts in relation to the whole, the balance, and the harmony between the various dimensions of human existence necessary for the healthy functioning of the whole organism (Pellegrino and Thomasma 1993). It is a balanced relationship between the physical, psychosocial, and intellectual elements of their lives. This could be a definition of what palliative care should be about.

The doctor/patient relationship relies on integrity and trust. Neither party must impose their values on the other. Overriding another person's values is an assault on their humanity and their person.

Using these principles and virtues enables carers to address some of the challenging moral or ethical issues near the end of life. Aspects such as people asking for or insisting on futile treatments, balancing ordinary and extraordinary treatment, the doctrine of double effect, and the relationship between killing and letting die have attracted much discussion and comment over the last four decades, and the debate has been considerably better informed by research, investigation, and dialogue between those in the palliative care community and their colleagues in the field of medical bioethics.

The developments in the provision and understanding of palliative care have enabled a more informed discussion of these topics, but resolution for many in our broader society is still a long way off. However, by attending to people as whole people within the context of their family whoever that may be, we stand a much better chance of meeting their needs – not just their physical needs but their psychological, their social, and their spiritual needs as well.

One aim of palliative care then is to care for people in a way that facilitates dying well. This notion is dependent on many variables that encompass the holistic dimensions of our existence. Dying well is likely to be different for everyone, and seeking a universal definition of what it means may be futile. Dying is, to a greater or lesser extent, a social event (Kellehear 2008), and denying the psychological, social, and spiritual aspects of the dying person leads to a less than optimal dying experience. Understanding the many dimensions of the approaches to and the nature of care then is a prerequisite to starting to get that way of caring right for each person and their family that we encounter as they approach the end of life.

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Quality of Life

2

Lukas Radbruch and Birgit Jaspers

Contents

Abstract

Improving the quality of life is considered a central goal of palliative care, together with the prevention and relief of suffering. However, there is no broadly accepted definition of palliative care. Quality of life may be defined as the gap between expectations, hopes, and ambitions and the present experiences (Calman gap). With progression of the underlying disease, and deterioration of physical and cognitive performance status, patients may still report good quality of life, if they reduce their expectations or shift the focus to other areas to find quality of life (response shift). However, patients experiencing rapid progression of severe illness may be overwhelmed with the

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_8

next steps of deterioration, and may not be able to adapt their expectations quickly. Using quality of life measures as a primary outcome parameter for palliative care may be difficult, as there are so many things that affect it that have nothing to do with the provision of palliative care.

A large number of assessment instruments have been published for quality of life. The Short Form Survey of the Medical Outcome Study (SF-36) and its even shorter forms SF-12 and SF-8 are most prominent for health-related quality of life. The Functional Assessment of Chronic Illness Therapy (FACIT) and the European Organization for Research and Treatment of Cancer (EORTC) family of tools are used extensively for disease-related quality of life. The Schedule for the Evaluation of the Individual Quality of Life (SEIQoL) is a prominent example for the assessment of the individual quality of life.

However, many palliative care patients can only complete short and simple assessment instruments. The EQ-5D uses only six items, but also single-items have been tested.

A number of concepts overlap to some degree with quality of life, such as overall happiness, meaning in life, sense of coherence, or quality of dying and death. However, with all these concepts, some components of the quality of end-of-life care and the quality of dying may be difficult or even impossible to measure.

1 Quality of Life: A Central Goal of Palliative Care

Following the definition of palliative care of the World Health Organization from 2002, quality of life is central to the concept of palliative care: *palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual* (Sepulveda et al. 2002).

This has been confirmed in a discourse analysis of a broad range of English and German definitions of palliative care (Pastrana et al. 2008), which found a striking agreement that prevention and relief of suffering and improvement of quality of life are considered as central goals of palliative care.

As improvement or at least maintaining the best possible quality of life for patients and families is per definition the main goal of palliative care, this merits a close look at the concept, and more specifically, how to define quality of life and how to operationalize and assess it.

However, this may not be easy, as the lack of a satisfactory definition of quality of life has been highlighted by Randall and Downie in their critical review of the philosophy of palliative care, though they note that *judging by volume of literature on the topic, the search for one has not been abandoned* (Randell and Downie 2006).

The strong focus on quality of life is not unique for palliative care, as other areas of medicine, especially those that deal with chronic (incurable) disease such as Endocrinology, Genetics, or Neurology – share this goal (Strawson 2014).

Palliative care is not restricted to the terminal phase, and indeed early integration of palliative care in the disease trajectory of severely ill patients is an emerging focus. However, many patients are facing death, or at least the sudden impact of a short prognosis, and are grappling with a drastic reduction of the remaining lifespan. For these patients, the question arises whether they can experience any quality of life at all, or how there can be any improvement of quality of life when facing death.

However, clinical experience shows that palliative care patients are able to experience good quality of life. In some patients, quality of life is astonishingly high. Relief of suffering with adequate symptom control can increase quality of life, but also other factors may be essential to maintain or even increase quality of life in spite of the prognosis, e.g., a feeling of connectedness.

Even though patients would not often use the term quality of life, they have a clear understanding how to fill the concept for themselves.

2 Quality of Life Concepts

There is considerable agreement that quality of life is a multidimensional construct integrating a broad spectrum of indicators of personal well-being (Felce and Perry 1995). In general, quality of life will be influenced by the degree that the needs of the individual are met. These needs will vary widely depending on the setting.

In the resource pool setting, quality of life will depend largely on regular, if possible daily, access to clean water, food, shelter and heating, and if possible money. In richer settings, coverage of these basic needs is taken for granted, and quality of life will depend more on the pursuit of professional and personal ambitions.

Maslow has described this in the hierarchy of needs (Maslow 1943, 1954), which starts from the basic needs of living and ends with the need for personnel growth (Fig. 1). The first four levels are deficiency needs, which motivate people when they are unmet. These needs will become stronger when they are not met: the longer you lack access to water, the more thirsty will you become. When a needs deficit on one level has been satisfied, motivation will be directed toward the next level of needs.

In contrast to the first four levels of deficiency needs, the top level represents a growth or being need. Self-actualization includes realizing personal potential, self-fulfillment, seeking personal growth, and peak experiences. This is not a deficiency that can be fulfilled, and most often growth needs will even become stronger when they are being tackled by the individual, with higher goals for self-fulfillment and peak experiences.

The hierarchy of needs does not mean that higher levels of needs are correlated with higher quality of life. An increase in the standard of living, either by economic progress in general or by climbing up the social ladder for the individual, does not necessarily result in an increase in quality of life.

The General Social Survey (GSS) in the US is performed since 1972 (gss.norc.org). It does not ask about quality of life, but includes some questions about happiness. General happiness is assessed as: "Taken all together, how would you say things are these days, would you say that you are very happy, pretty happy, or not too happy?" Happiness has been promoted as a stand-alone indicator of well-being, as overall happiness was related to longer lives (Lawrence et al. 2015).

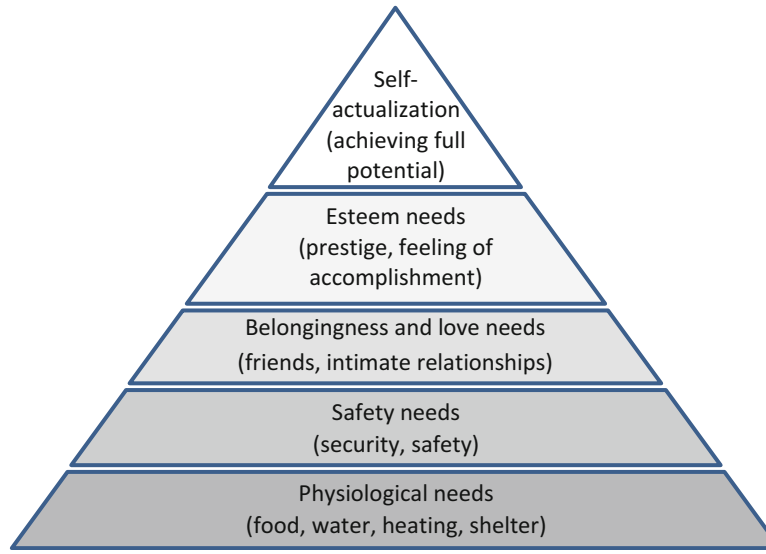

Fig. 1 Hierarchy of needs (Maslow 1943, 1954)

However, in spite of increased standards of living, due to technical advances and economic progress, the percentage of respondents rating themselves as very happy has remained roughly the same since 1972, with the 2014 level near the 1972–2014 average at 33% (Smith et al. 2015). Similar results have been reported for Great Britain (Blanchflower and Oswald 2004).

2.1 Health-Specific Quality of Life

For health care discussion, there is a high desire to assess and measure quality of life. For this purpose, the broad overall concept of quality of life had to be narrowed down to health-related quality of life. The World Health Organization has defined health not merely as the absence of disease, but rather as a state of complete physical, mental, and social well-being (World Health Organization 1948). In consequence, assessment instruments for health-related quality of life try to integrate these dimensions. The 36-item Short Form Health Survey (SF-36) developed in the Medical Outcomes Study is a prominent example of such an instrument (Ware and Sherbourne 1992).

2.2 Disease-Specific Quality of Life

With illnesses with a prolonged disease trajectory such as cancer, quality of life may be influenced by a number of disease- or treatment-related factors. Assessment of disease-specific quality of life, e.g., with the questionnaire of the European Organization for Research and Treatment of Cancer (EORTC) or the Functional Assessment of Chronic Illness Therapy (FACIT). Both instruments have a core questionnaire that assesses the main dimensions of quality of life, and a vast range of add-on modules for assessment of specific symptoms or common problems with specific diagnoses.

2.3 Individual Quality of Life

The standardized items of health- or disease-related quality of life questionnaires allow for the calculation of total and subscale scores. However, with the selection of items, there is also an inherent bias, as the patient's quality of life will only be captured when it is defined by the items in the questionnaire. If the patient finds that activities or experiences outside of these items make up part of his quality of life, this will not be included in the assessment.

This produces a dilemma for assessment: either a validated and highly standardized questionnaire is used, with calculated scores that allow easy comparison, but does assess only that part of quality of life that is represented by the items in the questionnaire, or a broader assessment is used, with a higher chance to capture all factors that contribute to the patient's quality of life, but does not allow for easy calculation of scores. This is Heisenberg's principle of uncertainty as applied to palliative care. This principle has been described in particle physics. Heisenberg stated that it is impossible to measure the position and the velocity of a particle at the same time. Either the position is assessed, but this invariably will cause a change of velocity, or the velocity is determined, but then this would involve a change in position. Similarly, assessment of quality of life will either allow assessment of the nature of well-being or of the extent of quality of life, but not both at the same time.

However, an attempt to capture the individual quality of life has been made with the Schedule for the Evaluation of the Individual Quality of Life (SEIQoL) (O'Boyle et al. 1995). This instrument first asks the patient which are the favorite domains that contribute to his quality of life, then assesses the contribution and the degree of impairment in each of these domains. A sum score can be calculated from this information. As the disease progresses along its trajectory, some of the favorite domains may change, but the scores still can be calculated and compared with previous quality of life scores.

3 Quality of Life Assessment

A large number of assessment instruments have been published for quality of life. A systematic review on outcome assessment instruments in

palliative care identified 80 instruments for assessment of quality of life, the most frequent domain in outcome assessment (Stiel et al. 2012). QOL assessment can be used in a number of ways, e.g., for outcome measurement, for cost effectiveness calculations, and as accountability measurement. However, quality of life assessment as an accountability measure has some disadvantage, as quality of life is influenced by so many factors such as adaptation to illness and functional disability that have nothing to do with the provision of palliative care. Quality of life assessment can also be useful in clinical care and care planning.

3.1 SF-36

The SF-36 is the best-known example for the assessment of health-related quality of life. It includes items assessing health-related limitations in eight dimensions: physical functioning, social functioning, physical role, emotional role, emotional well-being, pain, energy/fatigue, and general health perceptions. Evaluation requires a complex algorithm, as the resulting scores are converted in standardized scores with a range of 0–100, where the general US population would reach mean scores of 50 with a standard deviation of 10. In addition to the subscores on eight dimensions, two main scores can be calculated for the physical and mental well-being. The SF-36 has been extensively investigated in in a broad range of settings and languages (Gandek et al. 1998; Ware et al. 1998).

A shorter version has been developed with 12 items, which covers the same dimensions but results only in summary scores for physical and mental health (Ware et al. 1996). More recently, the SF-8 has been developed with eight single items assessing the same dimensions (Ware et al. 2001). Whereas the SF-12 is an exerpt of the SF-36, the SF-8 has similar, but not identical items compared to SF-36 and SF-12.

The SF-36 questionnaire may be too complicated for many patients with advanced disease requiring palliative care, and some questions may deemed inappropriate by the patients. For example, in our own experience, the question "Compared to one year ago, how would your rate your health in general now?" has been perceived as distressing by patients with advanced cancer and rapid deterioration in the last year.

3.2 FACIT

The Functional Assessment of Cancer Therapy (FACT-G) questionnaire aims at collecting data on the quality of life of cancer patients with 27 items in four domains: physical, social, emotional, and functional well-being. All items are rated on a 5-point Likert scale (0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, 4 = very much). All questions refer to the time frame of the last week. A general quality of life score is calculated as well as five subscores on physical, functional, social, sexual, and mental-emotional well-being (Cella et al. 1993). Higher scores represent lower QoL and higher impairment ("0 = best possible" to "108 = worst possible").

The questionnaire has also been useful in other patient groups and has been renamed Functional Assessment of Chronic Illness Treatment (FACIT). The core questionnaire can be augmented with add-on modules for cancer- (or other diseases-) specific, treatment-specific or symptom-specific problems (e.g., for bone pain or fatigue). The FACIT website lists information on modules and language availability (www.facit.org).

An add-on module is available for palliative care (FACIT-PAL), which adds 19 items to the core questionnaire, resulting in a total of 46 items (Lien et al. 2011; Siegert et al. 2014). As this taxes the capacity of patients with advanced disease and cognitive and physical impairments, a shorter version with 14 items in total has been designed, the FACIT-PAL14. This short version provides a sum score, but no subscores (range 0–56, higher scores = better quality of life) (Zeng et al. 2013).

3.3 EORTC

The European Organization for Research and Treatment of Cancer has developed the core questionnaire for quality of life EORTC-QLQ-C30 (Aaronson et al. 1993). The questionnaire includes

30 items on the general condition of the last 7 days, except for the questions about the physical well-being which refers only to the current situation. Five subscales on the physical, role, cognitive, emotional, and social functioning are summarized with 2–5 items each. Nine additional symptom scores on fatigue, nausea and vomiting, pain, dyspnoea, insomnia, loss of appetite, obstipation, diarrhea, and financial problems are calculated from 1–3 items each. All items are rated on a 4-point Likert scale (1 = not at all, 2 = a little, 3 = quite a bit, 4 = very much). Additionally, a global health and QoL index is calculated from two items on a 7-point Likert scale reaching from 1 = very bad until 7 = excellent. For the five functional subscores and for the global health index, higher scores represent higher quality of life, whereas higher scores in the symptom scales indicate higher symptom intensity, resulting in lower quality of life.

An algorithm for the calculation of a summary score has been introduced only recently (Giesinger et al. 2016). The questionnaire has been used and validated in a range of settings and languages.

As with the FACIT, a large number of additional modules are available, mostly on different cancer entities, but also on other topics such as fatigue or information (http://groups.eortc.be/qol/eortc-qlq-c30).

A shorter version with 15 items has been developed as a core questionnaire for palliative care patients, the EORTC-QLQ-C15-PAL (Groenvold et al. 2005). This questionnaire includes the symptom scales for pain, dypsnea, insomnia, appetite loss, and constipation, as well as abbreviated subscales for physical and emotional functioning, nausea, vomiting, and fatigue, and one of the two questions on general health. The EORTC-QLQ-C15-PAL has been promoted as the new standard for quality of life assessment in advanced cancer (Groenvold et al. 2006) and has even been found useful as a prognostic indicator in patients with advanced cancer (Lee et al. 2014).

3.4 SEIQoL DW

SEIQoL: This tool assesses five domains of the patient's individual quality of life with a structured interview (O'Boyle et al. 1992; Waldron et al. 1999). The patient is asked to name five domains of his life that he finds most important right now. He then is asked to rate his level of satisfaction with each of these domains, by drawing bars in a 100-mm box (0 = worst possible satisfaction and 100 = best possible satisfaction). In the original SEIQoL, the weight that each domain has for the patient's quality of life would be elicited in the interview. However, this process takes time, and most patients prefer a shorter assessment. The direct weighting version (SEIQoL-DW) uses a disk with five movable colored segments (O'Boyle et al. 1995; Hickey et al. 1996). The patient adjusts the segments according to the relevance (weight) he attributes to each domain. The cumulative products of level of satisfaction and weight represent the quality of life score, in a range between 0% and 100%, with higher scores representing higher QoL.

The most frequent domains named by patients with advanced cancer in the validation paper were family, health, social life, spiritual life, friendship/relationships, contentment/happiness, work, finances, marriage, mobility, and pain relief (Waldron et al. 1999). Other studies using the SEIQoL have confirmed the predominance of family and social relationships in other patient groups such as elderly patients or patients with amyotrophic lateral sclerosis or with congenital heart disease, with health issues only coming second (Neudert et al. 2004; Moons et al. 2005; Hall et al. 2011; Hamidou et al. 2017).

As the disease progresses, some domains that the patient has used for the SEIQoL rating may not be feasible or important for him anymore, e.g., work and career advancement may drop from the screen disease-related disability, or sport activities may become impossible because of physical impairment. However, other domains will then become more important. Allowing for changing domains in the quality of life assessment corresponds with the real life experience in palliative care, where patients sometimes explain that with progression of the disease lost abilities and chances are balanced by gaining a new focus on what they find really important in life.

However, completing the SEIQoL requires the ability to concentrate and the capacity for abstraction. It seems doubtful whether the majority of palliative patients are able to use this instrument as their physical and cognitive status and general condition often are rapidly declining. Use of the SEIQoL may be too time-intensive and not practicable in clinical palliative care routine.

3.5 Short Assessment Tools

Assessment tools that are well established in other settings often are not practicable in palliative care because of the limited physical, cognitive, or psychological status of patients. Assessment tools have to be short and simple to reduce the burden on the patient. Comprehensive questionnaires are feasible only for a minority of patients in the clinical setting of a palliative care unit (Stiel et al. 2011).

The EuroQoL consortium has produced a concise instrument, the EQ-5D. Five items cover one dimension each: mobility, self-care, usual activities, pain/discomfort, anxiety/depression. Two version are available, one with three response options (no problems/some or moderate problems/extreme problems), the other with five options (no problems/slight problems/moderate problems/severe problems/extreme problems). In addition, a thermometer scale is used for rating overall health (0 = worst health that can be imagined, 100 = best health that can be imagined).

3.6 Specific Palliative Care QOL Instruments

A number of specific tools for quality of life assessment have been developed, including the McGill Quality of Life Index, the Missoula-VITAS Quality of Life Index (MVQOLI), the Needs at the End-of-life Screening Tool (NEST), and the Quality of Life at the End of Life (QUAL-E) (more information at http://www.npcrc.org/content/25/Measurement-and-Evaluation-Tools.aspx). However, these instruments have been used less frequently and are available in fewer languages other than English compared to the more general quality-of-life questionnaires discussed above. The McGill index includes 20 items, the QUAL-E 26 items. The NEST questionnaire uses only 13 items, but with additional items, if the cut-off scores of any items are exceeded, so that the total length of the questionnaire can be extended up to 65 items. The MVQOLI uses three questions on five domains, one each on subjective assessment, function, and importance of the domain.

Patients at the end of life with reduced physical and cognitive function often need help for the completion of these questionnaires. Ideally for the palliative care setting, assessment of quality of life would be done with a single question. This approach has been recommended for specific area in palliative care, e.g., depression (Chochinov et al. 1997) or fatigue (Radbruch et al. 2008). However, using the single item "How do you feel today?" we found only moderate correlations with the global scores of EORTC-QLQ-C30 and FACIT-G (Stiel et al. 2011). Highest correlations were found with physical and functional subscales of the comprehensive instruments. Most patients seem to understand the single item as a medical question addressing these physical-functional aspects in the clinical routine.

Ongoing research in our department has investigated two alternative single items. The single item "How would you rate your overall quality of life during the past few weeks?" was taken from the EORTC QLQ-C30 quality of life questionnaire, but correlations of other instruments with this single item were inadequate as well. However, the second single item "How satisfied are you currently with your physical and emotional well-being?" correlated well with the total score and with the physical, emotional and functional subscales and moderately with the social well-being subscale of the FACIT. This single item seems suitable as a short screening instrument for quality of life in palliative care.

4 Quality of Life as a Static or Dynamic Concept

Measuring health-related or disease-related quality of life with standardized instruments fosters the attitude that quality of life is a static construct,

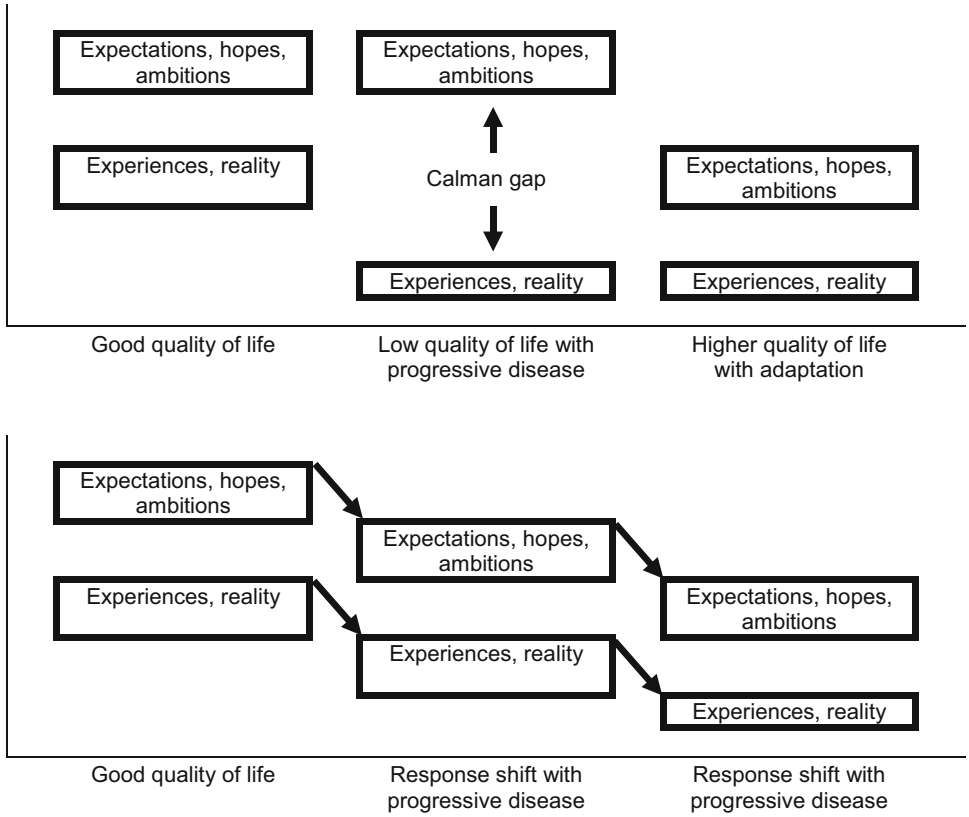

Fig. 2 Calman Gap and response shift

influenced predominantly by factors such as physical or cognitive performance status, physical symptoms, or social relationships. These contributing factors are to a large degree outside the influence of the patient. The patient's quality of life remains unchanged, if there are no aggravating factors (e.g., disease progression) or alleviating factors (e.g., effective symptom control).

However, this is contrary to the experience in clinical practice that quality of life depends to a major degree on the patient's needs, preferences, and expectations. In an influential approach, Calman proposed quality of life as the difference between the hopes and expectations of an individual and the individual's present experiences (Calman 1984). This difference has also been described as the Calman gap, and support a dynamic construct of quality of life.

In consequence, patients with severe cognitive or physical impairments may report high quality of life, if they have had time to adapt their hopes and expectations to the present situation (Fig. 2). This is similar to patients with chronic disabilities, who also quite often report normal or even high quality of life.

With progressive disease, patients often will reduce their hopes and expectations as they feel the deterioration. As the gap between experiences and expectations does not widen with the lower levels of expectations, patients will report no change in overall quality of life, even though their present experiences have become much worse. This is known as the response shift (Fig. 2).

However, adaptation takes time, and even experienced palliative care staff often underestimates the amount of time patients and caregivers need to adapt to a new situation. Patients experiencing rapid progression of severe illness may be overwhelmed with the next steps of deterioration, and may not be able to adapt their expectations quickly.

Defining quality of life as the difference between patient's expectations and present experience also means that quality of life can be improved in two ways, either by improving the experiences (e.g., with effective symptom control) or by lowering the expectations. This poses an inherent danger in palliative care, as lowering the expectations may be easier. Facilitating adequate adaptation of expectations to the deterioration with progressive disease may be perceived as very helpful by patients, but this should not be carried too far, as the patient and his caregivers also have a right to keep up their hopes and ambitions, even if they are clearly unrealistic in the face of the progressive disease.

Several studies have demonstrated the effect of response shift in patients with advanced cancer over time (Hagedoorn et al. 2002; Ahmed et al. 2004; Echteld et al. 2005) or compared to healthy controls (Stiefel et al. 2008; Fegg et al. 2010b). Response shift has also been discussed as a major confounder for the outcome evaluation in clinical trials (Ring et al. 2005; Verdam et al. 2015), and an expert panel recently recommended more research on response shift (Preston et al. 2013).

5 Concepts Related to Quality of Life

As there is no broad consensus on the definition of quality of life, it is not surprising that a number of concepts overlap to some degree with quality of life. Overall happiness (included in the General Social Survey) has already been discussed above.

Quality of life seems closely related to the search for meaning, as expressed in Viktor Frankl's famous quote "Those who have a 'why' to live, can bear with almost any 'how'" (Frankl 1962). A German workgroup has developed a Schedule for Meaning in Life Evaluation (SMiLE) that has been used in different palliative care settings (Fegg et al. 2008, 2010a). The evaluation uses a similar method as the SEIQoL, but patients are asked to name the major domains that contribute to the meaning they find in life. However, the domains that are selected by the patients closely overlap with those selected in the SEIQoL, with a predominance of family and social relationships. This raises the question whether there is a meaningful separation between quality of life and meaning in life, or whether the two concepts are correlated so closely that only quality of life needs to be assessed.

Making meaning is also an integral part of the sense of coherence concept, together with understanding and being able to influence the environments or events happening. The Sense of Coherence Scale (SOC) includes 29 items or 13 items in a short version (Antonovsky 1993), but a number of other versions has been used as well (Eriksson and Lindstrom 2005). Subscales for the three dimensions manageability, comprehensibility, and meaningfulness have been calculated, though Antonovky suggested to use only the total score of the instrument. A systematic review found a strong relationship between sense of coherence and quality of life: the stronger the sense of coherence, the better the quality of life (Eriksson and Lindstrom 2007). In addition, sense of coherence seemed to be a good predictor for good quality of life in longitudinal studies.

A quality of death index has been developed to describe the quality of life until the very end (Economist Intelligence Unit 2015). However, this is a macroeconomic indicator, compiling information on palliative care and healthcare environment, human resources, affordability of care, quality of care, and community engagement to compare the quality of palliative care available to adults in 80 countries. This does not provide information on individual patients.

On an individual level, the Quality of Dying and Death (QODD) questionnaire is used to interview family members after the death of the patient to evaluate the quality of care in the final stage of life (Curtis et al. 2002). The QODD includes 31 items assessing symptoms, patient preferences, and satisfaction with care. The total score ranges from 0 to 100 with higher scores indicating better quality of dying and death.

Other instruments have been developed for evaluation of the quality of dying, but a systematic review found only the QODD has been well validated and widely used (Hales et al. 2010). Shortcomings of the instrument have been critically

discussed, challenging that some components of the quality of end-of-life care and the quality of dying may be difficult or even impossible to measure (Curtis et al. 2013).

6 Conclusions and Summary

Quality of life assessment can be used in a number of ways, e.g., for outcome measurement, for cost effectiveness calculations, and as accountability measurement. Improving the quality of life is considered a central goal of palliative care, together with the prevention and relief of suffering. However, there is some variety in the definition and indeed the understanding of the concept of quality of life, and in consequence a range of assessment instruments have been developed.

The Short Form Survey of the Medical Outcome Study (SF-36) and its even shorter forms SF-12 and SF-8 are most prominent for health-related quality of life. The Functional Assessment of Chronic Illness Therapy (FACIT) and the European Organization for Research and Treatment of Cancer (EORTC) family of tools are used extensively for disease-related quality of life. The Schedule for the Evaluation of the Individual Quality of Life (SEIQoL) is a prominent example for the assessment of the individual quality of life.

However, many palliative care patients can only complete short and simple assessment instruments. With the limitations on assessment, the number of other factors influencing quality of life such as adaptation to illness and functional disability and the overlap of quality of life with other concepts such as meaning in life or sense of coherence some components of the quality of end-of-life care and the quality of dying may be elusive or even impossible to measure.

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Global Aspects of Palliative Care

3

Stephen R. Connor

Contents

Abstract

In this chapter we will look at the growth of modern palliative care globally from its humble beginnings to finally becoming part of mainstream health care; major developments and milestones in global development, including involvement of the World Health Organization (WHO), the HIV/AIDS Pandemic, the rise of non-communicable diseases, the millennium goals, and now the sustainable development goals; and the World Health Assembly resolution on palliative care. We will explore the current status of palliative care globally and look at future directions and challenges for palliative care to reach its goal of full access to those in need.

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_4

1 Introduction

What was once a small movement confined to high-income countries is slowly becoming an essential part of any modern health-care system. Hospice palliative care is part of the solution to what ails the current health-care system. Consistently, palliative care leads to effective symptom control (Shu-Yu et al. 2016), improved quality of life (Temel et al. 2010), less unnecessary hospitalization (Morrison et al. 2008), realization of dignity (Chochinov et al. 2011), and reduced cost both for patients and families as well as providers (Smith et al. 2014).

Yet palliative care still remains on the fringes of mainstream health care and many myths persist resulting in too few patients able to access any care or are referred on the brink of death. Eighty percent of the need for palliative care is in low- and middle-income countries, while 80% of the current palliative care that is available is confined to only 20 high-income countries that have managed to achieve advanced levels of integration into mainstream health care.

Persisting myths include that hospice or palliative care is a building where you are sent to die, that patients are given morphine and no longer communicate or become addicts, that having hospice and palliative care will cause you to give up and die sooner, that palliative care is just for people with cancer, and that palliative care is just for old people. In the United States, the median length of service is less than 3 weeks. There are still many people that fear the idea of hospice or palliative care simply because of an association with dying.

2 History of Modern Palliative Care Development Globally

Modern hospice care began in 1967 with the opening of St. Christopher's Hospice outside London. Dame Cicely Saunders, founder of St. Christopher's, had a vision for a place where those facing the end of life could be cared for with the principles of pain and symptom control and whole-person compassionate care, using an interdisciplinary team approach for both the ill person and their family. She pioneered the field of hospice care and became a beacon for all countries worldwide to learn this new approach to care. An education and training center was established at St. Christopher's where people from dozens of countries came to learn hospice care and then return to their home country to transplant this new approach to caring for the dying in their own setting and culture.

The term palliative care was introduced by Dr. Balfour Mount at the Royal Victoria Hospital in Montreal, Quebec, in 1974. The word *hospice* in French is understood to mean "home for the destitute" and was seen as an unacceptable term in Francophone Quebec. The word *palliate* originates from the Greek and translates as "to cloak," meaning that when we care for the dying, our interventions are meant to cloak or to prevent from seeing or experiencing pain or other suffering. Palliative care is the term generally used to refer to the practice of hospice and palliative care globally and encompasses hospice care. It also signifies the transfer of hospice principles into the wider health-care system including hospitals, long-term care facilities, clinics, primary care settings, and personal residences.

The hospice movement has grown slowly in the past 50 years but has mainly been confined to high-income countries.

3 Major Developments Globally

3.1 World Health Organization

Several significant developments have occurred in recent decades that have spurred the development of global palliative care. The World Health Organization (WHO) published the first monograph *Cancer Pain Relief* guidance on the assessment and treatment of cancer pain in 1986 that included a new WHO pain relief ladder. The ladder identified three simple steps for treating mild, moderate, and severe pain. This monograph was revised in 1996 with a guide to opioid availability. Also in 1990 WHO published the first definition of palliative care emphasizing symptom

management and pain control in a wider approach. This was followed in 2000 with the publication of an expanded definition of palliative care emphasizing treatment for all life-threatening illnesses from the time of diagnosis.

WHO's support for palliative care was crucial in its early development but was centered in the cancer department, giving the impression that palliative care was only for cancer though the WHO definition was much broader and referenced any life-threatening illness. There was also considerable attention to the palliative care needs of those with HIV/AIDS, especially before the advent of highly active anti-retroviral treatments. WHO has shifted its emphasis from communicable disease to the major cause of death being from noncommunicable diseases.

3.2 Noncommunicable Diseases (NCDs)

WHO's realignment around noncommunicable diseases is an opportunity for palliative care to be vocal about the necessity of its inclusion in all aspects of policy, program development, and service delivery. Following criticism that WHO was too focused on HIV and TB treatment while 66% of all deaths from all causes were due to NCDs, WHO has shifted its focus to put a major emphasis on NCDs.

A global UN dialogue on NCDs has continued since 2012, informed by the Global Action Plan for the Prevention and Control of NCDs 2013–2020. A Global Coordination Mechanism on NCDs continues this dialogue, and a Global Monitoring Framework for NCDs has been developed. Palliative care advocates were successful in getting an indicator for palliative care at the country level that measures opioid consumption against total cancer deaths. This is one of 25 WHO-approved indicators that countries can use to measure progress.

NCDs kill 38 million people each year, almost three quarters in low- and middle-income countries. Sixteen million of these deaths are considered premature in those before the age of 70. There were 17.5 million cardiovascular deaths, 8.2 million cancer deaths, 4 million deaths from respiratory diseases, and 1.5 million from diabetes, these four accounting for 82% of all NCD deaths. All of these conditions are appropriate for palliative care.

3.3 Sustainable Development Goals and Universal Health Coverage (SDG/UHC)

The SDGs are a UN initiative officially known as "Transforming our world: the 2030 Agenda for Sustainable Development." There are 17 aspirational goals with 169 targets. One of the goals (#3) is to "Ensure healthy lives and promote well-being for all at all ages." One of the targets under SDG3 is to "Achieve universal health coverage, including financial risk protection, access to quality essential health care services and access to safe, effective, quality and affordable essential medicines and vaccines for all."

Palliative care advocates were able to include palliative care in the description of the continuum of services under UHC. The continuum is Promotion – Prevention – Treatment – Rehabilitation – Palliation. This was a major achievement and allows palliative care to claim its place in the SDGs. Without palliation, UHC cannot be achieved. Unfortunately, despite several attempts, palliative care advocates have not yet been able to get WHO approval for a palliative care indicator to hold countries to account for palliative care development.

3.4 World Health Assembly (WHA) Resolution on Palliative Care

Perhaps the greatest achievement for global palliative care to date is the unanimous passage of WHA resolution 69.17 (World Health Assembly 2014) "Strengthening of palliative care as a component of comprehensive care throughout the life course." The WHA is the governing body of the WHO and is made up of all UN countries. It took 3 years of sustained advocacy to get this resolution on the WHA agenda. The WHO staff

then prepared a report to inform the resolution that used data from the WHPCA/WHO Global Atlas of Palliative Care at the End of Life (Connor and Sepulveda 2014). The Atlas describes the need for palliative care, the current status of palliative care delivery, the barriers to access, the limited resources devoted to palliative care, and recommendations for improving access to care.

The resolution calls for a series of actions by all countries and by the WHO itself to ensure that palliative care is part of every country's healthcare system with an emphasis on community-based primary health care. Specifically, countries are called upon to:

- Develop and strengthen policies to integrate palliative care into health systems
- Ensure adequate domestic funding and human resources
- Support families, volunteers, and caregivers
- Integrate palliative care in health professional curricula at all levels
- Assess domestic palliative care needs including for essential medicines
- Review and revise drug control legislation and regulation and add palliative care medicines to national essential medicine lists
- Support partnerships between governments and civil society
- Integrate palliative care into plans for management and control of noncommunicable diseases

The resolution further calls on WHO to:

- Ensure palliative care is integrated into all heath system plans
- Update or develop guidelines and tools on palliation in health system and across disease groups and levels of care, addressing ethical issues
- Support countries in reviewing and improving drug legislation and policy to ensure balance
- Explore ways to increase availability and accessibility of essential palliative care medicines
- Work with the International Narcotics Control Board and the UN Office on Drugs and Crime to promote availability of controlled substances for pain and symptom management and support accurate estimates for opioids
- Collaborate with UNICEF to promote pediatric palliative care
- Monitor global situation of palliative care to evaluate progress
- Encourage countries to adequately fund PC programs and research on palliative care models in low- and middle-income countries
- Report back on implementation of resolution

4 Current Status of Global Palliative Care

To date progress on meeting all these recommendations from the WHA resolution is occurring slowly. Some technical assistance documents have been published, six countries have been identified to host official WHO demonstration projects, and work has begun on revision of the original WHO cancer pain guidelines. However, access to opioids is still overly restricted in 75% of the world; there is no measure of how many professional schools have added palliative care curricula or audit of policies that have been changed to include palliative care. Funding for palliative care implementation has if anything decreased. A new audit of levels of development in palliative care is planned for completion in 2018, and it is hoped that the 42% of countries lacking any palliative care last measured in 2011 will be decreased.

Findings from the most recent assessment of the state of palliative care globally can be found in the *Global Atlas of Palliative Care at the End of Life (Connor & Sepulveda, 2014)*. The purpose of the Atlas was to paint a picture of palliative care globally by answering the following questions:

- What is palliative care?
- Why is palliative care a human rights issue?
- What are the main diseases requiring palliative care?
- What is the need for palliative care?
- What are the barriers to palliative care?
- Where is palliative care currently available?

- What are the models of palliative care worldwide?
- What resources are devoted to palliative care?
- What is the way forward?

The WHO's **2002 definition of palliative care** both for adults and children (World Health Organization 2017a) was used along with a definition of hospice. Some limitations in the definition are noted including lack of clarity on four points: first that palliative care is needed in chronic as well as life-threatening/limiting conditions, second that there should be no time or prognostic limit on the delivery of palliative care, third that palliative care is needed at all levels of care including primary and secondary as well as tertiary care, and fourth that palliative care is needed in all settings of care.

Palliative care has begun to be accepted as a **human right** in health care. There are a number of precedents for this belief including reference to the 1966 International Human Right to Health from the UN International Covenant of Economic, Social and Cultural Rights (Committee on Economic, Social and Cultural Rights (CESCR) General Comment 14 para.12), which calls for the right of everyone to the enjoyment of the highest attainable standard of physical and mental health. Further the UN Special Rapporteur on torture has said that denying access to pain relief can amount to inhumane and degrading treatment. It is governments that do not allow access to essential medicines such as opioids that are responsible, rather than clinicians. There are many other statements in support of this right.

In order to identify the main **diseases that require palliative care** and the number of these patients, the *Atlas* used WHO's most recent mortality data (2011). There were over 54.5 million deaths worldwide that year, most (66%) due to noncommunicable diseases. At minimum over 20 million of these were identified as needing palliative care. The primary diseases for adults included cardiovascular, cancer, pulmonary, HIV/AIDS, kidney, liver, dementias, multi-drug resistant TB, Parkinson's, rheumatoid arthritis, and multiple sclerosis. For children the major diseases included congenital anomalies, neonatal conditions, protein energy malnutrition, meningitis, HIV/AIDS, cardiovascular, endocrine-blood-immune disorders, cancer, neurological conditions, and kidney and liver diseases.

This was the first time that WHO acknowledged that all these conditions required palliative care. Prior to this publication, WHO only provided guidance on palliative care for cancer and HIV. Further the *Atlas* looked at the distribution of need for palliative care and found that almost 80% of the need is in low- and middle-income countries. The majority of those needing palliative care are adults 60 years or older (69%) with 25% aged 15–59 and 6% being children from birth to 14 years. While the number of over 20 million refers to those at the end of life needing palliative care, we effectively doubled that number to 40 million to account for all those needing palliative care prior to the end of or last year of life. Add several family members to this need and you have well over 100 million people annually that need palliative care services.

When assessing the **barriers to palliative care development**, we use the WHO public health model. The model has four components: (1) policy, (2) education, (3) medication availability, and (4) implementation of services. For palliative care to develop in an individual country, it is often best to use a simultaneous bottom-up and top-down approach. A country champion is needed to advocate for palliative care within the country and to eventually develop a prototype palliative care delivery program. However, this is difficult to do if there is no recognition of palliative care in government policies and regulations. Therefore, the lack of government policies is often a barrier that must be overcome initially.

Conducting a national needs assessment can be a helpful starting point to educate officials as to the scope of the need for palliative care and to demonstrate the gap in lack of services. Examples of comprehensive national needs assessments and other key policy documents can be found at http://www.thewhpca.org/resources/category/country-reports-and-needs-assessments. Other key policy documents that should be developed include:

- National standards for program operation
- Clinical guidelines for palliative care provision

- Inclusion of palliative care in national policies on NCDs, HIV, TB, cancer, and health-care priority setting documents
- Legal recognition of palliative care in health-care law and regulation including licensing
- Recognition of palliative care as an area of health-care specialization
- Regulation of access to controlled substances
- National strategy for implementation of services

Controlled substances, especially opioids, are either unavailable or so tightly controlled in 75% of the world that they are not available for palliative care (International Narcotics Control Board 2015). It is essential that unnecessary and overly burdensome regulations are removed or modified so that they can be used for palliative care. The WHO has a model list of essential palliative care medicines (World Health Organization 2017b) that should be available in all countries. This is often a long and difficult process that involves multiple ministries to approve including ministry of health, drug control authorities, police and internal affairs, and ultimately the legislative and executive bodies in the country.

Gaining access to medicines, especially oral morphine, is critical to successful palliative care development and has to go hand in hand with provision of **education** for health professionals. The World Health Assembly resolution on palliative care (2017) calls on all governments to ensure that palliative care education is provided at all levels of health professional training including undergraduate, graduate, postgraduate, and specialization training. Practically this means that basic palliative care curricula should be included in medical and nursing schools, additional courses and practicums should be provided during residency and internships, continuing education should include palliative care, and a pathway for specialty or sub-specialty qualification should exist. Further, palliative care content should be included in social work, psychology, and chaplaincy education.

In addition to health professional education, it is equally important for the public to be informed and sensitized to the need and availability of palliative care. Most people, particularly in limited resource settings, may assume that advance illnesses such as cancer inevitably result in unrelieved pain and suffering when we know that symptom relief and quality of life are possible and should be available to all citizens. Families faced with the need to care for seriously ill relatives also need practical hands-on training in caregiving to make it possible for loved ones to remain in the place they call home.

All of this should lead to the formation and growth of palliative care services **implemented** throughout a health-care system. While many initial hospice or palliative care programs begin as standalone programs effectively outside the mainstream health delivery system, the challenge to reach the majority of persons needing palliative care is to effectively integrate palliative care into all levels of health care including primary, intermediate, and tertiary levels in both the public and private health-care systems (Gomez-Batiste and Connor 2017).

5 Future Directions for Global Palliative Care

5.1 Low- and Middle-Income Countries (LMIC)

The future of palliative care depends on how successful we are in developing palliative care in limited resource settings. Since almost 80% of the need for palliative care is in LMICs, it is imperative that palliative care is successfully implemented there. There are a number of good models that have been described (Connor and Sepulveda 2014) that may be replicated, and there is a lot of work being done to develop, test, and implement models that are viable and sustainable in LMIC settings. Notably, WHO plans demonstration projects in six countries (Belarus, Jamaica, Oman, Malaysia, Thailand, and Zimbabwe) and the Worldwide Hospice Palliative Care Alliance another six (Bangladesh, Ethiopia, Jordan, Panama, Philippines, and Ukraine) that will hopefully develop and disseminate new models. The challenges are great, but it is critical that progress be made since less than 20% of current palliative care delivery is available in LMICs.

5.2 Community-Based Palliative Care

One of the critical factors in developing palliative care in limited resource settings is the degree to which palliative care is owned by the community. This is also critical in high-income settings but more so in LMICs. When resources are limited, there is a general tendency for people to take care of each other more readily and family connections are often closer. This is a strength, but so often without the support and training that palliative care provides, caregivers are left to helplessly witness unrelieved suffering. With modest investments in palliative care that support community care giving, community based palliative care can become mainly self-sufficient.

5.3 Medication and Education

In 75% of the current world, access to effective pain medication is so severely restricted (International Narcotics Control Board 2015) that it is essentially impossible to achieve pain relief and comfort for dying patients. This is the world's biggest drug problem. Notable efforts are beginning to change this severe imbalance, but a lot more work is needed to correct this situation. Fear of misuse of opioids has resulted in major interference in the practice of medicine throughout the world. Effective safeguards against misuse need to be in place, but the situation is so out of balance in most of the world that palliative care cannot be practiced effectively.

On top of this, education in palliative care and pain relief is still in its infancy worldwide. It is useless to train physicians and nurses in palliative care if essential palliative care medicines are unavailable. This includes not only opioids and other analgesics but other psychotropic medication including anti-anxiety and anti-depressant medication, anti-seizure, anti-emetic, and anti-psychotic medication. What is taught is forgotten in situations where relief of suffering is not possible. Most importantly bedside teaching, where real learning occurs, is not realistic if these medications are unavailable.

5.4 Funding

The ultimate test of whether palliative care is effectively implemented in a country is the willingness of governments to reallocate funding to palliative care, especially in non-hospital settings. In all countries most health-related funding flows to hospital care. What has been seen over and over is that hospice and palliative care reduce the need for unnecessary hospital care in favor of care in the community. The net result is usually a reduction in expense to the health-care system. The difficult part practically and politically is to shift funds now going to inpatient care to home care services. This requires evidence and political will. Corruption and self-interest often stand in the way, but this can and has been done in many countries.

6 Integration

Ultimately the future of palliative care is in its integration into the mainstream health-care system in every country. Palliative care will not succeed as a specialized form of care outside the mainstream of existing health-care delivery. Forty years ago many of us thought the need for hospice and palliative care would disappear in 20 years as we improved the care of dying patients. That has not occurred and the need for specialist palliative care is now well established worldwide. However, the majority of patients needing palliative care should be able to be effectively cared for by their primary health caregivers. This is where new development is occurring globally. Organizations like the International Primary Palliative Care Network and the European Association for Palliative Care's primary care task force have made great strides in promotion of palliative care as a core competency in family medicine, and oncology associations have called for early integration of palliative care in oncology practice. Still there are literally millions of health-care professionals that have never received training in palliative care and will need to do so.

7 Conclusion and Summary

The international hospice palliative care movement, now 50 years old, remains underdeveloped. Less than 10% of the global need for palliative care throughout the course of life-limiting illness is being met. The greatest need is in low- and middle-income countries where palliative care is available the least. Great strides have been made in identifying this need and getting the United Nations and international bodies to call for integration of palliative care throughout the life course. However, translating this progress to the ground is a long way off. It will require major improvements at the individual country level in setting policies that promote palliative care, education in palliative care for literally millions of health-care workers, removal of excessive restrictions on essential palliative care medicines, and resources and political will to implement both primary and specialized services. Further it will require major changes in the attitudes and beliefs of both the public and the health professions. Acceptance of palliative care at some level requires an acknowledgment that death and dying are essential parts of life and that care of those with life-limiting conditions and illnesses is an essential part of every health-care system. As the global population ages and confronts these realities, there is every hope that palliative care will grow and thrive in the future.

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Organization of Palliative Care in Different Parts of the World

4

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_6

Abstract

Palliative care has developed rapidly and heterogeneously in the past decade around the globe. In this chapter, we present an overview of palliative care development in different regions of the world with a pair of case studies of models of palliative care delivery within each region. The textbook is divided into subsections based on the following regions: Europe, North America, Latin America, Africa, Asia-Pacific, and Middle East. Regions were decided based on existing palliative care networks, where available. Information regarding palliative care development in each region is organized based on the World Health Organization's Public Health Strategy for Palliative Care: (1) policies, (2) medicine availability, (3) education, and (4) implementation of services plus (5) vitality (professional activity). This chapter is intended for the reader to gain a high-level view of the state of palliative care development in regions of the world and the challenges and successes within each region. Two case models per region give the reader a quick view into the diversity of palliative care services offered in different regions of the world and give the reader insight into regional-specific delivery models.

1 Introduction

The aim of this chapter is to provide an overview of palliative care development globally with supplementary case studies to describe an array of existing models of palliative care delivery.

Outside of Europe, North America, and Australia, generally, access to quality palliative care services is rare (WHPCA and WHO 2014). However, palliative care has seen a remarkable growth in the past few years. In 2011, 58% of the world's countries had at least one palliative care service, a 9% increase since 2006, with the greatest gains in Africa (Lynch et al. 2013). Still, only 8.5% of countries have achieved advanced integration of palliative care into service provision (Lynch et al. 2013).

This chapter outlines the development of palliative care in different regions of the world, organized by the facets of the World Health Organization's Public Health Strategy for Palliative Care, which include (1) policies, (2) medicine availability, (3) education, and (4) implementation of services (Stjernsward et al. 2007). In addition, due to the fact that the growth in palliative care has often been due to advocates in various countries, we include information on a fifth category: vitality (Centeno et al. 2007, 2016; Woitha et al. 2016b). Each subsection is divided into different geographical regions: Europe,

North America, Latin America, Africa, Asia-Pacific, and Middle East. The regions were mostly based on existence of regional palliative care networks, which often provide much needed information on palliative care development in their respective regions. Each region also contains two case studies of two models of hospice and palliative care service delivery, recommended by experts, for the reader to gain a deeper insight into the different types of models available in palliative care delivery globally. The case studies, therefore, do not necessarily represent the most developed palliative care service in the region, but are available to show the richness in different types of palliative care service delivery throughout the world.

In this chapter, palliative care is defined as "care given to improve the quality of life of patients who have a serious or life-threatening disease, such as cancer" (National Cancer Institute 2010). With its goal to "prevent or treat, as early as possible, the symptoms and side effects of the disease and its treatment, in addition to the related psychological, social, and spiritual problems" (National Cancer Institute 2010). Hospice care has the same principles but palliative care is offered earlier in the disease process, and hospice care is a form of palliative care and is usually limited to a terminal diagnosis (usually defined as having a life expectancy of 6 months or less) (National Cancer Institute 2010).

It is important to note that, in different regions of the world, the concept of palliative care versus hospice care may manifest itself in different ways. In the United States, patients are enrolled in a hospice when a physician estimates a life expectancy of 6 months or less, whereas a hospice in Uganda may, in practice, be providing palliative care, not limiting its patient population to a particular life expectancy.

2 Europe

A total of 32 countries which are part of the European Association for Palliative Care were included in this section (Fig. 1). We thank Mr. Eduardo Garralda (University of Navarra) for reviewing and providing guidance on this section.

2.1 Implementation of Services

According to the European Atlas of Palliative Care, in 2013, the UK had 308 palliative care hospital support teams, 189 inpatient hospices, and 272 day hospice/day care centers (Centeno et al. 2013b). In addition, it leads pediatric palliative care services with 46 pediatric home palliative care support teams, 241 pediatric palliative care units in tertiary hospitals, 42 pediatric inpatient hospices, and 31 pediatric day care services (Centeno et al. 2013b). There is much greater variation in Central and Eastern Europe, where certain countries have no known palliative care capacity (such as Uzbekistan), while others have advanced integration of services (Poland) (Lynch et al. 2013).

Specialized palliative care services in Europe have increased greatly from 1,449 to 5,000 over a period from 2005 to 2012 (Centeno et al. 2016). However, most of the service growth has been in Western Europe, with minimal growth in Central and Eastern Europe (Centeno et al. 2016). In 2012, there were 2,063 home-care teams, 1,879 inpatient palliative care services, and 1,088 hospital support teams in Europe (Centeno et al. 2016) (Fig. 2). Generalist palliative care provision remains an issue and there is a lack of valid, feasible, and measurable indicators to compare generalist palliative care services in Europe (Centeno and Garralda 2016).

The UK has consistently been identified as among the highest performing countries in palliative care according to the Quality of Death Index (The Economist Intelligence Unit 2015), and Western European countries generally show a high level of service provision, with most of the countries falling under levels 4a/4b (preliminary/advanced integration of services) according to the world map (Lynch et al. 2013).

2.2 Policies

Since the development of Recommendation (2003) 24, a national palliative care policy framework, by the Council of Europe (2003), many European countries have adopted laws or frameworks on palliative care. A recent study showed

Fig. 1 Member countries of the European Association for Palliative Care

that out of the 46 countries that took part in the survey in 2013, 12 European Union (EU) and 6 non-EU countries had national palliative care plans (Woitha et al. 2016a). Sixty-three percentage of European countries had a national law where PC provisions were identified, and 52% had national documents with standards and/or norms regarding palliative care provision (Woitha et al. 2016a). Sixty-seven percentage of countries had specific responsibilities for palliative care delivery within the Ministries of Health; some countries delegate the responsibility to one person (e.g., Latvia, Bulgaria), while others have a national office supervising palliative care provision (e.g., Italy). Figure 3 outlines a map of national palliative care plans/strategies and laws by country in Europe.

With regard to the financial resources for palliative care provision, 32 countries (out of 45) provide palliative care free of charge, and 19 countries provide free medications (Woitha et al. 2016a). Full payment was only required in Bulgaria, whereas the majority of the countries had some type of subsidized system for consultation costs and medications (Woitha et al. 2016a). However, national palliative care leaders report that major barriers to palliative care development in Europe include lack of a national plan, lack of adequate regulatory frameworks, and insufficient funding. Particularly, lack of funding allocated specifically for palliative care was seen as the greatest issue in 19 countries (Centeno and Garralda 2016).

2.3 Education in Palliative Care

Twenty-eight European countries (65% of responding countries) have palliative medicine in the curriculum of at least one medical

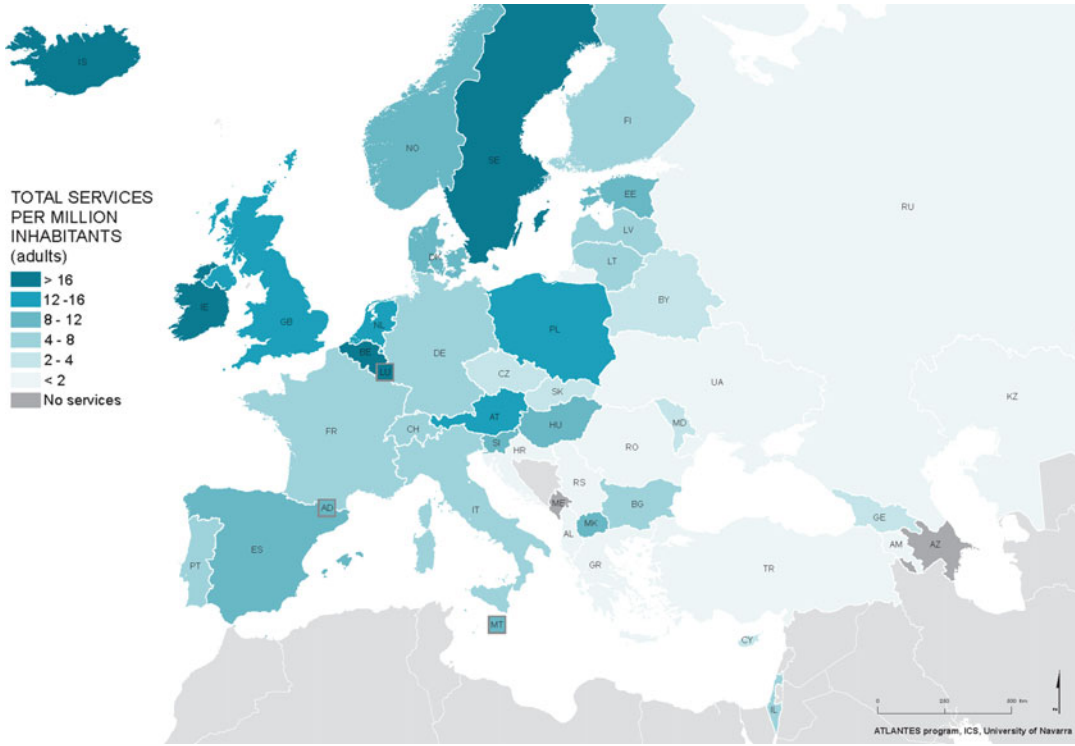

Fig. 2 Density of palliative care services in Europe. (Reproduced with permissions from authors) (Centeno et al. 2013a)

university, and in 13 countries, it is taught in all medical schools (Carrasco et al. 2015). Fourteen countries did not have palliative medicine in their undergraduate medical curriculum (Carrasco et al. 2015). In the United Kingdom (UK), Norway, Belgium, France, and Malta, palliative medicine is a required course in all medical schools. Seventeen countries reported having full professors of palliative medicine on faculty (Carrasco et al. 2015).

According to an expert committee on education convened by the European Association of Palliative Care, Norway, UK, Belgium, and France were rated highest in terms of undergraduate palliative medicine education (Carrasco et al. 2015). Another European study identified that 18 of 53 European countries had accredited specialization in palliative medicine, including Czech Republic, Denmark, Finland, France, Georgia, Germany, Hungary, Ireland, Israel, Italy, Latvia, Malta, Norway, Poland, Portugal, Romania, Slovakia, and the UK (Centeno et al. 2015).

2.4 Medicine Availability

There is a large difference in opioid availability and consumption between Western and Eastern Europe. In most Western European countries, opioids are available to cancer patients for no cost or subsidized >75% (Cherny et al. 2010). Though there are many Eastern European countries that also provide opioids for no cost or subsidized >75% (Czech Republic, Croatia, Latvia, Rumania, the Slovak Republic, Hungary, Estonia, and Serbia), there are also a large number of countries that lack essential medicines (Lithuania, Tajikistan, Belarus, Albania, Georgia, and Ukraine) (Cherny et al. 2010).

However, as availability does not necessarily equate to accessibility, accessibility remains an issue in many countries. Many Eastern European countries and Greece require special permits or physicians from only certain specialties to prescribe opioids (Cherny et al. 2010). In general, countries with the greatest number of regulatory

Fig. 3 National palliative care plans, strategies, and laws across Europe. (Reproduced with permissions from authors) (Centeno et al. 2013a)

barriers to accessibility also tended to have the most limited opioid formularies (Cherny et al. 2010).

2.5 Vitality and Advocacy

The European Association for Palliative Care (EAPC) was founded in 1988 with 42 founding members (EAPC 2016). It has grown significantly since its inception with members from 48 countries around the world and 57 National Associations from 32 European countries (EAPC 2016). Figure 1 shows a map of all the member countries of the EAPC.

The EAPC has been active internationally, partnering with national and international organizations, such as the International Association for Hospice and Palliative Care (IAHPC) and Worldwide Hospice Palliative Care Alliance (WHPCA) in different policy initiatives and petitions, and organizing annual palliative care congresses. In 2007, it led the Budapest Commitments, which aided national palliative care associations in defining clear goals, frameworks, and commitments in developing palliative care in their respective countries (Radbruch et al. 2007). And it partnered with IAHPC, WHPCA, and Human Rights Watch in creating the Prague Charter in 2013, urging governments to ensure the right to palliative care (Cleary et al. 2013d).

The EAPC has two official journals, the European Journal of Palliative Care and Palliative Medicine, and Palliative Medicine currently ranks the highest in terms of impact factor among other palliative care-related journals (EAPC 2016).

Across Europe, 37 countries have at least one National Association for Palliative Care (with some countries having more than one), 21 have published directories of palliative care services, 19 countries hold national palliative care congresses, 15 have a dedicated palliative care journal, and another 15 have palliative care research centers (Centeno et al. 2013b).

Palliative Care Model #1: PAL24, Madrid, Spain (Harding et al. 2013; Merino 2016; Plan Estratégico de Cuidados Paliativos de la Comunidad de Madrid 2010)

Palliative care in Madrid was started in the 1990s due to the tireless work of a few pioneers in palliative care. The first palliative care unit was opened at the Hospital General Universitario Gregorio Marañón and the first home-based service at Hospital Clínico San Carlos. Initially, palliative care was not available in all districts of Madrid, but following the Regional Palliative Care Plan in 2005, it was extended into all. Through the Regional Plan, palliative care and support teams were implemented in many new hospitals, and new beds and units were expanded in hospitals with already existing palliative care services. A pediatric palliative care unit was started in 2008 at the Hospital Infantil Universitario Niño Jesús de Madrid. Of note, the Spanish Healthcare System is publicly financed, and covers palliative care.

PAL24 (Platform Specific Palliative Care 24 Hours), a continuity of care model implemented in Madrid, is an innovative program that centralizes and coordinates palliative care resources in Madrid. The program is operational 24 h a day, 365 days a year, and its goals are to support caregivers at home and avoid unnecessary emergency visits to hospitals, support professionals taking care of patients at any level of care, and manage palliative care resources available throughout Madrid. The program is composed of six palliative care units, each with a doctor and a nurse, and services are provided through telemedicine (phone), advising professionals, and home-visits, when necessary. It uses INFOPAL, a system that allows for tracking of patients across hospitals and hospices, allowing for coordination and continuity of care. More than 500 professionals across

Palliative Care Model #1: PAL24, Madrid, Spain (Harding et al. 2013; Merino 2016; Plan Estratégico de Cuidados Paliativos de la Comunidad de Madrid 2010) (continued)

Madrid, including 11 home-care teams, 12 hospital-based teams, 289 palliative care beds, 6 teams from the Spanish Association Against Cancer, and a pediatric team, are working in coordination with the PAL24 team to deliver and coordinate services.

The service is housed and financed through SUMMA112, which is the Emergency Medical Service of Madrid. In 2015 alone, more than 22,000 contacts were made with PAL24, servicing over 86,000 patients.

Palliative Care Model #2: Hospice Casa Sperantei, Brasov, Romania (Hospice Casa Sperantei 2016)

Hospice Casa Sperantei was started in 1992 in Brasov and was the first charity providing care for end-of-life patients in Romania. Since its start, it has grown to be an important provider of palliative care services for the region, with over 100 staff members. In addition to its home-care program, which includes two rural teams in Fagaras and Zarnesti, the Hospice runs a 20-bed inpatient unit for adults and children.

The Hospice, furthermore, provides education on hospice and palliative care, not only in Romania but also to the Southeastern region of Europe. In 1997, it opened the Princess Diana Education Centre in Brasov, providing resources and training courses for medical and social care professionals, and in 2004, it opened the Nicholas Edeleanu Institute and Teaching Centre in Bucharest, offering resources and training for those interested in hospice and palliative

(*continued*)

Image 1 Hospice Casa Sperantei Team. (Photo provided by Dr. Daniela Mosoiu)

Palliative Care Model #2: Hospice Casa Sperantei, Brasov, Romania (Hospice Casa Sperantei 2016) (continued)

care. Through both teaching centers, the Hospice has trained more than 15,000 individuals, and it offers Master's and Certificate-level programs for healthcare providers.

The Hospice provides services free of charge, and most of its operating budget is supported through international and national grants, and also through Local Authorities and taxpayers, who can direct part of their income tax to the Hospice. The Hospice was supported by 400 volunteers in 2015, amounting to 18,000 volunteer hours donated (Image 1).

3 North America

For North America, the focus will be on the United States and Canada, since no information was available for Greenland. Figure 4 shows a map of the countries included in this subsection (three countries). We thank Dr. Diane Meier (Center to Advance Palliative Care, USA) and Dr. Jose Pereira (Pallium Canada, Canada) for reviewing and providing guidance on this section.

3.1 Implementation of Services

In North America, Canada and the United States (US) have advanced integration of palliative care in to the health system, but Greenland had no identifiable palliative care activity (Lynch et al. 2013). The US had a ratio of 1:48,000 of hospice/palliative care services to population and Canada had a ratio of 1:67,000 (Lynch et al. 2013). According to the Economist Intelligence Unit, the US and Canada were ranked 9 and 11, respectively, in the Quality of Death Index overall scores (The Economist Intelligence Unit 2015).

In USA, about 67% of hospitals have palliative care programs, with 90% having palliative care programs if the hospital had 300 beds or more (Dumanovsky et al. 2016). However, there is regional variation with New England having 88% and east south central part of the United States having only 42% of hospitals with palliative care programs (Dumanovsky et al. 2016). Hospitals owned by a for-profit entity, those in the South of the United States, and hospitals with fewer than 50 beds are least likely to report palliative care services (Dumanovsky et al. 2016).

Fig. 4 Countries included in North America

The first hospice opened in the US in 1973, and since then, has grown to 6,100 in 2014, with a majority (59.1%) being free-standing/independent hospices (National Hospice and Palliative Care Organization 2015b). There are about 4,400 board-certified palliative care physicians, but research shows that there is an estimated shortage of at least 6,000–10,000 palliative care physicians based just on current palliative care need in the US (Lupu and American Academy of Hospice and Palliative Medicine Workforce Task Force 2010). Considering the rapid growth in the population over age 65, the workforce needs have been grossly underestimated.

3.2 Policies

In the United States (US), the Medicare Hospice Benefit (passed by Congress in 1982) is the major source of hospice payment and reimbursement in the country, paying for 85.5% of hospice patients in 2014 (National Hospice and Palliative Care Organization 2015b). In 1993, under President Clinton's healthcare reform, hospice was included as a nationally guaranteed benefit (National Hospice and Palliative Care Organization 2015a). The passage of the Patient Protection and Affordable Care Act in the US in 2010 provided many additional opportunities for palliative care growth, by shifting healthcare delivery models from volume to value, which promotes the palliative care model of team-based approaches. However, patients are only eligible for reimbursements for non-hospice forms of home care if they have "skilled needs," i.e., they require a nurse or physical therapist (The Economist Intelligence Unit 2015). The passage of the Act required state Medicaid programs to allow children with life-limiting illnesses to concurrently receive both hospice care and curative treatment (National Hospice and Palliative Care Organization 2015a). Less than a fraction of 1% of the National Institutes of

Health's research budget is dedicated to palliative care, placing significant limits on the adequacy of the evidence base supporting palliative care clinical delivery (Gelfman et al. 2013).

In Canada, the Canadian Health Act (CHA), enacted in 1984, is the most important law that governs the provision of health care in general, though there is no law that specifically governs hospice and palliative care (Williams et al. 2010). Health care service delivery, with a few exceptions, is the responsibility of the Provinces and Territories in this highly-federalized system. Therefore, there has evolved significant variation in how palliative care services are organized and delivered across the country as it is dependent on regional and provincial/territorial policymakers and funders (Williams et al. 2010). A patchwork has evolved in which there are centers and regions of excellence in terms of high levels of access to various hospice and palliative care services in some jurisdictions, and other regions in which some components are either not available or not fully integrated in the regional or provincial jurisdictions (Williams et al. 2010).

There is currently no national policy or strategy related to the provision of hospice palliative care services in Canada. National guidelines have instead been developed by national and provincial palliative care organizations (Williams et al. 2010). However, there is currently a national planning strategy underway in Canada, and in November 2016, a Consensus Statement of the Palliative Care Lay Panel made recommendations that will be vital to the development of policy options and implementation plans for Canada in the spring of 2017 (Covenant Health 2017).

3.3 Education in Palliative Care

The US does not have a mandatory palliative care curriculum for medical schools. In fact, one large review of the literature found that US medical students had little to no mandatory training in palliative care (Aldridge et al. 2016), and in 2015, only 20% of schools had a separate course in palliative care, most of which are elective (Dickinson 2016).

In 2006, the American Board of Medical Specialties approved hospice and palliative care as a medical specialty (National Hospice and Palliative Care Organization 2015a). Currently, palliative care is an accredited postgraduate fellowship program by the Accreditation Council for Graduate Medical Education (Connor 2007). Furthermore, the Hospice and Palliative Care Nurse Association offers certification for advanced practice nurses, registered nurses, and nursing assistants (Connor 2007).

In Canada, there has been significant work done over the last two decades related to integrating palliative care education across the learning continuum, from undergraduate and postgraduate curricula, to continuing professional development (CPD) for health professionals already in practice. Pallium Canada has been the most active national organization with respect to CPD (Pallium Canada 2017). It has been developing and implementing CPD-level education programs across the country since 2001 (Pallium Canada 2017). Their Learning Essentials Approaches to Palliative Care (LEAP) courses are interprofessional and bilingual (English and French) and various versions cover many different healthcare settings (Pallium Canada 2017). The materials are also used in undergraduate and postgraduate curricula (Pallium Canada 2017). More advanced, intermediate courses for professionals wanting to develop more in-depth skills is also offered by Victoria Hospice and McMaster University (Williams et al. 2010). The Educating Future Physicians in Palliative and End-of-Life Care (EFPPEC) project, which ran from 2004 to 2009, implemented a palliative care education team and program in each of Canada's 17 medical schools, though there has been variable update across schools (TAFMC).

For over a decade, there has been a specialized-level palliative care nursing certificate program offered by the Canadian Nursing Association and a 1-year added competency residency program accredited at several medical schools by the College of Family Physicians of Canada (CFPC) and the Royal College of Physicians (RCPSC). In 2015, both the CFPC and the RCPSC granted palliative care formal subspecialty status and will be

accrediting 1- and 2-year palliative care residency programs (CHPCA 2016).

3.4 Medicine Availability

According to data from the International Narcotics Control Board (INCB), which includes both North and South America in their regional reporting of the Americas, from 1980 to 2006, the Americas had a steady increase in total morphine equivalents consumption (Gilson et al. 2013). Canada and the United States drive morphine consumption trends in this region (Gilson et al. 2013). As opposed to Asia or Africa, substance use disorder, in the form of illegal drugs and diversion of prescription drugs, has remained a major problem in Canada and the US (International Narcotics Control Board 2015). It is important to note that in Canada, the majority of opioid prescriptions (about nine out of ten) are related to chronic pain prescriptions for patients who do not have a concurrent serious illness. Total morphine equivalents in Canada in 2014 in mg per person was 967 and 733 without including methadone (Pain and Policy Studies Group 2014a).

In the US, the Centers for Disease Control, in 2016, released guidelines for prescribing opioids for chronic pain (Dowell et al. 2016) to try to address the exponentially increasing sale of prescription opioid and opioid-use related deaths. Opioid overdoses have quadrupled between 1999 and 2015 even though there has not been an overall change in the amount of pain Americans report (Centers for Disease Control and Prevention 2016). In fact, opioids, both prescription and illicit, are the main driver of drug overdose deaths in the US (Centers for Disease Control and Prevention 2016).

3.5 Vitality and Advocacy

The National Hospice Organization was founded in the US as early as 1978 as a professional membership organization, and in 2000, changed its name to the National Hospice and Palliative Care Organization (NHPCO 2015a). The National Coalition for Hospice and Palliative Care was founded in 2001 (NCHPC 2017); it leads advocacy efforts in the US through its member organizations and started the National Consensus Project for Quality Palliative Care in 2002, a task force to "further define and underscore the value of palliative care and to improve upon the delivery of palliative care in the United States" (NCHPC 2017). It has been involved in developing and disseminating versions of the *Clinical Practice Guidelines for Quality Palliative Care* in 2004, 2009, and 2013 (NCHPC 2017). In addition, in 2013, the Patient Quality of Life Coalition was formed, working to improve quality of care for patients and families with serious illnesses by promoting policies to expand access to high-quality palliative care (Patient Quality of Life Coalition 2017).

The National Palliative Care Research Center (NPCRC) coordinates research in palliative care across the US, as most medical schools do not yet have departments or divisions in palliative care (National Palliative Care Research Center 2013). The Center to Advance Palliative Care, which partners closely with the NPCRC, provides tools, training, technical assistance, and metrics to help implement and integrate palliative care into healthcare organizations (CAPC 2017).

In Canada, the Canadian Palliative Care Association, now known as the Canadian Hospice Palliative Care Association (CHPCA), was established in 1991 (CHPCA 2016) and the Canadian Society of Palliative Care Physicians (CSPCP) in 1993 (CSPCP 2014). The CHPCA has been important in acting as a national voice in policy, awareness, and education; it has developed a model to guide to hospice and palliative care in 2002, and it represents more than 500 programs and services and more than 30,000 members (Williams et al. 2010).

Palliative Care Matters has also been important in Canada in bringing together experts and organizations nationally and internationally to help develop a national palliative care strategy and to ensure that palliative care becomes a part of Canada's universal healthcare model (Covenant Health 2017).

Palliative Care Model #1: ProHEALTH Care Support, New York, USA (Lustbader et al. 2016)

ProHEALTH Care is a large multispecialty practice with multiple locations throughout the New York metropolitan area, and employing 900 providers. Within ProHEALTH Care is ProHEALTH Care Support, a home-based palliative care program that provides care in the context of a Medicare Shared Savings Program Accountable Care Organization (ACO).

The palliative care team is comprised of six registered nurses, two social workers, two doctors, one data analyst, and three administrative staff. The team also has 12 volunteers, who visit patients at their homes. Each nurse makes about five home visits and five phone calls per day and is responsible for about 90 patients, working in concert with a social worker and physician. Most patients are seen at their home at least once a month with two telephone calls per month, with additional visits as needed.

One interesting aspect of this model is the importance of telepalliative care, where patients and/or their caregivers may have a virtual visit with any team member through a smart phone or laptop. The nurses also report support from physicians via telemedicine when visiting a patient's home. Patients have 24/7 access by telephone or telemedicine, and about 20% of patients utilize the service. Patients with advanced heart failure, chronic obstructive pulmonary disease on home oxygen, metastatic cancer, or severe dementia qualify for the program, identified through an algorithm developed by the ACO using claims data.

This model is unique in its use of telemedicine with specialty-level palliative care and 24/7 coverage for patients. Comparing patients receiving this home-based care model to those receiving usual care, cost per patient for Medicare parts A, B, and D was $10,435 lower than the cost per patient receiving usual care, and $12,000 lower in the last 3 months of life. Furthermore, hospital admissions were 34% lower in the final months of life than those receiving usual care, and had 35% greater hospice utilization rate as compared to usual care recipients.

This innovative model of palliative care may provide significant savings for healthcare systems while still providing excellent care to patients by providing 24/7 access and meeting patient desires at end of life by with a majority (87%) dying at home rather than in the hospital (Image 2).

Palliative Care Model #2: Edmonton Regional Palliative Care Program, Canada (Canadian Medical Association 2015; Bruera et al. 1999; Fainsinger et al. 2007)

The Edmonton Regional Palliative Care Program was established in 1995 with the goal of increasing access to care for terminal patients with cancer to palliative care services. The Program initially consisted of a tertiary palliative care unit and a weekly multidisciplinary palliative care clinic in the local cancer center and has since expanded to include home care, hospice care, hospital care, and additional outpatient clinics.

The Regional Program's Administrative Office coordinates delivery of care, ensuring standards are met, and coordinating funding, program development, education, and research. The Family Physicians and Home Care are able to offer 24-h care to patients and with the Alberta Health Care Insurance Plan, able to bill for visits with palliative care patients. Hospices provide an important part of the Program, especially

(*continued*)

Image 2 ProHEALTH Care Support Palliative Care Team. (Photo provided by Dana Lustbader)

Palliative Care Model #2: Edmonton Regional Palliative Care Program, Canada (Canadian Medical Association 2015; Bruera et al. 1999; Fainsinger et al. 2007) (continued)

when patients may not have the resources or may not want to die at home. The Tertiary Palliative Care Unit allows for care for patients with symptoms that are difficult to manage. The Palliative Care Consulting Service was also formed in order to provide consultations to acute care facilities and the community, providing consultation services for home care, long-term care, and community hospitals, with 24-h coverage throughout the year.

Palliative care services are provided through family doctors and nurses and are supported by a multidisciplinary team of dieticians, occupational therapists, homemakers, chaplains, pharmacists, physiotherapists, recreational therapists, rehabilitation therapists and assistants, social workers, volunteers, and palliative care consultants.

One unique aspect of the program is its research base and a model for providing standardized care through tools developed either at Edmonton or adopted for the interdisciplinary teams such as the Edmonton

Palliative Care Model #2: Edmonton Regional Palliative Care Program, Canada (Canadian Medical Association 2015; Bruera et al. 1999; Fainsinger et al. 2007) (continued)

Symptom Assessment System, the Mini-Mental State Questionnaire, the CAGE Questionnaire, The Palliative Performance Scale, Mean Equivalent Daily Dose of Parenteral Morphine, and the Edmonton Staging System for Cancer Pain. This allows for standardization and coordination of transfers of care, allowing ease of communication across different institutions within the Edmonton Region, supported by research and evidence. A regional database was developed to allow for generation of reports and continuous process improvement, including evaluating aspects of the program. The databases have allowed for research demonstrating decreases in death in acute care facilities and cost-savings for the region. The program's strength in research and evidence has allowed it to continue developing programs, including an educational curriculum in the undergraduate medical school and a Palliative Medicine Residency Program and incorporation of PhD personnel into research programs.

4 Latin America and the Caribean

A total of 18 countries were included in this section (Fig. 5). We thank Ms. Liliana de Lima (International Association for Hospice and Palliative Care) for reviewing and providing guidance on this section.

4.1 Implementation of Services

In 2012, there were 922 palliative care services across Latin America, with ratios ranging from 16.06 services per one million persons in Costa Rica to 0.24 services per one million persons in Honduras (Pastrana et al. 2012). The services offered are often concentrated in the most highly developed countries in terms of palliative care development. Argentina, Mexico, and Chile had the highest number of services in the region, with 151, 119, and 277 total services, respectively (Pastrana et al. 2012). According to the World Map of Palliative Care, there were no Latin American countries in the highest level (advanced integration of palliative care into the healthcare system), but Costa Rica, Chile, and Uruguay were categorized into the second highest category of preliminary integration (Lynch et al. 2013). There are 44 day care centers across all of Latin America, with the highest concentration in Costa Rica (1.63 day care centers per one million persons) (Pastrana et al. 2012).

There are 600 specialists in palliative care in the region, with the majority (70%) practicing in the three most developed countries in terms of palliative care (Chile, Mexico, and Argentina) (Pastrana et al. 2012) .

Fig. 5 Countries included under the umbrella of the Latin American Association for Palliative Care

4.2 Policies

National palliative care programs exist in many Latin American countries. However, one SWOT (strengths, weaknesses, opportunities, threats) analysis of palliative care development in Latin America showed that in eight countries, health policies were a significant barrier to palliative care development (Pastrana et al. 2015). National palliative care programs/plans exist in Brazil, Chile, Cuba, Mexico, Panama, Peru, and Venezuela (Pastrana et al. 2012).

According to the Atlas of Palliative Care in Latin America, published in 2012 by the Latin American Association for Palliative Care (ALCP for its Spanish acronym), three countries had national palliative care laws (Mexico, Colombia, and Chile), and all countries mentioned palliative care in the national HIV/AIDS Program and national primary care program (Pastrana et al. 2012). However, three countries did not mention palliative care in their corresponding national cancer control plan (Bolivia, Guatemala, and Paraguay) (Pastrana et al. 2012). Only five countries had a monitoring/auditing program in place (Chile, Costa Rica, Cuba, Panama, and Venezuela) (Pastrana et al. 2012).

4.3 Education in Palliative Care

There is uneven offering of education in palliative care across the region. Four countries in Latin America have an official palliative care specialty or subspecialty (Brazil, Venezuela, Costa Rica, and Colombia), with the first accreditation in Colombia in 1998. In six countries, palliative care training can be obtained via a course or diploma (Argentina, Chile, Cuba, Mexico, Panama, and Uruguay) (Pastrana et al. 2012). Postgraduate training in palliative care is offered in ten countries (Argentina, Brazil, Colombia, Costa Rica, Cuba, Guatemala, Mexico, Paraguay, Uruguay, and Venezuela) (Pastrana et al. 2012).

In many countries, including Bolivia, El Salvador, Honduras, and Nicaragua, there is no mention of palliative care in medical school training, while, on the other hand, Cuba and Uruguay have palliative care offerings throughout their medical schools either as a separate offering or part of another course (Pastrana et al. 2012).

4.4 Medicine Availability

According to the Global Opioid Policy Initiative, Chile and Argentina have the highest opioid consumption in the region (which included Latin America and the Caribbean), though consumption even in those two countries is considered moderate when compared to international levels (Cleary et al. 2013a). Morphine consumption was higher than the global mean (6.24 mg/capita) only in Argentina in 2014, according to the Pain and Policy Studies Group (2014c). All countries except Anguilla had injectable morphine, and six countries (Dominican Republic, Ecuador, El Salvador, Honduras, Paraguay, and Trinidad and Tobago) did not have immediate release morphine available (Cleary et al. 2013a).

Jamaica, Anguilla, and St. Lucia allow nurse prescription with special permit or authorization, and Uruguay allows nurse prescribing in emergencies (Cleary et al. 2013a). All countries allow oncologists to prescribe opioids, although six countries required special permits (Argentina, Bolivia, Brazil, Ecuador, Honduras, and Mexico) (Cleary et al. 2013a), and family doctors and surgeons are also allowed to prescribe, but more countries required special permits (and Anguilla allows surgeons to prescribe only in emergency situations) (Cleary et al. 2013a).

4.5 Vitality and Advocacy

Palliative care in Latin America began in the 1980s with support from local leaders and international experts (Bruera 1993). In addition to publishing the Atlas of Palliative Care in Latin America, the ALCP has been implementing a regional palliative care congress every 2 years which has had a positive influence in the development and advancement of the field in the Region. In addition, the ALCP serves as a source

of information and dissemination for news, updates, and networking (Pastrana et al. 2012). The countries with the highest number of members in the ALCP are Brazil and Argentina (Pastrana et al. 2012). Figure 5 shows a map of the countries included under the umbrella of the ALCP.

In addition to the regional association, 11 countries have at least 1 national palliative care association, with some having more than 1 (Brazil, Costa Rica, and Mexico) (Pastrana et al. 2012). Chile has the greatest number of research teams in palliative care (27 teams), and nine countries had identifiable palliative care research teams (Pastrana et al. 2015). Only Brazil has a national journal covering palliative care topics, and 13 countries have national conference on palliative care (only Bolivia, Guatemala, Honduras, Nicaragua, Dominican Republic, and Venezuela did not have national conferences) (Pastrana et al. 2012). Mexico and Argentina were the most active in terms of projects or agreements with organizations in other countries (Pastrana et al. 2012).

Latin American national palliative care leaders report international cooperation in research and training initiatives as important components for the region in terms of vitality, especially with institutions from the UK, Spain, Canada, and United States, and with countries in the region like Mexico or Argentina (Pastrana et al. 2012).

Palliative Care Model #1: Palliative Care Unit, Hospital Universitario Austral, Buenos Aires, Argentina (Mutto 2016)

Information for this case model was provided by Dr. Eduardo Mario Mutto, Hospital Universitario Austral.

The Hospital Universitario Austral (HUA), accredited by Joint Commission International, is located 50 km from Buenos Aires. Its Palliative Care Unit (PCU) began in March 2013 and consists of three doctors, two nurses, a psychologist, three volunteers and two chaplains. The PCU has morphine (oral/parenteral), methadone (oral), oxycodone (oral) and fentanyl (parenteral/transdermal) available.

Patients are cared for in the inpatient unit, outpatient clinic, the emergency service, and, in some cases, at home. All patients also receive weekly phone calls. Most patients reside in districts near HUA (within a radius of 50 km) and belong to the middle class and have some form of private medical coverage, though some patients come from neighboring countries and from throughout Argentina.

Since its establishment, 600 patients have been treated, referred by the following hospital services: Medical Clinic 34%; Oncology 23%; Emergency 14%; Spontaneous 10%; Hepatology 4%; Other 15%. An average of 15 first-time consultations and 60 active follow-up patients are treated monthly. About 50.5% of patients die in the hospital; 26.5% at home and 23.4% at another hospital.

The team prioritizes research and teaching medicine and nursing students at the university. The team tracks four patient care indicators: Place of death; integrated care; contact with primary caregiver; evaluation of symptoms using the Edmonton Symptom Assessment System. Students receive theoretical classes with a practical component in the PCU, and students can take a Palliative Medicine elective in their fifth year and are able to complete a senior thesis in palliative care. In 2017, a postgraduate course in palliative care will be available for doctors and nurses.

There is a close relationship between the PCU and Hospice Buen Samaritano (HBS), located 3.5 km from HUA, providing palliative care to patients in difficult financial situations. In 2015, an agreement was made between the HUA and the HBS for a joint training fellowship in palliative care (Image 3).

Image 3 Hospital Universitario Austral in Argentina Palliative Care Team. (Photo provided by Eduardo Mutto)

Palliative Care Model #2: Palliative Care Clinic, El Salvador (López Saca 2016)

Information for this case model was provided by Dr. José Mario López Saca, Clínica de Cuidados Paliativos.

There is one hospice in El Salvador and six pain and palliative care units in public hospitals providing free care but with few physicians with formal training and with limited access to opioids. In 2013, an internal medicine physician with 2 years of palliative care training from La Clínica Universidad de Navarra, Spain, started a private palliative care clinic in the capital with an oncologist, an oncology-trained nurse, and a psychologist with experience working with hospice patients.

Previously, palliative care units did not exist in the country, and therefore, the team took steps to gain approval from the National Council of Public Health, which authorized the clinic through the Medical and Nursing Surveillance Board. Requirements were created that provide the basis for similar initiatives.

Thus, the Palliative Care Clinic started with the aim of providing support and

Palliative Care Model #2: Palliative Care Clinic, El Salvador (López Saca 2016) (continued)

control of symptoms for patients with both advanced cancer and noncancer patients through outpatient consultation, day clinic, and home care. In the outpatient clinic, patients with higher functional capacity are managed where pain is usually the main symptom. At the day clinic, patients receive medications, including palliative chemotherapy or intravenous antibiotics. The largest proportion of patients is cared for at home. The clinic, although private, provides free care for patients who cannot pay. In the past 4 years, the number of patients has been increasing, and currently, the team manages about six patients per month at home.

Due to the growing number of patients, the multidisciplinary team has also grown; currently, there are two palliative doctors, two outpatient nurses, one part-time psychologist, and ten home-care nurses.

The team has a continuous training plan in place; two Saturdays a month, there is a

(*continued*)

Image 4 Palliative Care Clinic in El Salvador Palliative Care Team. (Photo provided by José Mario López Saca)

Palliative Care Model #2: Palliative Care Clinic, El Salvador (López Saca 2016) (continued)

team session, and once a month, there is an online session with teams abroad (Spain, Guatemala, Argentina and Chile). One semester per year, a basic palliative care course is given to the nurses who provide home care. The team also runs a palliative medicine course that has been taught from 2013 at the medical school as an elective in the fifth year of medicine. Interest has grown exponentially, and starting from 2017, the course will be mandatory for sixth year students.

The unit has a strong relationship with the General Directorate of Medicines, the institution responsible for the supervision of opioids in the country, and there are currently two or three pharmacies in San Salvador that have extended-release morphine, liquid morphine, methadone tablets, extended- and immediate-release oxycodone tablets, fentanyl patches, and liquid fentanyl. The mechanism for obtaining the opioid at home is now faster, but there are still barriers to certain opioids in El Salvador (Image 4).

5 Africa

Africa differs from much of the rest of the world in its delivery in palliative care and level of burden of specific diseases such as HIV/AIDS, which predominates in Africa, even over malignant diseases, and tuberculosis (WHPCA and WHO 2014). Furthermore, due to the fact that Africa hosts the majority of children, globally, in need of palliative care (49%), the balance in need of various different types of palliative care service provision differ from the rest of the world (WHPCA and WHO 2014). A total of 54 countries (Fig. 6) were included in this section. We thank Dr. Emmanuel Luyirika (African Palliative Care Association) for reviewing and providing guidance on this section.

5.1 Implementation of Services

Uganda, South Africa, and Kenya have the highest number of hospice and specialized palliative care services (Rhee et al. 2017). The first hospice in Africa was started in Zimbabwe in 1979 (Di Sorbo et al. 2010). Since then, there has been a large growth in palliative care in Africa, accounting for most of the growth in palliative care globally from 2006 to 2011 (Lynch et al. 2013). According to the global update of the

Fig. 6 Countries included under the umbrella of the African Palliative Care Association

world mapping project in palliative care, Africa was the most prominent region for progress of countries from Group 3 to 4 (isolated/generalized provision to initial/advanced integration into the health system) (Lynch et al. 2013). However, no palliative care services were identified in 28 countries, and countries, like Zimbabwe, have moved dramatically between different levels of palliative care service provision based on political volatility (Lynch et al. 2013). Ratio of hospice palliative care services to population ranges from 1:237,000 in Swaziland to 1:41,412,000 in Ethiopia (Lynch et al. 2013).

Radiotherapy is particularly important for palliation in the African context. Although there were 277 machines in the continent in 2010, 60% of these machines were housed in two countries (South Africa and Egypt) (Abdel-Wahab et al. 2013). Furthermore, 29 countries, at the time of the study, had no radiotherapy machines, and 7 countries had only 1 radiotherapy machine (Abdel-Wahab et al. 2013). There is need to advocate for African countries to invest in radiotherapy as a palliative care treatment modality in order to improve the quality of life for patients with cancer and in need of palliation.

5.2 Policies

In 2002, the first African declaration at Cape Town was passed, recognizing palliative care as

a right for all adults and children with life-limiting illnesses, and declaring pain and symptom control as a human right (Mpanga Sebuyira et al. 2003). The Declaration also stated the importance of ensuring palliative care at all levels of the healthcare system (Mpanga Sebuyira et al. 2003).

In April 2012, the African Union adopted the "Common Position on Controlled Substances and Access to Pain Management and Dugs" stating the need for focusing on greater access and availability of opioids and the "Declaration of Non-communicable Diseases" which included palliative care (Rawlinson and Luyirika 2014). In September 2013, the Ministers of Health of 21 African countries adopted a consensus statement entitled, "Consensus Statement for Palliative Care Integration into Health Systems in Africa: Palliative Care for Africa," which agreed on focusing on greater access and accountability in providing palliative care services (Rawlinson and Luyirika 2014). The statement also outlined six objectives critical for countries in integrating palliative care into health systems, including the importance of developing policy frameworks to integrate palliative care into hospital and community home-based care services; to integrate palliative care services into national health budgets; to ensure availability of and access to essential medicines in pain and symptom control; to integrate palliative care into nursing, medical, and other relevant health training curricula (including social workers, pharmacists, psychologists, and clergy); to share best case practices across the continent; and to develop partnerships across the continent (APCA 2013).

In 2014, at the seventy-seventh World Health Assembly, WHA67.19 was passed, which called for strengthening of palliative care as a component of comprehensive care throughout the life course; the document urged member states to develop and strengthen policies in palliative care; to ensure adequate funding and human resources for palliative care initiatives; to provide basic support through multi-sectorial partnerships; to include palliative care in education and training; to continually assess palliative care needs; to review legislation and policies for controlled medicines; to update lists of national essential medicines; to foster partnerships; and to implement and monitor actions (Sixty-seventh World Health Assembly, May 24, 2014).

More recently, in August 2016, at the Fifth International African Palliative Care Association Conference's second African Ministers of Health session on Palliative Care, representatives from 26 African countries agreed upon the Kampala Declaration, reasserting the importance of strengthening palliative care in Africa and reaffirming the commitment of Ministries of Health in implementing WHA67.19 and committing to invest in technologies to improve quality and palliative care services and to provide leadership to ensure implementation of WHA67.19 (APCA 2016a).

At the individual country level, to date, there are seven African countries with stand-alone national palliative care policies (Malawi, Mozambique, Rwanda, Swaziland, Tanzania, Botswana, and Zimbabwe), and one in the process of being adopted Uganda (Luyirika et al. 2016). Three African countries (Uganda, South Africa, and Tanzania) have integrated palliative care into their national health policies and strategies, and Uganda and South Africa have recognized palliative care as an examinable subject (Rawlinson et al. 2014). Uganda is unique in that it is the first country in Africa that has changed its laws to allow nurses and clinical officers with proper training to prescribe oral morphine (Jagwe and Merriman 2007). A more recent study shows that 22% (12/48) countries have stand-alone palliative care policies (Rhee et al. 2017). In general, Francophone countries lag behind Anglophone countries in terms of palliative care development and service implementation (Human Rights Watch 2015).

5.3 Education in Palliative Care

Palliative care education is provided by five overarching types of organizations: national palliative care associations, such as the Hospice and Palliative Care Association of South Africa; nongovernmental palliative care organizations, such as Hospice Africa Uganda, Mildmay Uganda, and

Island Hospice; universities, such as the University of Cape Town and Makerere University; the African Palliative Care Association; and other global organizations, such as the International Association for Hospice and Palliative Care (Rawlinson et al. 2014).

Higher level education in palliative care is now available in several countries in Africa, including South Africa, Uganda, and Tanzania (TRUMH 2015). The Institute of Hospice and Palliative Care in Africa in partnership with Makerere University, also provides training across Africa through certificate-, diploma-, and Bachelor's-level courses (with plans to release a Master's in Palliative Care soon) to healthcare professionals, done through distance learning combined with a few months of in-person learning (Hospice Africa Uganda 2016b). The University of Cape Town in South Africa offers postgraduate palliative care through a distance education program (Ens et al. 2011). Zambia, Uganda, South Africa, Kenya, Ghana, and Egypt reported some form of physician accreditation (Rhee et al. 2017).

Mildmay Uganda provides the only multidisciplinary pediatric palliative care diploma on the African continent (Rawlinson et al. 2014).

5.4 Medicine Availability

Despite the great need of opioids on the continent, according to data from the International Narcotics Control Board (INCB), Africa consistently reports the lowest morphine and total morphine equivalence consumption globally from 1980 to 2009, with a small decrease in consumption from 2004 to 2006 (Gilson et al. 2013). The countries with the highest morphine consumption in 2014 were, in order, South Africa, Seychelles, Swaziland, Rwanda, and Mozambique, though all were still below the global mean (Pain and Policy Studies Group 2014b).

As reported by the Global Opioid Policy Initiative, codeine and morphine are the primary medicines on formulary, but none of the 25 countries covered in the study had all seven essential opioids available (the seven essential opioids, as per the IAHPC, are codeine, immediate release oral morphine, controlled release oral morphine, injectable morphine, oral immediate release oxycodone, transdermal fentanyl, and oral methadone) (Cleary et al. 2013b). Six of the countries (Cote d'Ivoire, Liberia, Libya, Rwanda, Sierra Leone, and Tunisia) reported no oral immediate release morphine, and Sierra Leone and Tanzania had the most limited formularies with only two medications on the formulary (Cleary et al. 2013b).

Medicines were free in about half of the countries studied, and in those countries where medicines were not free, costs were usually borne fully by the patient (Cleary et al. 2013b).

Prescribing privileges were least restrictive for oncologists, where almost all studied countries except for Egypt, Liberia, and Morocco, always allowed for oncologists to prescribe opioids. Four countries (Kenya, Sierra Leone, Tanzania, and Uganda) allowed nurse prescriber privileges with special permit or authorization, and Madagascar, Malawi, and Sudan allowed nurse prescribing in cases of emergencies (Cleary et al. 2013b). Most countries had considerable restrictions to opioid accessibility (Cleary et al. 2013b).

5.5 Vitality and Advocacy

Palliative care growth in Africa has largely been due to the dedicated work of activists and civil society organizations on the ground and nongovernmental organizations and institutions. Currently, national palliative care organizations, such as the Palliative Care Association of Uganda, the Hospice and Palliative Care Association of South Africa, and the Kenyan Hospice Palliative Care Association provide policy-level support, education, advocacy, and mentorship in their respective countries (Harding et al. 2013). The African Palliative Care Association (APCA) provides country-level support to governments, national palliative care associations, and individuals in countries that are trying to start palliative care in their respective countries. Figure 6 shows a map of the countries included under the umbrella of the APCA. There are national palliative care associations in countries like Botswana, Malawi, Mozambique, Zambia, and Zimbabwe (APCA 2016b).

Palliative Care Model #1: Hospice Africa Uganda, Kampala, Uganda (Hospice Africa Uganda 2016a)

Hospice Africa Uganda (HAU) was started in 1993. It is a nongovernmental organization funded mostly by grants and donations, providing palliative care in Uganda. Since its conception, it has become an internationally renowned model for palliative care provision in Africa. HAU currently operates hospices in three locations in Uganda, and the core of its work is its outpatient services and home visits. In addition, it provides outreaches to communities, sees consultations at Mulago National Hospital, and conducts monthly visits to partner hospitals. It also provides innovative models such as mobile clinics.

HAU has also been core to advocacy in Uganda. Through its Morphine Production Unit, it produces morphine for the rest of the country. It has played a key role in advocating for a national palliative care policy as well as for nurses to be able to prescribe basic medications for palliative care in Uganda.

HAU has also grown outside of Uganda, providing education to healthcare providers across Africa through its Institute of Hospice and Palliative Care in Africa and its International Programs Department. It offers short courses, diplomas, and a Bachelor's in palliative medicine, and it is planning to start offering a Master's. Upon finishing the course, trainees are aided by HAU in building palliative care capacity in their hospital or country.

HAU provides medications free of charge to patients, and charges, for those who are able to pay, 10,000 Ugandan shillings per visit (equal to about $3 USD). The team is made up of a core team of nurses overseen by a Nurse Supervisor and a Clinical Director, who is a doctor. The team also

Palliative Care Model #1: Hospice Africa Uganda, Kampala, Uganda (Hospice Africa Uganda 2016a) (continued)

consists of social workers and lay counselors. They also have a team of Community Health Volunteers, who identify and provide linkage to care to eligible patients for community outreaches (Image 5).

Palliative Care Model #2: Radiation and Isotope Center Khartoum (RICK), Khartoum, Sudan (Gafer and Elhaj 2014)

Information for this section was provided by Dr. Nahla Gafer and Dr. Shaima Sideeg, Radiation Isotope Center Khartoum.

The palliative care team at the Radiation and Isotope Center Khartoum (RICK), the main oncology center in Sudan, was started by Dr. Nahla Gafer after receiving training at Hospice Africa Uganda. It started in 2010 as an outpatient clinic, as the first site of PC in Sudan, and in 2011, with funding from the African Palliative Care Association, opened a palliative care ward. The palliative care unit has nine beds and the outpatient service is open 5 days a week, providing care to patients from oncology units at RICK and from other hospitals. A home care service was also started in 2011 where staff volunteered to conduct home-care once a week on Saturdays. Patients' families provide transportation for personnel, showing a strong partnership between the care team and the community in which they work.

Since its inception, the palliative care unit has introduced liquid oral morphine to RICK and has improved availability to opiate and non-opiate palliative care medications; opiates are now available all week, including on holidays, though some regulatory barriers are still in place. Palliative care is available in

(*continued*)

Image 5 Hospice Africa Uganda Team. (Photo provided by Eddie Mwebesa)

Palliative Care Model #2: Radiation and Isotope Center Khartoum (RICK), Khartoum, Sudan (Gafer and Elhaj 2014) (continued)

two additional institutions in Sudan, through educational initiatives at RICK, and the three institutions coordinate in providing trainings for healthcare workers in Sudan.

The palliative care service has 24/7 coverage, and it works with the emergency room where there is a section dedicated for oncological emergencies, including for palliative care patients. The team also provides a specialized service for patients who need additional help with dressing and special needs. The team is working closely with the Ministry of Health to continue expanding its services and palliative care availability throughout the country.

RICK sponsors the palliative care team, and additional funds come from the local community. Palliative care services are provided free to all patients, even to those not from Sudan (Image 6).

6 Asia-Pacific

A total of 15 countries (Fig. 7) were included in this section. We thank Dr. Ednin Hamzah (Hospis Malaysia) and Dr. Young Seon Hong (Asia-Pacific Hospice Palliative Care Network) for reviewing and providing guidance on this section.

6.1 Implementation of Services

Development of palliative care across Asia is very heterogeneous (Lynch et al. 2013). Hong Kong

Image 6 Radiation and Isotope Center Khartoum, Sudan Team. (Photo provided by Shaimaa Sideeg)

and Singapore have achieved advanced levels of palliative care integrations, but many countries in the region have limited to no palliative care services (Lynch et al. 2013). In Western Asia, most countries range from one to four services throughout the region (Lynch et al. 2013). Australia and New Zealand rank second and third, respectively according to the Quality of Death Index (The Economist Intelligence Unit 2015) and have among the best hospice/palliative care service to population ratios of 1:67,000 and 1:89,000, respectively (Lynch et al. 2013).

According to the world mapping of palliative care, Japan, Singapore, South Korea, and Malaysia perform the best in terms of ratio of hospice/palliative care services to population, ranging from 1:183,000 in Japan to 1:250,000 in Malaysia; Pakistan performed the worst in the region with a ratio of 1:90,404 (Lynch et al. 2013).

According to the 2015 Quality of Death Index by The Economist Intelligence Unit, six countries from the Asia Pacific region were included in the top 20 Quality of Death Index scores, including Australia, New Zealand, Taiwan, Singapore, Japan, and South Korea (The Economist Intelligence Unit 2015).

A more recent article published by the Asia Pacific Hospice Palliative Care Network showed higher development of palliative care in East Asia compared to South and Southeast Asia, with South Korea, Taiwan, Japan, and Hong Kong having 13, 29, 35, and 59 beds per one million inhabitants, respectively (Yamaguchi et al. 2014). Australia had 107 specialist palliative care services, and New Zealand had 35 inpatient hospices and 41 beds per million inhabitants (Yamaguchi et al. 2014).

Hospices in Asia have a long history of being a grassroots movement, supported mainly by volunteers, nongovernmental organizations, and charities (religious and secular). Although there are many case studies of successful initiatives, in the long run, without integration into the health system, such programs may not be sustainable in the long run (Loucka 2012). As mentioned above, different models of hospice and palliative care delivery have been developed, each catered to the realities of the context of each region. For example, in East Asia (Mainland China did not participate in this particular survey), Hong Kong has the highest number of in-patient hospices (76) while Japan and Taiwan, though very developed in palliative care, have 0 (Yamaguchi et al. 2014). However, Japan has the highest number of hospital palliative care teams at 541, and Taiwan has the highest number of certified palliative care physicians at 562 (Yamaguchi et al. 2014). In Southeast Asia (without responses from Indonesia and Myanmar), Singapore has the highest level of service provision with 28 specialist palliative care service beds/one million inhabitants but has 0 oncology or general

Fig. 7 Member sectors of the Asia-Pacific Palliative Care Network

hospital-based palliative care units, while Malaysia, having 7 beds/one million inhabitants has the highest number of palliative care units, palliative care outpatient clinics, and home palliative care services at 19, 23, and 23, respectively (Yamaguchi et al. 2014).

6.2 Policies

The Asia Pacific region is very vast with very different cultures and levels of development. However, there have been significant advances in individual countries in recent years, and there are certain countries with much improvement in palliative care policies in the region. For example, Singapore has recently developed a national palliative care strategy, and Japan, which performed poorly in the 2010 Quality of Death Index, has jumped up to the top 20 in Quality of Death Index scores partially due to the institution of a new cancer control program and the incorporation of palliative care centers into the national budget (The Economist Intelligence Unit 2015). Taiwan,

ranked at number 6 in the Quality of Death Index, includes palliative care in its National Health Insurance, which allows for reimbursement of services (The Economist Intelligence Unit 2015). Bangladesh has incorporated palliative care into its National Cancer Strategy & Plan of Action (LCPC, October 8, 2016).

However, other countries still lag in policy development; the Philippines does not have any government-led strategy for the development and promotion of national palliative care, and in India and China, which together make up a significant portion of the world's population, has very little in terms of national palliative care policies (The Economist Intelligence Unit 2015). India has recently withdrawn its National Program for Palliative Care, which allocates a portion of the national budget for palliative care (although recent legislative changes have made it easier for doctors to prescribe morphine in India) (The Economist Intelligence Unit 2015). China has no national strategy or guidelines with limited use and availability of opioids, although the Ministry of Health officially endorsed the establishment of palliative care departments in hospitals in 2008 (The Economist Intelligence Unit 2015).

6.3 Education in Palliative Care

Flinders University (Australia), working with the Asia Pacific Hospice Palliative Care Network (APHN), has developed a Graduate Certificate in Palliative Care course, offered to students from the Asia Pacific region, with a particular emphasis on resource-challenged areas, though the program is currently not available (Hegarty et al. 2014). The course is being offered in Singapore through a distance-learning curriculum, in partnership with the National Cancer Center Singapore (Hegarty et al. 2014). There are also important advances at the country-level. Sri Lanka's Post-Graduate Medical Institute has approved a postgraduate diploma in Palliative Medicine for doctors, to be rolled out in 2017 (LCPC, October 8, 2016), and Bangladesh appointed its first Palliative Medicine professor in 2015 (LCPC, October 8, 2016).

The APHN has also, in concert with the Lien Foundation, started the Lien Collaboration for Palliative Care, where, through a "Training-the-Trainer" program, they are focusing on palliative care development in resource poor countries through a collaborative of 40 international healthcare experts in palliative care, training 140 healthcare professionals in the Asia Pacific Region (LCPC, October 8, 2016). The Lien Collaboration has also recently released a documentary on the recent development of palliative care in Bangladesh, Myanmar, and Sri Lanka (LCPC, October 8, 2016).

Palliative care is recognized as a specialty or subspecialty in Australia (Bolognesi et al. 2014), Taiwan, Singapore, Japan, Hong Kong, Mongolia, Malaysia, India, and the Philippines (data was not available for the other five sectors: Korea, Thailand, Indonesia, Vietnam, Myanmar) (Asia Pacific Hospice Palliative Care Network 2016). Taiwan had the shortest number of years required (1 year) while Australia (Bolognesi et al. 2014), Malaysia, Singapore, and India require 3 years for specialization/subspecialization (Yamaguchi et al. 2014). Hong Kong requires 4 years, but either concurrently with either advanced clinical oncology or through a dual certification process with internal medicine (Yamaguchi et al. 2014). However, the lack of specialist training in many countries in Asia continues to be a major barrier to the growth of the palliative care field (Hamzah 2016).

6.4 Medicine Availability

Asia, similar to Africa, with many countries that are still considered "developing," represents a small proportion of total morphine equivalents consumption globally (Gilson et al. 2013). Opioid consumption has remained stable, with most of the growth coming from Japan and South Korea (Gilson et al. 2013). New Zealand and Australia have much higher morphine consumption than any other country in the Asia-Pacific and are the only two countries in the region with morphine consumption higher than the global mean (Pain and Policy Studies Group 2014e).

Codeine and morphine were the most commonly available formulations in the region, and China, the Philippines, and Malaysia had all seven essential medicine formulations available, while Hong Kong (China), South Korea, Thailand, and Vietnam had six of seven available (Cleary et al. 2013c). Of the 20 countries studied by the Global Opioid Policy Initiative, 11 provided medications at no cost of <25% of the cost to patients. Except for Japan, South Korea, Indonesia, Nepal, and Bhutan, all other countries had four or more restrictive regulations to opioid accessibility (Cleary et al. 2013c). In fact, opioid restrictions continues to be a big barrier to the growth of palliative care in many countries in Asia (Hamzah 2016).

Nurses are allowed to prescribe with special permits or authorization in the Philippines, Bhutan, and Pakistan (Cleary et al. 2013c). All countries allowed oncologists to provide opioids, although eight countries required special permits or authorizations; China did not allow family physicians to prescribe opioids, and Bangladesh allows family physicians to prescribe only in cases of emergencies (Cleary et al. 2013c). In Japan, Taiwan, the Philippines, and Vietnam, physicians require a special license to prescribe opioids (Yamaguchi et al. 2014).

6.5 Vitality and Advocacy

The first regional conference to support palliative care development in Asia was held in 1989 and a second in 1996, both in Singapore (Goh 2002). The third, in Hong Kong, was held in conjunction with the 1997 fourth Asia Pacific Cancer Congress, where a decision was made to form a separate legal identity (Goh 2002). The Asia Pacific Hospice Palliative Care Network (APHN), based in Singapore, was formed in 2001 to develop and support the development of palliative care in Asia; it consisted initially of 14 sectors including the following: Australia, Hong Kong, India, Indonesia, Japan, Korea, Malaysia, Myanmar, New Zealand, Philippines, Singapore, Taiwan, Thailand, and Vietnam (Goh 2002). Mongolia was added as a sector in 2015 (Hamzah 2016). Figure 7 shows a map of the member sectors of the APHN.

Due to the heterogeneity of cultures and tradition as well as development economically and in relation to palliative care, the APHN has recently shifted its strategy to focusing on capacity building in certain countries with lower levels of palliative care development (Hamzah 2016). Currently, it is working closely with advocates focused in four countries: Bangladesh, Myanmar, Sri Lanka, and India (Hamzah 2016).

Palliative Care Model #1: Neighborhood Network Palliative Care Service, Kerala, India (Kumar 2007)

The Neighborhood Network in Palliative Care (NNPC) is a community-based project, aimed at empowering local communities to look after their own chronically ill and dying. In the program, community volunteers play an active role in planning, evaluating, monitoring, and modifying the program.

Community volunteers give 2 h a week to care for the sick in their area. They are trained through 16 h of interactive theory sessions and four clinically supervised days. The volunteers then form groups of 10–15 members, supported by trained doctors and nurses, to identify those who are ill in their community and organize and plan interventions. The group may work with existing palliative care facilities or may build their own. Volunteers make regular home visits to follow up on patients that are seen by the palliative care team, identifying and addressing nonmedical issues, linking the patient to the healthcare provider.

The program provides an additional layer of support through trained volunteers who visit patients in between outpatient or inpatient visits, resulting in better psychosocial and spiritual support and better

(*continued*)

Palliative Care Model #1: Neighborhood Network Palliative Care Service, Kerala, India (Kumar 2007) (continued)

identification of psychosocial needs, including financial problems.

The NNPC is comprised of more than 4,000 volunteers, 36 physicians, and 60 nurses. In less than 5 years, the NNPC model resulted in the establishment of 68 community-based palliative care initiatives in northern and mid-Kerala, which covers about 12 million persons. The project is supported by raising money locally through donations of less than 15 cents.

Development of palliative care in Asia has been most difficult in rural areas. Programs such as NNPC provide information on innovative models that can be utilized in settings with constrained resources (financial and human resources), to assist professionals in delivering high quality palliative care to patients (Image 7).

Palliative Care Model #2: Hospis Malaysia, Kuala Lumpur, Malaysia (Hamzah 2016)

Hospis Malaysia is one of the first hospices in Malaysia providing community palliative care. It was started in 1991, run from a donated room in a hospital, and the nurse would go out into the community to see patients. Since then, Hospis Malaysia has grown into a team of 4 doctors, 18 nurses, 1 occupational therapist, 1 pharmacist, 1 Patient Care and Volunteer Coordinator and many nonclinical support staff (Public Relations, Finance, General Manager, Research Assistants, rotating support staff), and provides home-care services, day care services, hospital consults and bereavement support. Hospis Malaysia also provides education and training in the undergraduate medical curriculum of six

Palliative Care Model #2: Hospis Malaysia, Kuala Lumpur, Malaysia (Hamzah 2016) (continued)

universities in Malaysia as well as postgraduate training to family medicine physicians (4-week practical training rotations), and specialist palliative care training for internists (6 month rotations; palliative care is a subspecialty of Internal Medicine in Malaysia). The hospice in collaboration with APHN also runs its own workshops on different topics (palliative care nursing, communication skills; ethics; hope and suffering; pain and symptom management; pediatric palliative care and grief and bereavement) that are held yearly and is open to anyone who would like to participate from the Asia-Pacific region; about 300 persons participate in the short courses each year.

Hospis Malaysia is unique among hospices in its area in that it uses an internally developed web-based electronic health record system, to keep track of patient records and allowing the Medical Director to work with nurses in following patients even when not physically in the country. The system is also used as an audit tool to monitor various indicators of care. Due to the fact that funding from the government has been inconsistent, the hospice is unique in the way that it has approached long-term financial planning. It has four core departments: Clinical; Education, Training, and Research; Communications & Fundraising; and Finance & Administration. It has approached running the hospital like a business model with middle- and long-term strategies and has built a strong donor engagement plan, providing financial stability and growth. It sends out frequent newsletters to donors on progress and has focused on educating the donor base on what palliative care is and the importance of palliative care in the community.

Hospis Malaysia also has an internal auditing system, run by two Research

(*continued*)

Image 7 Session with patients at neighborhood network palliative care service in India. (Photo provided by Suresh Kumar)

Image 8 Hospis Malayisa, Malysia Team. (Photo provided by Ednin Hamzah)

Palliative Care Model #2: Hospis Malaysia, Kuala Lumpur, Malaysia (Hamzah 2016) (continued)

Assistants that provide ways of keeping track of outcomes, such as pain control, to allow for continuous improvement in processes and quality improvement.

Palliative Care Model #2: Hospis Malaysia, Kuala Lumpur, Malaysia (Hamzah 2016) (continued)

A strong base of management and clinical leadership has led to strong growth in clinical and education growth, which in turn has led to a greater role in national advocacy (Image 8).

7 Middle East

Due to the fact that the Middle East does not have an umbrella palliative care organization, we use the WHO's Eastern Mediterranean Regional Office (EMRO) in summarizing developments in this section, and therefore, some of the countries overlap with other regions. Figure 8 shows a map of the countries (22 countries) included in the WHO's EMRO. We thank Dr. Hibah Osman (Balsam Center) for reviewing and providing guidance on this section.

7.1 Implementation of Services

The availability and distribution of palliative care services across the Middle East is uneven. Higher levels of development are seen in Cyprus, Israel, Lebanon, and Jordan, which have inpatient palliative care beds, interdisciplinary palliative care, and pain teams (Silbermann et al. 2015b). The world map's updated study on palliative care services showed the following countries with higher levels of service provision in the region: Bahrain with a ratio of 1:791,000, Kuwait with 1:1,492,000, Jordan with 1:1,579,000, and Lebanon with 1:2,112,000 (Lynch et al. 2013). In absolute numbers, Saudi Arabia has the highest number of active PC services in the region, followed by Egypt and Jordan (Osman et al. 2017), but these services are not covered by government or reimbursed by private insurance (Osman 2016).

7.2 Policies

Information on national palliative care plans in the Middle East is scarce (Silbermann et al. 2012). Kuwait has palliative care-related regulations, Morocco and Kuwait are awaiting to pass a law regarding palliative care provision; Jordan has incorporated palliative care into its National Cancer Control Plan (Shamieh 2016), and Egypt has National Guidelines on management of acute and chronic pain as well as management of other physical symptoms (Silbermann et al. 2012).

Some preliminary results from a study on palliative care development in the region suggest that although Morocco and Qatar are the only countries with national palliative care programs; several other countries (Kuwait, Jordan, Egypt, and Lebanon) have programs under development (Osman 2016). Tunisia is unique in that it has a stand-alone national palliative care plan (Osman et al. 2017).

7.3 Education in Palliative Care

There is a need for more educational programs and curricula in the Middle East region. Many providers continue to seek education from countries with more advanced programs in Europe and North America (Shamieh et al. 2010).

According to one study of providers in the Middle East showed that one of the top barriers to providing palliative care included not having opportunities for training for health care professionals in palliative care (Silbermann et al. 2015b). Even countries that fare better in terms of opioid consumption in the region do not do so well in terms of palliative care training. For example, palliative care is being integrated into nursing curricula in Lebanon but not yet into medical school curricula, and there are no postgraduate training opportunities in the country. The Lebanese Ministry of Public Health launched, in 2011, a National Committee for Pain and Palliative Care to further progress in this area (Osman 2015a).

The country that stands out in terms of palliative care education is Saudi Arabia. It established the first fellowship training program in palliative medicine in Arabic countries at King Faisal Specialist Hospital and Research Center in 2000, and its graduates have been crucial in helping to set up palliative care programs in other Arabic-speaking countries such as the United Arab Emirates, Qatar, and Egypt (Al-Shahri 2009). Only Saudi Arabia and Lebanon have official certified licensing programs for palliative care physicians, and Egypt, Jordan, Qatar, Iran, and Oman have developed other licensing programs (Master's or Diploma) (Osman et al. 2017).

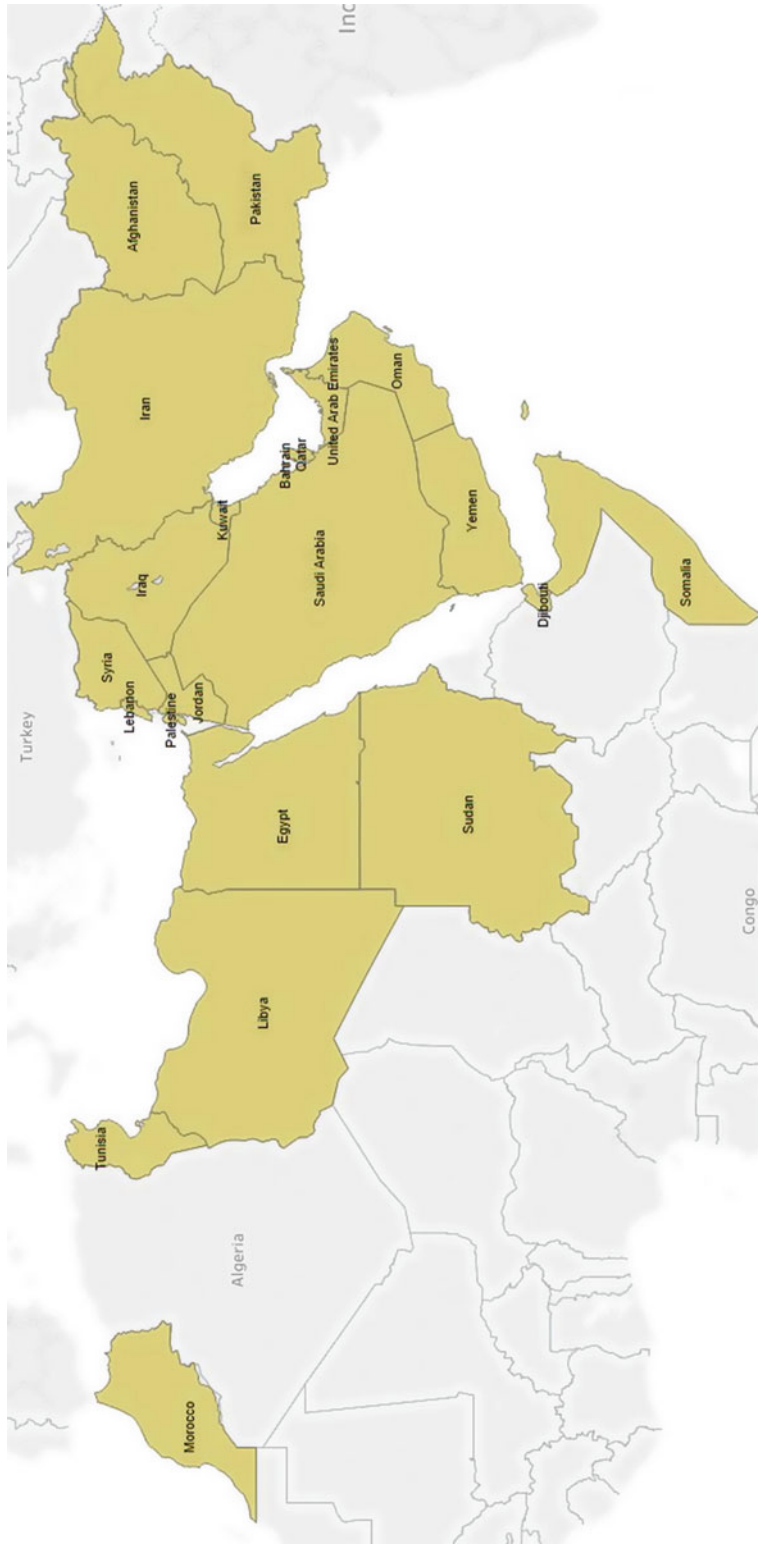

Fig. 8 Countries included in the World Health Organization's Eastern Mediterranean Regional Office

7.4 Medicine Availability

Opioid consumption and availability is, overall, very poor in the Middle Eastern countries. According to the Global Opioid Policy Initiative study in the Middle East, Lebanon and Bahrain had the greatest opioid consumption in 2011, though there was no data available for some countries more developed in palliative care, such as Jordan (Cleary et al. 2013d). The study showed, furthermore, that most countries had considerable regulatory restrictions to opioids (Cleary et al. 2013d).

According to data by the Pain and Policy Studies Group, the mean consumption of morphine in 2014 in the EMRO was 0.384 mg/capita compared to the global mean of 6.24 mg/capita. The group showed that Saudi Arabia had the highest morphine consumption in 2014, followed by Tunisia and Jordan (Pain and Policy Studies Group 2014d).

Another study pooled data from the International Narcotic Controls Board Report for 12 Middle Eastern Countries (Lebanon, Jordan, Syria, Qatar, United Arab Emirates, Saudi Arabia, Oman, Bahrain, Kuwait, Iraq, Egypt, and Yemen) and found that those 12 countries had lower opioid consumption than all regions globally except for Africa and Central America (Wilby and Wilbur 2017).

Furthermore, in addition to the fact that opioid consumption in the Middle East is much lower than Western countries, opioid consumption is also distributed unequally across the region. For example, in 2009, compared to the US, with opioid consumption of 29,487 sold-defined daily doses (S-DDD) per million inhabitants per day, Saudi Arabia had levels around 200 S-DDD, while Pakistan and Iraq had below 10 S-DDD per million inhabitants (Silbermann et al. 2012).

7.5 Vitality and Advocacy

The Middle Eastern Cancer Consortium (MECC), which includes Egypt, Jordan, Palestine, Israel, Cyprus, Turkey, and the USA, provides training and support in palliative care for those working in the oncology field (Silbermann et al. 2015a). It works closely with Ministries of Health in the region to help promote palliative care programs and activities (Silbermann et al. 2015a). Morocco, Tunisia, Lebanon, Jordan, Saudi Arabia, Kuwait, and Iran reported having national palliative care associations, though not all are currently active (Osman 2016; Osman et al. 2017).

Palliative Care Model #1: The Lebanese Center for Palliative Care – Balsam, Lebanon (Osman 2015a)

Information for this case model was provided by Dr. Hibah Osman, Balsam Center.

The Balsam Center in Lebanon is a non-governmental organization providing home-based care in Beirut. It has been in operation since 2009. The team is composed of one social worker, one outreach coordinator, three physicians (one part-time), five nurses, and clinical pharmacist and a clinical psychologist. Since its opening, it has cared for over 500 patients and families with 159 new patients enrolled in 2015. The Center trains palliative care teams in hospitals across the country and launched a large capacity building project in collaboration with the Ministry of Public Health, the World Health Organization, and Ain WaZein Hospital. It also serves as a training site for medical, nursing and social work students and has developed several courses including a mandatory module for 4 weeks to second-year medical students at the American University of Beirut.

Currently, the team expanding its research capacity and is undertaking a study to evaluate the impact of home-based palliative care on the cost of healthcare and quality of life for patients with advanced illness in partnership with GlobeMed, the American University of Beirut, and the Lebanese American University. The study aims to obtain data that would encourage integration of palliative care into

(*continued*)

Palliative Care Model #1: The Lebanese Center for Palliative Care – Balsam, Lebanon (Osman 2015a) (continued)

health. The team is also leading a project sponsored by the World Health Organization and in collaboration with the University of Navarra in mapping palliative care development in the Eastern Mediterranean Region.

The Balsam Team is involved in advocacy within the community, organizing awareness activities and engaging students at universities. The Team released a Short Film in October 2015, highlighting experiences of patients and families with the aim of helping others better understand palliative care.

The Team has recently launched a distance support program. Through telemedicine, the team is able to keep support patients and families that are located in geographical areas that are difficult to access (Image 9).

Palliative Care Model #2: King Hussein Cancer Center, Jordan (Shamieh 2017; Shamieh and Hui 2015; Shamieh et al. 2017)

Information for this case model was provided by Dr. Omar Shamieh, King Hussein Cancer Center.

The King Hussein Cancer Center (KHCC) is the largest tertiary cancer center in Jordan and treats more than 3,500 new cancer patients each year, more than 50% of patients with cancer in the country, as of 2016. In 2017, a new expansion is planned to open which will double the size of inpatient capacity (total of 370 beds) and will increase the outpatient capacity five times in space and also will double the outpatient capacity to two- to threefolds. This will enable KHCC to receive the majority of cancer cases in Jordan.

Palliative Care Model #2: King Hussein Cancer Center, Jordan (Shamieh 2017; Shamieh and Hui 2015; Shamieh et al. 2017) (continued)

The palliative care service at KHCC is the largest comprehensive palliative care program in the country and covers all medical and surgical oncology specialty services, including the emergency department. It comprised of an outpatient clinics, inpatient consultation service, inpatient service, a specialized palliative care unit, and a home-based palliative care program. The team is made up of American Board Certified palliative care physicians, registered nurses with training in palliative care and wound management, two clinical pharmacists, a social worker with experience in palliative care counseling, and a spiritual advisor. The service has available, as needed, a clinical psychologist, clinical dietitian, and physical and respiratory therapists.

The outpatient clinics operate 5 days a week and seeing about 10–15 patients per day. The inpatient consult team, in 2016, saw over 400 inpatient consultations. The KHCC palliative care unit has eight single-bed rooms with 24/7 visiting hours. The outpatient clinics operates 8 half-days a week from Sunday to Thursday and sees about 10–15 patients per clinic day. Home care expanded to four teams covering within a 100-mile radius of Amman, Jordan; each team consisting of two nurses and a driver and operating 5 days a week with weekend visits conducted when necessary. In 2016, the team provided for 2,300 visits.

The KHCC palliative care serves as a high-quality model of palliative care in the region for its education and international collaborative research and is a designated center of excellence for patient care. It is a WHO-designated regional center for

(*continued*)

Image 9 Balsam Center, Lebanon Team. (Photo provided by Hibah Osman)

Image 10 King Hussein Cancer Center, Jordan Team. (Photo provided by Omar Shamieh)

Palliative Care Model #2: King Hussein Cancer Center, Jordan (Shamieh 2017; Shamieh and Hui 2015; Shamieh et al. 2017) (continued)

palliative care education and training and many trainings are offered throughout the year. It provides postgraduate palliative clinical training for nurses from the University of Jordan and provides 1-month mandatory placements for the internal medicine residents. The team is very active in

Palliative Care Model #2: King Hussein Cancer Center, Jordan (Shamieh 2017; Shamieh and Hui 2015; Shamieh et al. 2017) (continued)

collaboration with the Jordanian Ministry of health in building capacity and services for palliative care across Jordan.

The KHCC is unique for its flexibility in reimbursement, allowing patients to receive palliative radiotherapy and procedures

(*continued*)

Palliative Care Model #2: King Hussein Cancer Center, Jordan (Shamieh 2017; Shamieh and Hui 2015; Shamieh et al. 2017) (continued)

according to needs and goals of care. The team is able to provide a range of palliative interventional procedures. The team provides respite care for patients with severe distress or caregiver burnout, and the service runs a 24-h phone help line and patients have access to KHCC's emergency department for emergency services (Image 10).

8 Conclusion and Summary

Though there has been much growth in palliative care development globally, development has been unequal. In many regions, such as Africa, Asia, and the Middle East, regulatory barriers to opioids still present a major challenge to palliative care development. In all regions, service provision is very unequally distributed, with some countries ranking among the top countries in the world in terms of palliative care integration and service implementation while other countries in the same regions have progressed very little; this is particularly pronounced in Africa, Asia, and Latin America. The major barrier in the Middle East seems to be a lack of education and training opportunities for those interested in palliative care as well as access to opioids, and it still lacks a regional palliative care network to assist in advocating for greater services and training in the region. Educational opportunities continue to be a barrier in many countries in Asia and Africa, although program development has increased greatly in Africa in recent years. Regional palliative care networks such as EAPC, ALCP, APHN, and APCA are essential in Europe, Latin America, Asia-Pacific, and Africa in aiding growth and development in palliative care at the country level.

Still, palliative care has come a long way over the past decade. It is now starting to be integrated into public health systems. International organizations, such as the WHO, European Union, and governments are gaining interest in palliative care and are integrating palliative care into policies and strategies. More patients have access to opioids than in the past, and there is now a field in medicine dedicated to the training and practice of palliative care. Globally, especially in regions that have identified barriers to palliative care, there has been vast growth in the past decade, and new and innovative models of palliative care delivery, influenced by local cultures, have expanded access to many. Key advocates in countries working with and for regional and national palliative care associations are vital in the continued growth in palliative care. Though there remains much work to be done, there has also been much progress in palliative care development globally.

Finally, this chapter has focused on regional palliative care organization and networks. However, before ending this chapter, we would be remiss not to mention the important role of international palliative care organizations such as the International Association for Hospice and Palliative Care, the Worldwide Hospice Palliative Care Alliance, and the International Children's Palliative Care Network in coordinating and advocating for improved hospice and palliative care access across all dimensions of the WHO Public Health Strategy at the global level.

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Development of Palliative Care: Past, Present, and Future

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_2

Abstract

Palliative care is an essential element of any health care system and a component of comprehensive and integrated care. Access to good palliative care is a basic human right. Palliative care has evolved since its modern foundation: the *British Hospice model* proposed building comprehensive models of care (responding to all dimensions of needs of patients). Palliative care has since spread into all the different settings of the health care systems.

Key evolution of palliative care provision includes:

- The design and implementation of public health models as national or regional palliative care programs, and the policy proposed by the WHO in the World Health Assembly Resolution WHA67.19 in 2014: "*Strengthening of palliative care as a component of comprehensive care throughout the life course.*"
- The shift from the institutional and late care of terminal cancer patients toward the timely community- and population-based perspective and links to chronic care models.
- Initiatives of *compassionate communities* which aim at involving society to change attitudes toward end of life and propose integrated care at the community level.

1 Aims of This Chapter

To describe the development of palliative care from the initial experience of the British Hospices in the 1960s toward the public health approach from the 1990s onwards.

2 Definitions and Concepts in a Historical Perspective

2.1 Short History of Early Modern Palliative Care

Modern palliative care was initiated at St Christopher's hospice in 1967 (The term "palliative care" was first used by Dr. Balfour Mount at the Royal Victoria Hospital in Montreal Canada in 1974. The English word "hospice" translated in French speaking Canada as poor house, and In Spanish it means "house for abandoned children") by Cicely Saunders, who created a conceptual frame to identify the multidimensional needs of patients and their families and the concept of treating "total pain," defined as the suffering that encompasses all of a person's physical, psychological, social, spiritual, and practical struggles. A new model of care was proposed to respond to those multidimensional needs with symptom control, emotional support, and communication as the main elements; the patient and family as the unit of care; and promoting quality of life as the main purpose of care. To provide this approach, the practice of a competent interdisciplinary team was developed with contributions from all disciplines. This concept was initially provided in British inpatient hospices, with strong commitment and community and social support, with great success focused mainly on the care of patients with terminal cancer and very limited prognosis in hospice units across the UK.

2.2 Diversification and Spread into Other Systems

Gradually by the 1970s, this model of care developed different types of organizations, such as

home care services (St Christopher's), outpatient clinics and day care (St Luke's), and support teams (Thelma Bates). Palliative care was also extended into other settings such as acute bed hospitals (Royal Victoria Montreal), cancer institutes (Royal Marsden), support teams (St Thomas'), and comprehensive networks, and to look after other types of patients (AIDS (Krakauer et al. 2007), motor neuron disease, organ failure, etc.). From the mid-1970s to the late 1980s, palliative care services were disseminated into many other countries (Europe (Luczak 1993; Kaasa et al. 2007; Mosoiu et al. 2007), and some low- and middle-income countries (Stjernswärd 2002; Davaasuren et al. 2007)), adapting gradually to their health care systems and cultures.

2.3 The Public Health Programs

In the 1990s, the concept of palliative care as a public health topic was developed at the WHO, and several regions and countries (Catalonia and Extremadura in Spain (Gómez-Batiste et al. 1992; Herrera et al. 2007); Alberta, Canada (Fainsinger et al. 2007); Kerala, India (Kumar 2007); and others) developed palliative care programs with systematic planning and aims of coverage and equity.

During the 1990s, theory, education, and research were extended in many countries, academic positions were established, pre-graduate and postgraduate medical and nursing training developed, training for other members of teams created, and the specialty of palliative medicine established. It is now a recognized specialization in at least 30 countries. Experience, evidence, organizational indicators and standards, and many clinical procedures were developed during this period and added to textbooks and specialized journals (Connor and Sepulveda 2014).

2.4 Palliative Care in the Twenty-First Century

More recently and related to the increased prevalence and mortality of people with all chronic conditions, the concept of a palliative care approach has been developed, alongside the need for timely identification of people with all types of advanced chronic conditions in all settings of care, using community and population perspectives (Gómez-Batiste et al. 2012). In May 2014, the World Health Assembly approved the resolution on palliative care, "Strengthening of palliative care as a component of comprehensive care throughout the life course," to promote the concepts of palliative care for all people in need, from the time of diagnosis, in all settings of care (World Health Assembly 2014). Tools to identify patients at these so-called first transitions have been developed, and the concept of a palliative care approach in all settings is currently being extended, with public health policies implemented to develop these approaches.

Palliative care has been adapted to growing needs, extending from the focus on the care of patients with terminal cancer in institutions and interventions based in prognosis toward a wider perspective that includes the concept of "life-limiting" illness and early intervention; the care of persons with all types of serious chronic diseases and conditions, not just cancer (Murray et al. 2005); and planning based on prevalence, rather than mortality (Table 1).

This change in perspective has radically altered the scope of palliative care and its provision, toward a public health, global, population, and community perspective, introducing the concepts of the palliative care approach in all settings (Stjernsward et al. 2007; Stjernsward and Gomez-Batiste 2008), in combination with the initial concept based on specialist services, in the context of universal health care coverage and access (World Health Organization 2015a, b).

2.5 Summary of Key Current Concepts in Palliative Care

As a result of all these transitions, palliative care can be operationalized by several definitions and concepts (Table 2).

Table 1 Conceptual transitions in palliative care in the twenty-first century. (From Gómez-Batiste et al. 2017c)

	From	Change to
Concepts	Terminal disease	Advanced progressive chronic disease
	Prognosis of weeks or months	Limited life prognosis
	Cancer	All chronic progressive illnesses and conditions
	Progressive course	Progressive course with frequent crises of needs and demands
	Mortality	Prevalence
Model of care and organization	Dichotomy curative or palliative	Synchronized, shared, combined care
	Specific or palliative treatment	Specific and palliative treatment as needed
	Prognosis as criteria for intervention of specialist services	Complexity/ severity as criteria
	Late identification in specialist services	Early identification in community and all settings
	Rigid one-directional intervention	Flexible intervention
	Passive role of patients	Advance care planning
	Fragmented care	Integrated care
Perspective for planning	Palliative care services	Palliative care approach everywhere
	Specialist services	Actions in all settings of health care
	Institutional approach	Community approach
	Services' approach	Population approach
	Individual service	Systems approach

2.5.1 Updated Definition of Palliative Care According to the WHO Ad Hoc Technical Advisory Group on Palliative and Long-Term Care (TAG) (Gómez-Batiste et al. 2017a)

Definition of Palliative Care. Palliative care is the comprehensive and integrated care of persons with advanced chronic conditions and limited life prognosis and their families.

Definition of Palliative Care. Palliative care is the prevention and relief of suffering of any kind – physical, psychological, social, or spiritual – experienced by adults and children living with serious, chronic, complex, and life-limiting health problems and the promotion of dignity, best quality of life, and adjustment to progressive illnesses, using best available evidence. It is a person-centered accompanying of patients and their families throughout the illness course, including at the end of life that optimizes quality of life, promotes human development and well-being, and maximizes dignity.

Palliative care is a basic human right and an essential component of comprehensive and integrated care for persons with serious chronic, complex, and life-limiting health problems that should be practiced by health and social care providers of many disciplines, as well as palliative care specialists, and should be provided in any health care setting, including patients' homes.

Key principles of palliative care provision include the concepts of **comprehensive care** (responding to all multidimensional needs of patients and families), **integrated care** (into all services and settings, with coordination of care), **quality** (responding with effectiveness and efficiency), and **universal access** (equity, coverage, integration into all levels of the health system). The **values** of compassion and commitment are needed to care for persons who are in a frail

Table 2 Levels of the palliative care model. (Adapted from Gómez-Batiste et al. 2017a)

Targets and time
Palliative care is needed by persons suffering from all types of serious complex/chronic or progressive conditions in all settings
It is applicable early and timely in the course of serious chronic, complex, or life-limiting health conditions/illness in conjunction with disease-modifying or potentially curative therapies, for people living with long-term sequela of diseases or treatments, and to neonates and children with serious congenital or acquired health problems
Model of care
Palliative care starts with a multidimensional assessment of physical, emotional, social, and spiritual needs, values, and preferences of patients and their families followed by a systematic approach to care
It focuses on the essential needs of patients and their families such as spirituality, dignity, autonomy, hope, growth and well-being, and key relationships
It uses ethical principles and advance care planning to identify patients' priorities and goals in the case of children, the developmental stage, for care at the end of life, and shared decision-making along the process
It never hastens nor postpones death intentionally
It provides family care and personalized bereavement support for adults and children as needed
It should be integrated into standard responses to humanitarian disasters
Model of organization
Palliative care should be integrated into every setting of the health care system and should be accessible by anyone in need
It should be a standard part of training for medical and nursing students, primary care providers, and health care workers
It should be practiced by medical doctors, nurses, social workers, spiritual supporters, community health workers, therapists, volunteers, and other allied health professionals and caregivers, with adequate training
It should use a three-level structure: palliative care approach in all settings, general basic palliative care, and specialist palliative care with adequate skills at each level
It is best practiced by a competent interdisciplinary team
It uses care management principles to prevent crises and assure integration and continuity of care along the different settings
It encourages active involvement in care giving by family members, communities, and community members
It has proven its effectiveness in addressing patients and families' needs, and efficiency in the provision of care
Much avoidable pain and suffering continues to exist at the end of life. In both resource-rich and resource-poor countries, fewer than 14% of people currently access any end-of-life palliative care. The only way that palliative or end-of-life care can reach the vast majority of people who need it in any country is by integrating its availability in all settings for care: hospitals, care homes, and the community

and vulnerable situation (Gómez-Batiste et al. 2017a).

By operating as an *approach*, palliative care can be provided:

1. To all patients with progressive life-threatening illnesses
2. At all times. Be introduced at diagnosis of a life-threatening illness, not just in the last weeks or days
3. In all dimensions. Help integrate physical, social, psychological, and spiritual, not just the physical
4. In all settings. Extending its reach to people in hospitals, care homes, and most strategically in the community
5. In all regions of the world not just in economically developed countries
6. To all family members. Support family caregivers, at all stages (before, at the time of death, and after)
7. To all ages: applied to children with life-threatening illnesses as much as adults
8. To all society: Promote a public discourse about living in the face of dying and maximizing individual and community assets to promote individual and community growth

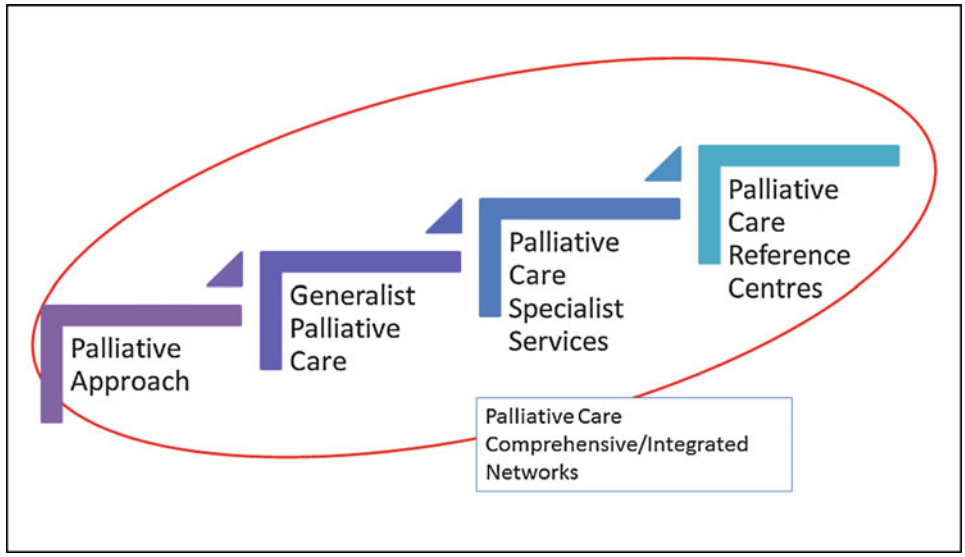

Fig. 1 Levels of palliative care complexity. (Adapted from Luyirika et al. 2017)

2.6 Models of Palliative Care Organization and Provision

2.6.1 Models of Organization

Persons with palliative care needs are cared for and attended to in all settings of the health care system (European Association for Palliative Care 2009). Palliative care can be provided in all of these settings with different levels of complexity and organization, according to the needs of patients and their families. In the context of universal coverage, all health care services need to address palliative care (Gomez-Batiste et al. 2008a).

2.6.2 Levels of Organization

Several levels of palliative care organization can be identified (Fig. 1). In the evolution of palliative care organization, there are also transitional models which can be the first actions prior to developing a specialist service.

2.6.3 Palliative Care Approach in All Settings of Care

Most health services attend to persons with advanced chronic conditions in different proportions and at different times in their disease process evolution. To assure quality of care and universal coverage for palliative care patients, the palliative care approach must be implemented in all services in the health system, especially primary care (for early identification and with a population perspective) and other services with highest proportions of palliative care needs.

The conventional medical services attending higher proportions of patients with palliative care needs are primary care, oncology, geriatrics, HIV/AIDS, and nursing or care homes. But all services have patients in need of different proportions of palliative care involvement.

There are measures that can be taken in any service to guarantee good quality of palliative care:

1. Establish and document a policy for palliative approach.
2. Identify patients in need using validated tools; these would identify needs, stratify the population at risk, and determine the prevalence.
3. Establish protocols, registers, and tools to assess patients' needs and respond to most common situations.
4. Train professionals and integrate palliative care training and review in the conventional training process (sessions, etc.).
5. Increase accessibility to continuing and emergency care, home care (if primary care services), and access for families in hospitals.
6. Identify the carers of patients and give them support and care, including bereavement support.

7. Increase team approach to jointly assess, plan, and implement care.
8. Establish links and criteria for intervention and access to palliative care specialized services in the area.
9. Evaluate results of the palliative approaches.

2.6.4 Primary Versus Specialist Palliative Care

With upwards of 61 million people needing palliative care annually and a very limited number of specialists, it is essential to the future of palliative care that primary care providers have the skills and knowledge to provide palliative care in their practices. An estimated two-thirds of those needing palliative care could be cared for without having to see a palliative care specialist (Connor and Sepulveda 2014). Additionally, specific times could be devoted to attend to those patients with higher needs. Some examples could be specific outpatient clinics in an oncology service for advanced patients, or specific times for bereavement or family support, specific home care visits, or programs of telephone support. In hospitals, patients with palliative care needs can be placed in designated areas (with individual bedrooms, etc.). Or in outpatient clinics, specific times and days can be devoted to these patients. This can also be the first stage before implementing a palliative care specialized service. To help differentiate primary and specialist palliative care, Quill and Abernathy (2013) distinguished the essential skill sets of each:

Primary Palliative Care

- Basic management of pain and symptoms
- Basic management of depression and anxiety
- Basic discussions about:
  - Prognosis
  - Goals of treatment
  - Suffering
  - Code status

Specialty Palliative Care

- Management of refractory pain or other symptoms
- Management of more complex depression, anxiety, grief, and existential distress
- Assistance with conflict resolution regarding goals of methods of treatment
  - Within families
  - Between staff and families
  - Among treatment teams
- Assistance in addressing cases of near futility

2.6.5 Specialized Palliative Care Service

A specialized palliative care service is a health care resource devoted specifically to attending to the complex needs of patients with progressive chronic life-limiting conditions and their families and to give support to other services. It is composed of a competent interdisciplinary team with advanced training and clearly identified by patients and other services.

There are different models and types of specialist services worldwide: Support teams (at home, hospitals, or comprehensive systems in territories), units, outpatient clinics, day hospitals, hospices, and comprehensive networks.

The key factors in the foundation of specialized services are leadership, training, institutional support, and the definition of the mission, values, aims, and internal and external consensus on the model of care and organization (Gómez-Batiste et al. 2008b). The most relevant aspect of the structure is a highly competent interdisciplinary team and the process/activities of PCS are well described (Table 3). The most relevant outcomes are the improvement of the quality of life of persons attended and their relatives. The most relevant criteria for success are the combination of good leadership, a competent team, institutional support, strategic planning, systematic quality assessment, and performance improvement. In most countries that recognize palliative care as a specialty, it is as a subspecialization.

Palliative care services can have diverse models of organization – according to needs of patients and the settings – including inpatient care (in specialist units or support to other services), outpatient clinics, home care, day care, phone/online support, continuing care, or emergency palliative care.

Palliative care services have demonstrated effectiveness, efficiency, and generate improvement of the quality of life of patients and their families (Gomez-Batiste et al. 2008c; World Health Organization 2016).

Table 3 Common activities (process) of palliative care specialist services. (Adapted from Gómez-Batiste and Connor 2017)

Care of patients: Interdisciplinary whole person assessment; care plan development; skilled medical, nursing, psychosocial, and spiritual intervention; follow-up and continuity of care
Care of families and bereavement follow-up
Ethical decision-making and advance care planning
Continuing care and case management
Liaison of resources
Support of other teams
Team work: meetings, roles, support, relations, climate
Registration and documentation
Evaluation of results
Internal training
External training to other services
Research and publications
Quality assessment and performance improvement
Volunteers
Advocacy
Links to society

In many countries, a "service" is an administrative concept, and can include different activities or resources (outpatients, inpatients units, support teams, etc.). In others, every activity will be named "service." A "palliative care team" is the specialized professional group providing these services or activities.

2.6.6 Elements of Specialized Palliative Care Services

- **Outpatient Clinics and Day Care**: Can be based in any setting of the health care system, and are crucial for early palliative care intervention and shared flexible models of cooperation (Gómez-Batiste and Connor 2017).
- **Mobile (or Support) Teams**: Interdisciplinary teams acting in support of other services. Can be based in Hospitals, Community/Home, or serve a district (acting in all or various settings).
  - The basic mobile team will include a medical doctor and at least one nurse, complemented by others, including psychosocial and spiritual professionals, therapy providers, and community health workers. Volunteers enhance the mobile team.
- **Inpatient Units** (called hospices in some locales with beds): Can be based in any setting of the health care system (hospitals, intermediate care centers, long-term nursing homes)
  - Adapted to the organization of health care inpatient services
  - Must respect privacy, and allow presence and access of families
  - Units may specialize in caring for different types of patients (cancer, organ failure, geriatric, children, AIDS, dementia, etc. or be mixed)
  - Can be based in acute, mid-term, or long-term settings or as individual stand-alone facilities
  - Size and resources vary according to country and setting, regulations, and standards
  - Processes and model of care are common to all services
  - Outputs and costs (mean age, length of stay, mortality) will be different according to types of patients.
- **Hospices**: Organizations exclusively devoted to care of advanced/end-of-life care patients, and can include all types of activities including home and inpatient care. Generally owned by NGOs but can be part of any system. The British Hospices were the first organizations implementing modern palliative care in the 1960s following the leadership/model of St Christopher's Hospice.
- **Comprehensive/Integrated Networks:** Organizations of **specialized** palliative care, serving a population and acting in all settings of this scenario (hospitals, intermediate settings, nursing homes, community) in an **integrated** way. In small districts, a **specialized** support team can be the only **specialized** resource needed to care in all settings. In districts with different providers, a common care pathway could be the formula for integrated care. In metropolitan districts, a complex integrated model can include various levels of complexity.

3 Population/Territorial Palliative Care: Integrated Models

The population and territorial perspectives are the key elements of a public health approach. The aim is to build an integrated model, bringing together all services involved.

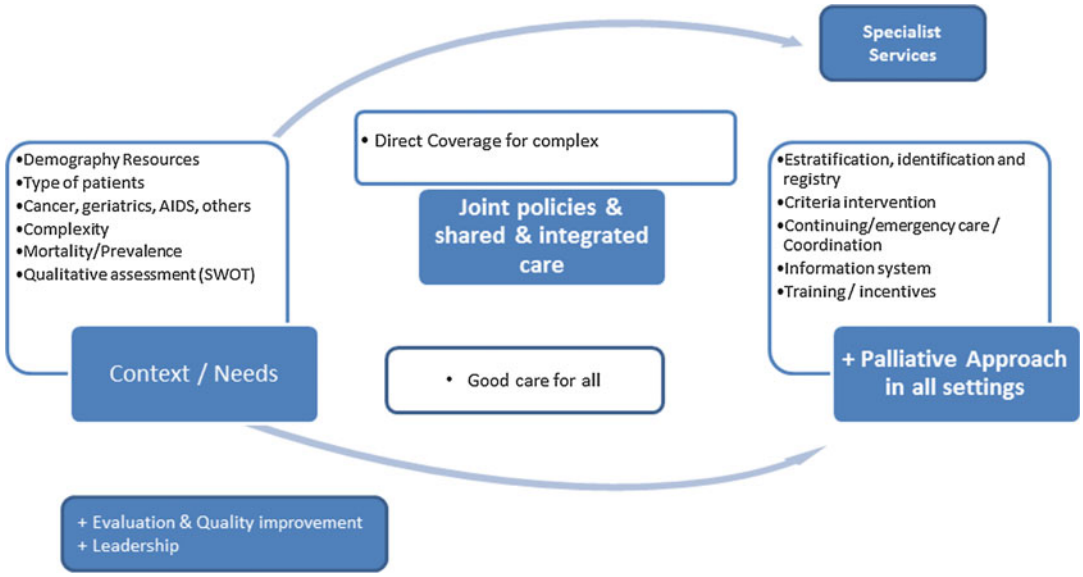

Fig. 2 Population and territorial approach for integrated palliative care. (Adapted from Luyirika et al. 2017)

A policy for a territory must start with an assessment of needs and context, mixing quantitative and qualitative methods. The aging proportion is a key factor. Once done, the next step might be to stratify the population, identifying the different groups that could be in need (McNamara et al. 2006; Murtagh et al. 2014). There are several tools to identify the people in need (Maas et al. 2013; Gómez-Batiste et al. 2017b). The most frequent figures in our context (21% of population over 65 years old) are that 4% of the population have complex chronic conditions, and may need intermittent and gradual palliative care interventions, the 1.5% are people with advanced/progressive chronic conditions and a limited life prognosis (Gómez-Batiste et al. 2014), and 0.4% have added social vulnerability (isolation, poverty, limitation of access, etc.). The next step is to define the roles of services, the pathways for patients (specially focused in transitions), and combined with an information system, incentives, training for professionals, and quality improvement. The most relevant factors for success are leadership and a funding model which incentives integrated over fragmented care (Fig. 2).

Policies for these different populations at risk must include the aims of care, the clinical issues, the ethical issues, and organizational issues (Fig. 3).

4 The Public Health National Policies and Practices

1. Establish a formal national or regional policy with participation of patients and all stakeholders (professionals, managers, policymakers, funders)
2. Determine (or estimate) the population- and setting-specific mortality and prevalence and needs assessment
3. Elaborate, agree, and validate an adapted tool for the identification of those in need of PC
4. Establish protocols to identify these patients in existing services
5. Establish clinical protocols and guidelines to assure good comprehensive, person-centered care for the identified patients
6. Identify the specific training needs, train professionals, and insert palliative care training in all settings
7. Promote organizational changes in primary care, specialized palliative care service, conventional services, and integrated care across all settings in districts
8. Identify and address the specific ethical challenges

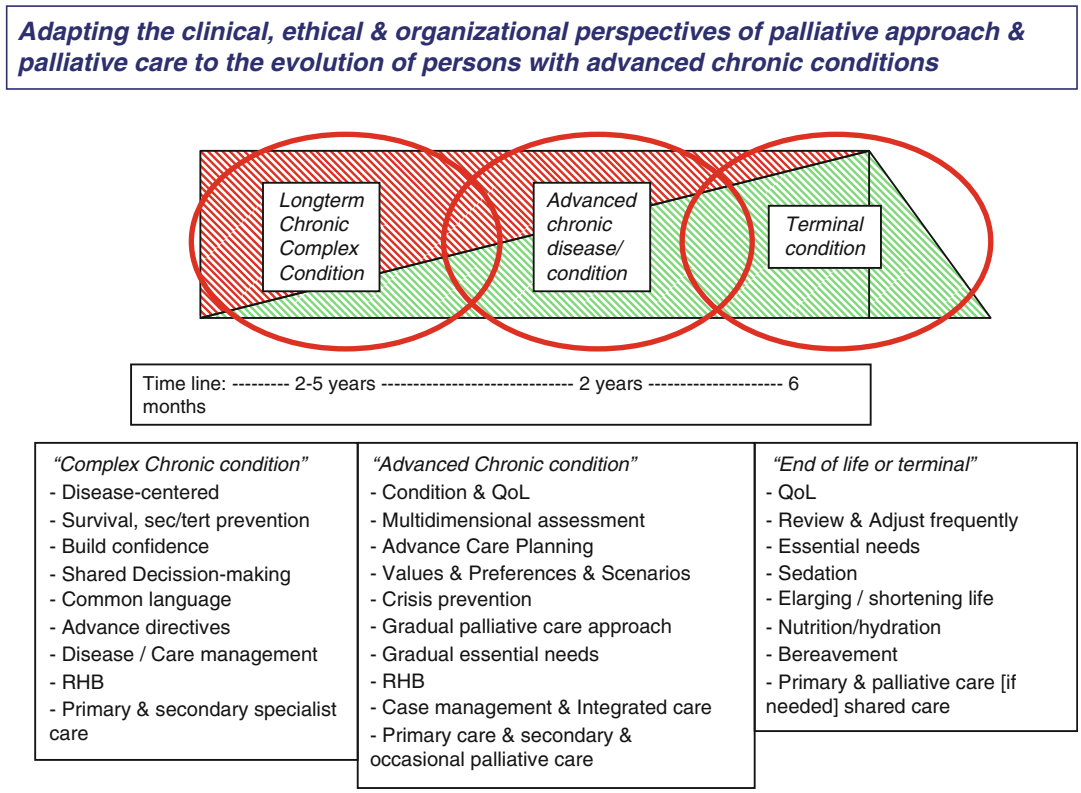

Fig. 3 Clinical, ethical, and organizational aims in different phases of evolution of chronic conditions. (Adapted from Gómez-Batiste et al. 2017a)

9. Insert palliative approach in all policies for chronic conditions (cancer, geriatrics, dementia, HIV, other, etc.)
10. Establish and monitorize indicators and standards of care and implementation plans and generate research evidence

Most of palliative care plans must be adapted to the extension of palliative care to all patients, at all phases, in all services. We can propose a recommendation to build up **National or Regional Programs**.

5 The Social Involvement: Compassionate Communities

In recent years, a new approach has been developed, as a necessary complement of the public health perspective. The programs of compassionate communities propose a new perspective of social involvement, empowering society and its organizations to participate in the change of culture and vision about end of life and in the design and evaluation of services (Kellehear 2013). It is a very interesting approach, which opens the scope of palliative care toward end of life and improves the so far paternalistic relationship of palliative care networks and services with society, frequently focused only in volunteers and funding (Abel et al. 2013; Abel and Kellehear 2016). The most relevant aims of these programs are to change the cultural and social approaches to end of life and dying, and also to provide integrated systems of care, especially for people combining a limited life prognosis and social vulnerability.

6 Conclusions and Summary

Palliative care has evolved since its modern foundation in the 1960s from the *British Hospice model*, from where the comprehensive model of

care (responding to all dimensions of needs of patients) and microorganization (as the team approach) were built. From this context, palliative care has been extended into the settings of the health care systems, with different organizational *models of teams and services*. A more developed model is *the comprehensive and integrated network in territories*. The other key evolutions moved from the institutional and end-stage care of terminal cancer patients to the timely, community- and population-based perspective and links to the chronic care models. The other key element has been the design and implementation of public health models as national or regional palliative care programs, and the policy proposed by WHO in the World Health Assembly Resolution WHA67.19: "*Strengthening of palliative care as a component of comprehensive care throughout the life course*." More recently, there are new initiatives of *compassionate communities* with the aim of further involving society in the cultural changes toward end of life and propose integrated care at the community level (Kellehear 2015).

Palliative care is a key element of any health care system, and access to good palliative care is a basic human right (Human Rights Watch 2009).

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Policies on Palliative Care in Different Parts of the World

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_7

Abstract

The WHO public health strategy for palliative care requires enabling policy as one of its three key pillars (alongside drug availability and education) (Department of Health 2003). A major recent driver of palliative care as a core component of health systems around the world has been the World Health Assembly Resolution on Palliative Care (Department of Health 2008a). Expansion of access to appropriate, high-quality of palliative care for adults and children irrespective of country will require the emerging field of global health palliative care research (Department of Health 2008b) to inform the WHO public health strategy. In recent years, we have also greatly increased the evidence base which underpins and supports appropriate policy (Economist Intelligence Unit 2015). In this chapter, we draw on recent policy developments from different parts of the world: from the birthplace of the modern palliative care movement, the UK; from South Africa, which has promoted a strong model of advocacy, provider networks, and academia; from Southern and Eastern Africa, which have advanced policy and provision rapidly in recent years; and lastly from the field of pediatric palliative care, which has specific policy considerations.

1 Palliative Care Policy in the UK

1.1 Postwar Britain

The UK National Health Service was developed in 1948 with the aim of bringing good health care to all from "cradle to grave" (Aneurin Bevan). In this economically challenging postwar period, much of the focus initially, within the NHS, was on delivering care to those living with acute and chronic conditions. Prior to this time, families and religious communities were central to the delivery of care to the dying. It was not until the 1950s, with the work of Dame Cicely Saunders, that the modern hospice movement began.

1.2 The Hospice Movement in England

In 1967 Dame Cicely Saunders founded St Christopher's Hospice in South London. Saunders' compassionate and holistic approach to care recognized the needs of the individual and revolutionized care delivery for the dying – "*y*ou matter because you are you, and you matter to the end of your life" (Dame Cicely Saunders). Subsequently, more charitable hospices across the UK were created to care for dying people. Therefore, unlike other specialties

within medicine, palliative care developed largely outside of NHS settings.

In the 1990s, two organizations were formed "The National Council for Palliative Care" (formerly "The National Council for Hospice and Specialist Palliative Care Services," a single body to speak on behalf of palliative care service providers) and "Hospice UK" (formerly "Help the Hospices" the national voice of hospice care) with the aims to improve end of life care for all and to extend the breadth and reach of hospice care, respectively. However, government reports in subsequent years identified variations in quality of end of life care, particularly in areas of social deprivation and for those dying from nonmalignant conditions. In response to these reports, there was a policy drive to improve care for people approaching the end of life in England, Northern Ireland, Scotland, and Wales.

1.3 Policies, Programs, and Strategies

In 2003 a white paper was published by the Department of Health (Building on the Best Department of Health 2003) which set out to improve choice within the NHS. This included a commitment to spend £12m over 3 years to improve end of life care (The End of Life Care Programme 2004–2007), through the implementation of tools and methods beyond specialist palliative care, including the "Liverpool Care Pathway for the Dying Patient," which had been developed in hospice settings and was translated for hospitals; the "Gold Standards Framework" for general practitioners to identify and support those with palliative care needs; and initiatives to support care homes in the delivery of end of life care.

In 2008, a review of the NHS led by Lord Darzi (High Quality Care for All Department of Health 2008a) recognized a need to improve quality of care, as evidenced through patient outcomes and experiences, safety, and effectiveness. Within the review, end of life care was identified as one of the eight priority areas. That same year, the "End of Life Care Strategy," (Department of Health 2008b) the first major end of life care policy, was launched. This strategy recognized the distancing of death from British society, with the majority of individuals dying in hospital and many people failing to consider in advance their preferences and priorities for end of life and therefore not dying in the place they would have chosen nor receiving the quality care they needed. The strategy communicated a need for a whole system approach to improving end of life care with improvements in identification of those approaching the end of life, care planning and discussions about preferences and priorities, coordination of care, high-quality care wherever it is delivered, careful management of the last days, and support for carers throughout the illness and into bereavement.

Another initiative from the "End of Life Care Strategy" was "Dying Matters," launched in 2009, which focuses on changing attitudes at a population level by actively encouraging people to consider their preferences and priorities for end of life, before the end of life. Within the "Dying Matters" initiative, there is also a campaign aimed at general practitioners called "Find your 1%," which encourages GPs to identify those patients who may be in the last year of life (estimates suggest that is 1% of the population), and proactively start discussions about preferences and priorities.

1.4 Highs and Lows

In both 2010 and 2015, the UK was voted as number 1 in the "Quality of Death Index" (Economist Intelligence Unit 2015), which has often been attributed to the strong links between palliative care in the NHS and Hospice settings, alongside meaningful community engagement. However, this ranking was shaken in 2013 when reported failings in the implementation

and use of the "Liverpool Care Pathway for the Dying Patient (LCP)" resulted in an independent review by Baroness Neuberger (More Care, Less Pathway Department of Health 2013) and its subsequent withdrawal. This intervention which had been developed from best practice in the hospice setting, the model for the development of palliative care as a specialty, was withdrawn due to failings in implementation and use but also fundamentally due to the lack of evidence to underpin its use. For many, in the immediate aftermath of the withdrawal of the LCP, there were a resultant vacuum and fears around how to meet the needs of those approaching the end of life. The review however also recognized the need to return to the fundamental tenet of palliative care – "You matter because you are you" (Dame Cicely Saunders) – focusing on the individual and their needs through the development of individualized care plans.

In response to the review, an alliance of 21 national organizations was formed to give direction to, and focus upon, improving the care of people who are dying and their families. In 2014 they published "One Chance to Get it Right" (Leadership Alliance for the Care of Dying People 2014) which included five priorities for improving care for people who are dying: identifying that a person is dying, communicating sensitively with the patient and those close to them, making a holistic assessment of their needs (physical, psychological, spiritual, and social), respecting their wishes, and establishing an individualized care plan, including place of care and death.

1.5 Ambitions and Commitments

The "Ambitions for Palliative and End of Life Care"(National Palliative and End of Life Care Partnership 2015) published by the National Palliative and End of Life Care Partnership in 2015 took forward the focus on individualized care and whole system and community approach. They identified six key ambitions to achieve quality end of life care: each person is seen as an individual, each person gets fair access to care, maximizing comfort and well-being, care is coordinated, all staff are prepared to care, and each community is prepared to help. Aligned with this was the new national commitment on end of life care (Our Commitment to you for end of life care Department of Health 2016), published by the Department of Health in 2016, which focused not only on care that individuals deserve to receive, irrespective of care setting, but also on the steps to achieve that through improving care quality and increasing accountability and transparency, leadership and identification and dissemination of innovation, and working closely with voluntary and community services. This renewed focus on learning within and across organizations and care settings will be further strengthened by the forthcoming merger of the National Council for Palliative Care and Hospice UK, to provide a clear single vision for high-quality end of life care in England for the future.

2 Palliative Care Policy in South Africa

Palliative care has not been articulated in South African government policy to date. However, in 2014, South Africa was part of the WHO executive committee that sponsored the WHA resolution 67.19 on palliative care which was adopted unanimously and to acclaim by all member states. The SA Minister of Health, Dr. Aaron Motsoaledi, acknowledged the responsibility of the Department of Health to ensure the implementation of the WHA resolution in South Africa. To this end, he appointed a National Steering Committee for Palliative Care and provided clear terms of reference to guide the work of the committee. He charged the committee to create "a revolution in health care through palliative care."(National Steering Committee on Palliative Care 2017) The first action of the steering committee has been to

develop a National Policy Framework and Strategy for Palliative Care.

2.1 Background

Palliative care in South Africa has largely been provided by nongovernmental organizations since the first hospices were established in the 1980s. These hospices are charity organizations and raise funds for the provision of palliative care from the general public, corporates, and trusts and, as they are outside of the formal health-care sector, have received little funding from the government. However, with the recognition of palliative care as part of Universal Health Coverage (World Health Organisation) and evidence of the benefit of palliative care for patients and families, increasing attention has been paid to the importance of integrating palliative care into the South African health system. The South African government has undertaken an ambitious project to establish a National Health Insurance (NHI) (Department of Health Republic of South Africa 2015) to ensure that everyone in South Africa has access to quality health care with financial risk protection so that the cost of care does not put people at risk of financial hardship. Palliative care is written into the NHI as an essential component of primary health care.

There have been a number of champions for palliative care that have influenced the efforts to develop a National Policy Framework and Strategy for Palliative Care. The Hospice Palliative Care Association (HPCA) of South Africa was established in 1987 by 15 hospices in an effort to share best practice in palliative care, to support the work done by hospices, to develop standardized training courses in palliative care, and to advocate for the provision of palliative care. The care provided to hospice patients has been the most effective advocacy for palliative care, but as this care is provided respecting people privacy and ensuring confidentiality, it is often only family members and friends experiencing this care that understand the importance of palliative care. To date, HPCA and member hospices have been the leading providers of palliative care education. In 1989, HPCA developed the Short Course in Palliative Nursing, a year's course to train nurses in palliative care at the request of the South African Nursing Council. This course is presented at ten hospices in different provinces in South Africa. The HPCA Palliative Care Institute has 24 different courses in palliative care including an e-learning course as an Introduction to Palliative Care to assist health-care professionals to develop basic knowledge and skills in the discipline.

The other key palliative care service is the Gauteng Centre of Excellence for Palliative Care at Chris Hani Baragwanath Academic Hospital in Soweto, Wits Centre for Palliative Care, within the University Of Witwatersrand School Of Clinical Medicine and provides undergraduate and postgraduate training. Palliative care was initially provided to relief suffering among cancer patients within the Department of Internal Medicine as early as 1999. The service was later complemented by the N'doro Project (Hongoro and Dinat 2011), funded by Irish Aid and DFID, which responded to the high mortality rate due to HIV before the South African government agreed to the rollout of antiretroviral treatment. In 2007, Gauteng Department of Health established the Gauteng Centre of Excellence for Palliative Care with 18 fully funded posts and subsidy for staff transport to conduct home visit. The leadership provided by Wits Palliative Care in the formal health sector has been a strong influence in the drive to integrate palliative care into the health system. The Centre has developed a strong education and research focus to guide this integration.

In 2001, the HPCA sponsored the development of postgraduate training in palliative medicine at the University of Cape Town through donor funding from the Diana Princes of Wales Memorial Fund (Ens et al. 2011). This was the first and for many years the only postgraduate training in palliative medicine on the continent of Africa, and UCT has been influential in the development of

palliative care champions and leaders in many African countries. UCT was also undergoing a review of the undergraduate medical curriculum in 2001, and this provided an opportunity to integrate palliative medicine into the family medicine training curriculum at UCT.

HPCA established a pediatric palliative care portfolio and through donor funding developed a curriculum to teach children's palliative care and to support member hospices in establishing children's palliative care programs. One of the early children's hospices is Sunflower Hospice established in Bloemfontein in 1998. The founder of the hospice, Joan Marston, still working as a volunteer, went on to lead the HPCA pediatric palliative care portfolio and was instrumental in establishing the International Children's Palliative Care Network (ICPCN) and was the first CEO of ICPCN. The Bigshoes Foundation (BSF) started the first hospital-based pediatric palliative care program at the Chris Hani Baragwanath hospital in Soweto in 2006 and expanded to Durban in 2008 and to Cape Town in 2009. The BSF developed a multidisciplinary pediatric palliative care consultation model that worked closely with the primary care teams providing care and support to hospitalized children that also ensured continuation of care through liaison with community-based services.

Substantial international funding for palliative care development was received by HPCA in 2004 which allowed us to scale up development and the mentorship programme to establish additional hospice services in South Africa. The HPCA palliative care standards were further developed with guidance from the Council for Health Standards Accreditation of Southern Africa (Cohsasa). Emerging home-based care organizations were assessed in a stepwise fashion to become members of HPCA following a development plan with experienced palliative care staff providing training and mentorship to assist in meeting the goals of the development plan. Hospices were awarded stars according to their level of development, and HPCA engaged Cohsasa to conduct a survey of hospice compliance with standards and awarded the hospice five stars upon accreditation through Cohsasa.

In 2009, HPCA signed a memorandum of understanding with the Department of Correctional Services to provide training and mentorship to staff in correctional services and to inmates. This followed screening a television documentary "on the conditions of offenders in South African prisons. Harrowing footage showed a terminally ill offender suffering excruciating pain as he lay dying." A pilot project linked Highway Hospice in Durban with Durban Westville prison to ensure palliative care would be provided in correctional services facilities as well as a referral process for inmates who were released having served their sentence or having received compassionate parole (Sithole and Dempers 2010). The partnership with HPCA and DCS has led to a training course in spiritual care developed as a partnership between prison chaplains and hospice spiritual counselors.

Key events in the development of the National Palliative Care Policy include the following:

A meeting of African and international leaders in palliative care funded by DPWMF in Cape Town in 2002 resulting in the Cape Town declaration and the establishment of a steering committee to develop a pan-African organization which was to become the African Palliative Care Association (Mpanga Sebuyira et al. 2003).

In 2009, HPCA established the Alliance for Access to Palliative Care, a group of individuals from different organizations including the National Department of Health and the National Department of Correctional Services, the Gauteng Centre of Excellence for Palliative Care, and other academic institutions. The involvement of government assisted in bringing the need to integrate palliative care into government strategy to the fore and in developing champions for palliative care within government. The academic institutions have identified the need for palliative care to be integrated into undergraduate training for health professional and social workers.

At the recent palliative care conference held in Kampala and co-hosted by the African Palliative Care Association and the Worldwide Palliative Care Alliance African, health ministers attended a preconference meeting which resulted in the Kampala Declaration on Palliative Care (African

Palliative Care Association 2016). "African Ministers of Health and representatives of country delegations at the 2nd Session of the African Ministers of Health on Palliative Care" stated their commitment to (1) "invest in essential technologies that contribute to quality palliative care services"; and (2) to "provide leadership at the highest level to ensure the implementation of the WHA 67.19 Resolution on "strengthening palliative care as a component of comprehensive care throughout the life course in Africa."

2.2 The National Steering Committee for Palliative Care

Seven task teams were established to guide the work of the committee. These are task teams on policy, education and training, drug availability, vulnerable persons, families and careworkers, funding, and ethics. The Policy Task Team and Steering Committee initially focused on developing a draft Policy Framework and Strategy for Palliative Care and, together with the Funding Task Team's work on costing the Policy, presented the policy document to the Technical Committee of the National Health Council (TechNHC) in February 2017. The TechNHC recommended the policy for approval at the next meeting of the National Health Council. The next actions for the Policy Task team are to decide on models of care and clinical pathways and to review and update clinical guidelines for palliative care.

The Education and Training Task Team conducted research into palliative care curricula and internationally identified core competencies for different health-care practitioners. A survey of palliative care training for undergraduate medical students was carried out across the eight medical schools with seven of these responding to the survey which provides the foundation for development of recommendations for standardized training in the undergraduate curriculum. The initial survey has been adapted for schools of social work, nursing, and rehabilitation sciences. In addition, the HPCA e-learning course Introduction to Palliative Care has been identified as a method of training practitioners already qualified so that they can enroll on the course in order to develop the basic knowledge and skills in palliative care equivalent to the level of graduate students.

The Task Team for Vulnerable Persons has developed a statement regarding access to palliative care for people with disabilities, children, older persons, refugees and asylum seekers, inmates of correctional services facilities, and residents of institutions ranging from TB hospitals to children's homes and care homes for the elderly.

The Drug Availability Task Team has drafted a position paper on the availability of essential palliative care medicines and has submitted this to the Department of Health. The task team has also reviewed the essential medicines lists (EMLs) and made recommendations to the National EML committee. Building on years of lobbying for nurse prescribing of medicines including opioid medication, the task team has made representation to the Director-General (DG) of Health to license nurses with appropriate training to prescribe opioids. Some of the barriers to nurse prescribing have been the Pharmacy Council not permitting pharmacists to dispense a nurse's prescription and delays in the South African Nursing Council's review of the SA Nursing Act which intends to revise the scope of practice of nurses. The DG has advised that hospice- and palliative care-trained nurses can be licensed under the current regulation 56a of the Nursing Act and hospices have written to the DG for this authority.

The Task Team for Supporting Families and Careworkers has drafted a statement on the need for caring for carers and spiritual care for families and all categories of health-care workers. The task team will update the guidelines for caring for carers and develop spiritual care guidelines for the health-care setting. The Ethics Task Team has drafted a paper on ethical issues in care of patients with advanced illness and a position statement on euthanasia and assisted suicide. The paper states that euthanasia is not a clinical practice and that the doctor's duty is to heal where possible, to relieve suffering, and to protect the best interests of their patients and not to hasten death.

The draft Policy Framework and Strategy for Palliative Care identifies the related South African policies and legislation that will enable South Africa to integrate palliative care in to the public health-care system and advocates that palliative care be available from conception to death across a continuum of care. While the policy acknowledges the importance of specialist-level palliative care services in tertiary institutions, it recognizes that the majority of services will need to be provided at district level within community settings. For this reason, it recognizes the need to include palliative care as an integrated, patient-centered, and health system-based service within the current program to reengineer primary health care in South Africa (Barron and Pillay).

The policy framework is based on three overarching goals that include health systems strengthening, ensuring adequate numbers of health-care providers trained in palliative care and effective governance and leadership to support the implementation of the policy. A monitoring and evaluation framework with indicators for each goal is provided as well as a suggested implementation plan for South Africa's provinces.

While the steering committee assisting with the development of the palliative care policy for South Africa realizes that this integration will not be achieved overnight, it truly believes that a progressive realization of peoples' right to palliative care has the potential to revolutionize health care in the country.

3 Palliative Care Policies in East and Southern Africa

3.1 Introduction

One of the highest commitments of any government is to set out what it tends to do in form of a policy. Palliative care is a relatively new discipline and is not fully integrated in many of the health systems in Africa. Getting governments to develop policies that embrace the introduction, funding, and implementation of palliative care as a health service delivery component and as a discipline taught to health workers is a key issue.

3.2 Palliative Care in Disease-Specific Policies

As the HIV epidemic became a major disease in sub-Saharan Africa and before antiretroviral medications became available, the health systems were inundated with several patients who needed palliative care. This caused many health service providers especially in the nongovernment sector to respond with palliative care programs for patients who had developed AIDS. Eventually governments and funders of HIV programs picked best practices and also started taking it up. Subsequent development of national HIV strategic plans and implementation plans included palliative care (Harding and Higginson 2014). As a result, a number of countries have palliative care that included a number of disease-specific policies such as HIV and cancer.

In Kenya palliative care was included in the Kenya National AIDS Strategic Plan 2005/2006–2009/2010 under the objective on improving the quality of life; the government included a budget of 830 million Kenya Shillings to cover the service for AIDS patients (United Nations Educational Scientific and Cultural Organisation). In addition when Kenya developed its National Cancer Control Plan of 2011–2016, palliative was a major component of the planned national cancer response. Other included in the national HIV and cancer-related guidelines and policies (Republic of Kenya Ministry of Public Health and Sanitation and Ministry of Medical Services 2011). These policies recognize the role of palliative care as part of the HIV and cancer care plans throughout the disease trajectory. In the Uganda National HIV Strategic Plan 2007/2008–2011/2012, palliative care was stated as a major component of care and treatment under objective 7 on increasing access to prevention and treatment of opportunistic infections, including tuberculosis (Uganda AIDS Commission). In addition palliative care is also

recognized and is mentioned in the Uganda Cancer Institute Act of 2016 which gives the Uganda Cancer Institute autonomy. The Uganda National Cervical Cancer Control plan also has palliative care as a specific and important part of the national response (Ministry of Health Uganda 2010).

In the United Republic of Tanzania National Cancer Control Strategy of 2013–2022, palliative care is a key component of the objective 3 focusing on care and treatment (The United Republic of Tanzania Ministry of Health and Social Welfare). The government commits to offer the best care they can afford to all patients with cancer and who are in need of it.

In Zimbabwe, palliative care is part of the Zimbabwe National HIV and AIDS Strategic Plan of 2015–2018 and is included in their national response and continuum of care for people with HIV/AIDS under community care and support (Government of Zimbabwe). The Zimbabwe National Cancer Control Strategy 2013–2017 includes palliative care as part of the planned continuum of services including cancer prevention, early detection (early diagnosis and screening), diagnosis and treatment, palliative care and rehabilitation, and cancer surveillance and research (Zimbabwe Ministry of Health and Child Welfare). In the Malawi National HIV and AIDS Strategic Plan (2011–2016) under strategy 2.5, palliative care is a major strategic action which is aimed at to improving access to psychosocial support and quality palliative care for terminally ill patients (National AIDS Commission Malawi 2011).

In The Kingdom of Swaziland, the Second National Multisectoral HIV and AIDS Strategic Plan 2006–2008 under the thematic area on care, support, and treatment, palliative care was a key component (The Government of the Kingdom of Swaziland 2006). All these disease-specific plans and policies have resulted into a significant investment in palliative care in those countries that have resulted into development of national palliative care associations and or palliative care desks at ministries of health being instituted.

In addition using the disease-specific resources, training of palliative care providers has happened in all these countries, and they have also set a stage for the development of stand-alone national palliative care policies in seven of these countries.

3.3 Palliative Care in National Health Sector Plans

Within the Ugandan National Health Sector Plan 2015/2016–2019/2020, the seven priorities include strengthening the national health system including governance; disease prevention, mitigation, and control; health education, promotion, and control; curative services; rehabilitation, and palliative care services (The Republic of Uganda Ministry of Health 2015). This puts palliative care among the key priorities for the health sector in Uganda.

3.4 National Stand-Alone Palliative Care Policies

From 2011, the African Palliative Care Association working with its partners and ministries of health in Africa has supported eight countries to develop stand-alone palliative care policies. These countries are Malawi, Tanzania, Rwanda, Swaziland, Zimbabwe, Botswana, Mozambique, and Uganda. Seven of these countries had already approved and ratified the policies by beginning of 2017 while Uganda is yet to finalize (Luyirika et al. 2016). These policies cover most aspects of palliative care in those specific countries.

3.5 Other Legal Frameworks

In some of the countries, some other key legal frameworks have been established to support palliative care implementation. In 2004 Uganda introduced a statute that allowed appropriately trained nurses and clinical officers to prescribe oral liquid morphine as a way of improving access to opioids among palliative care patients. This statute has resulted in more patients accessing oral morphine in areas where they would not

have had access because previously it was only doctors who were allowed to prescribe and yet they are few (Government of Uganda 2004).

3.6 The Impact of the Palliative Care-Related Policies on Health Systems and Palliative Care Implementation in African Countries

As a result of the different policy frameworks developed in several African countries, the health systems are being impacted positively.

Human resources are being developed, and several palliative care courses are running on the continent including Bachelor of Science in Palliative Care Degree and Diploma in Palliative Care for Africa (Distance Learning), Hospice Africa Uganda; Clinical Palliative Care Course for nurses and clinical officers at Hospice Africa Uganda; Diploma in Palliative Care at Nairobi Hospice in collaboration with Oxford Brookes University (UK); MPhil in Palliative Medicine, University of Cape Town (African palliative Care Association 2017); as well as a pediatric palliative care diploma at Mildmay Uganda. This has resulted into the development of the initial team of specialist palliative care providers in Africa who are running programs.

Palliative care service delivery and coverage is also improving given the improving policy framework and there a number of providing institutions. Global Atlas of Palliative Care at the End of Life of 2014 also highlights the improvement with one of the countries in the region approaching full palliative care integration into the health system (Connor and Sepulveda Bermedo 2014).

Medicines and essential technologies are another aspect of palliative care delivery that is improving on the continent though from a very low base. Increasing access to opioids in Africa has been documented by the UICC with countries such as Malawi, Uganda, and Ethiopia using different models to do this (UICC).

Financing palliative care is a major challenge on the continent, but with increasing coverage in various policies in countries, some degree of government commitment is emerging and is augmented by donor support especially through nongovernmental palliative care providers. In a thesis by Amandua Jacinta, most of the palliative care providers in Uganda drew their funding largely from donors, self-generated funds with some government support (Amandua 2013).

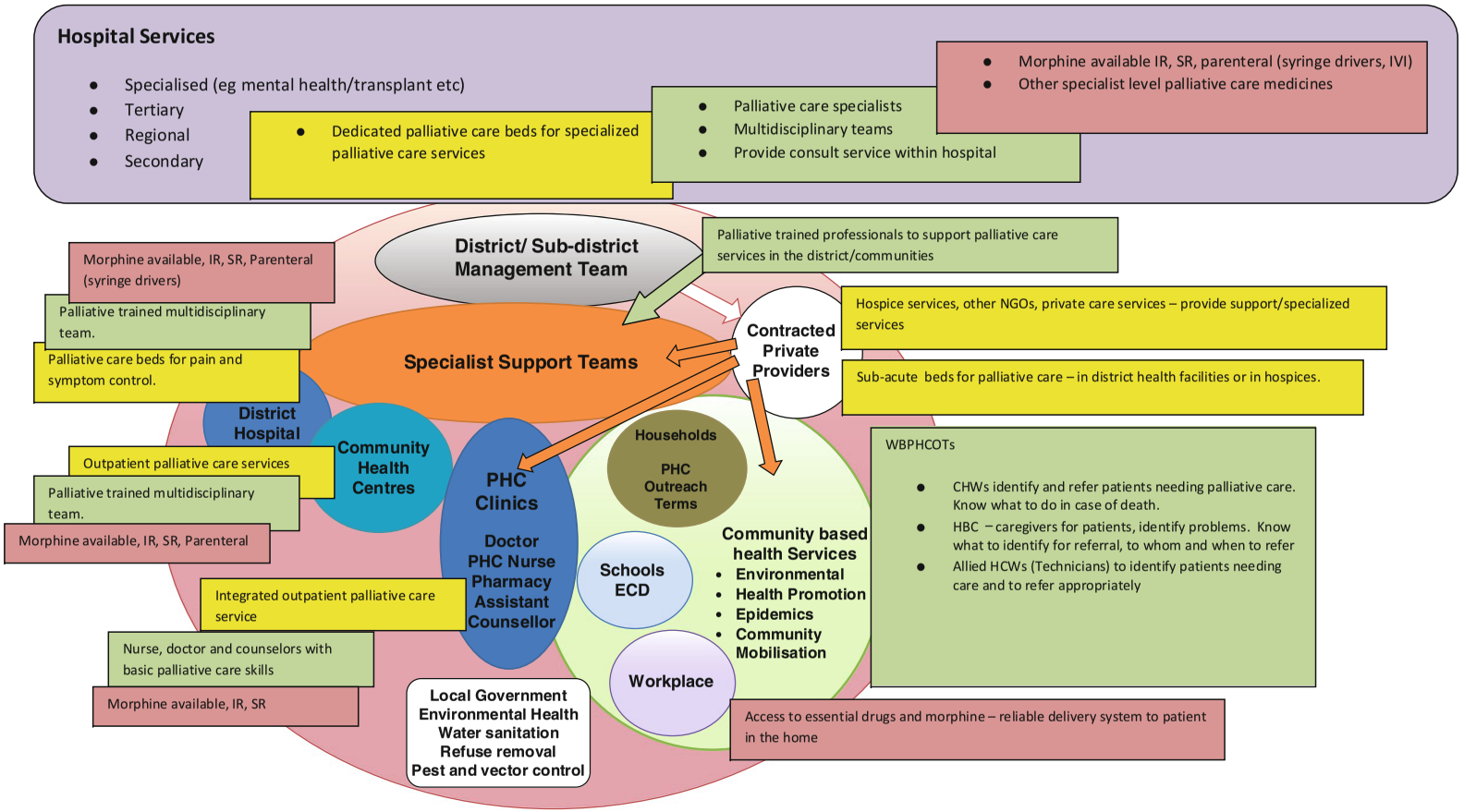
Health information including data collection and use is a key aspect of the palliative care service development. In Africa this is still a major issue that policies have not yet fully impacted.

Leadership and governance have been shown by some of the African governments that have developed policies that include palliative care.

4 Pediatric Palliative Care Policy

4.1 Context

The need for children's palliative care globally has until recently gone largely unrecognized, with the development of palliative care services for adults developing at a greater rate than that for children. Recently it was estimated that there are over 21 million children worldwide who would benefit from palliative care provision with more than 8 million children requiring specialist palliative care services (Connor et al. 2017). However, development has not kept pace with the need, with some countries, such as South Africa, where palliative care is relatively well developed, providing palliative care for less than 5% of those children requiring care (Connor et al. 2014). A systematic review of the provision of children's palliative care around the world completed in 2011, noted that 65.6% of countries globally had no known children's palliative care activity, with only 5.7% having provision that was reaching mainstream providers (Knapp et al. 2011). While developments have occurred in the past 10 years, some of which can be seen in the WHPCA global atlas for the provision of palliative care at the end of life (Connor and Sepulveda Bermedo 2014), there is still a long way to go for provision to meet



(DHS Strategy 2015 with modification to include integrated palliative care services at hospital and district levels)

the needs of children with life-limiting and life-threatening conditions (Downing et al. 2016, 2014a).

Approximately one quarter of the global population is under the age of 15, i.e., 26%, with that figure rising to around 40% in low-income countries (2014 World Population Data Sheet 2014). Challenges to the provision of children's palliative care will vary from country to country and include the following:

- The large number of children in some countries requiring palliative care due to the prevalence of conditions such as HIV, e.g., in Zimbabwe 113.3 children per 10,000 need palliative care (Connor et al. 2017), and conversely the relatively small numbers requiring palliative care in other countries, e.g., in Australia 21.0 children per 10,000 need palliative care
- Late presentation and underdiagnosis in constrained health-care systems, many of which have limited access to curative treatment
- A lack of access and availability of essential medicines for use in palliative care such as analgesics, with a lack of pediatric formulations
- A lack of education and therefore knowledge and skills for the provision of children's palliative care, thus leading to a lack of confidence among health workers and the need for a change in attitude toward the provision of children's palliative care
- A lack of specialist children's palliative care health professionals to provide not only clinical care but education and training and leadership
- Financial burden and inability to pay for care and treatment by the families, leading into a spiral of poverty
- A lack of awareness and understanding of children's palliative care
- The lack of government health policy, strategies, work plans, and funding for the provision of children's palliative care in the majority of countries worldwide (Downing et al. 2012, 2016; Downing and Ling 2012; Marston and Chambers 2012; Mwangi-Powell et al. 2015).

Many of these challenges could be addressed through an appropriate and comprehensive national palliative care policy for the provision of children's palliative care yet, at the same time, these challenges can make it hard to encourage governments to have a policy on children's palliative care.

4.2 Inclusion of CPC in National Policies

Differences exist with regard to whether there is a need for specific policies on children's palliative care within a country or whether a national palliative care policy should and will encompass children as well, ensuring that they are given full recognition and will not get forgotten or sidelined. It is important to remember that there are differences between children's and adult palliative care and that service provision and policy should reflect that difference, for example, ethical issues and how consent for treatment is provided, the broader range of people who may be involved in their care, and different use and preparations of medications (Marston and Chambers 2012; Amery 2009). Thus, if an overarching palliative care policy is to be in place, it is important that it recognizes these differences and that children are integrated throughout the policy and that an integrated approach, as outlined in the World Health Assembly Resolution(World Health Assembly 2014), is promoted.

Alongside the disparities in the provision of children's palliative care globally (Knapp et al. 2011; Downing et al. 2016; Harding et al. 2010), the provision of policy for children's palliative care varies and is at different stages of development and integration. Examples of policy from a range of countries including Uganda, Swaziland, New Zealand, Serbia, Ireland, and the UK will be discussed to illustrate some of these disparities.

Uganda has often been recognized as the country leading the development of palliative care in sub-Saharan Africa, with the provision of palliative care seen as reaching integration (Connor and Sepulveda Bermedo 2014; Clark

and Wright 2007) and capacity building not only for within Uganda but across the region (Merriman 2013; Rawlinson et al. 2014). However, despite this and the leadership from the Palliative Care Association of Uganda (PCAU), Uganda is only now in the process of approving a policy for palliative care (the detail of which has been described elsewhere in this chapter). Within Uganda they have taken the integrated approach with the assumption that children are included/implied throughout and that when talking about provision of care, education, access to medications, etc., the policy is talking about both adults and children. Indeed, in the background to the policy, children's palliative care is defined, and the governments set out their commitment to providing palliative care for all children and adults, and in discussing the principles underpinning the policy, the section on equity states that "The palliative care services shall be provided country wide while ensuring equity with respect to gender, age, and disease conditions with specific considerations for vulnerable groups of the population (Health TRoUMo 2014)," thus laying the foundation not only for children in terms of age but also for the wide ranging conditions for which children require palliative care. Similarly, the National Palliative Care Policy in Swaziland (2011) lays out the policy of universal access to palliative care as a guiding principle and includes an objective of "ensuring the delivery of palliative care services for persons with life-limiting illnesses at all levels, including children, as part of the comprehensive package"(Ministry of Health Kingdom of Swaziland 2011).

The situation within New Zealand – a high income country (World Bank 2017) – is very different, and demonstrates the complexity of the development of policy and frameworks for children's palliative care in a country. In September 2012, The "Guidance for integrated paediatric palliative care services in New Zealand"(Bycroft et al. 2012) was published which recognizes that there had been a variety of key documents within the country that have framed the development of children's palliative care. These include the following:

The Child Health Strategy (New Zealand Ministry of Health 1998a)

Through the Eyes of a Child: A National Review of Paediatric Specialty Services (New Zealand Ministry of Health 1998b)

The New Zealand Palliative Care Strategy (Health NZMo 2001)

Palliative Care: Report of the Palliative Care Expert Working Group to the Cancer Control Steering Group (New Zealand Ministry of Health 2003a)

New Zealand Cancer Control Strategy (New Zealand Ministry of Health 2003b)

The New Zealand Cancer Control Strategy Action Plan 2005–2010 (Cancer Control Taskforce 2005)

Specialist Palliative Care Tier Two Service Specification (New Zealand Ministry of Health 2014)

Gap Analysis of Specialist Palliative Care in New Zealand (New Zealand Ministry of Health 2009)

Positioning Palliative Care in New Zealand: A review of government health policy in relation to the provision of palliative care services in New Zealand (Palliative Care Council of New Zealand 2010)

While it was important that each of these was seen in the wider policy environment within the country, it is interesting to note that it was key documents addressing both adults' and children's palliative care, as well as general pediatric care, that were involved in shaping the children's palliative care services. This is in contrast with the development of the policy on children's palliative care in the Republic of Ireland, where a palliative care needs assessment undertaken in 2005 (Department of Health and Children and Irish Hospice Foundation 2005) estimated that there were approximately 1400 children living with a life-limiting condition, many of whom could not access care and for whom there was a lack of coordination of care. This was followed by the development of a policy – Palliative Care for Children with Life-Limiting Conditions in Ireland – A National Policy (2009) (Department of Health and Children (DOHC)

2009), which sets out the vision and framework for the development of services for children needing palliative care in Ireland. Following this there was a further needs assessment that looked at the need for respite service for children with life-limiting conditions and their families in Ireland (Irish Hospice Foundation (IHF) and Laura Lynn Ireland's childrens hospice 2013), with the most recent work of the National Development Committee for Children's Palliative Care (NDC) established in 2010, being to look at how things have progressed since the implementation of the policy, i.e., from policy to practice 2010–2016. Thus, a clear progression can be seen in the development of the national policy, its evaluation, and recommendations for ongoing service provision.

The UK is an example of a country where adults' and children's palliative care has developed alongside each other and in many ways separately. Together for Short Lives, the national body for children's palliative care, is working hard to influence policy in the UK on Children's palliative care, with ongoing work culminating in the development of an All-Party Parliamentary Group for Children who need palliative care (2017), which seeks to educate, inform, and motivate parliamentarians to take action to continue to develop children's palliative care services for all in need around the country.

For countries with limited palliative care delivery for both adults and children, there are opportunities for an integrated approach to the development of adult and children's palliative care services, where the two can develop alongside and be integrated with each other. An example of this can be seen in Serbia, where an EU-funded project "The development of palliative care in the Republic of Serbia"(European Union 2010) was implemented between March 2011 and November 2014. An important aspect of this project was the development of a national model of palliative care service delivery, for both adults and children, following the adoption of a national palliative care strategy by the Serbian Ministry of Health in 2009 (Government of Serbia 2009). While initially there was a lack of awareness of the need for children's palliative care, this was dispelled through a national needs assessment for children's palliative care. Alongside the provision of education and the development of palliative care services, a comprehensive model of care and service delivery appropriate for Serbia was set up that addressed both adult and children's palliative care service provision. This final document, adopted by the Ministry of Health in October 2013, addresses issues such as the assessment of requirements in terms of resources, operational procedures, referral protocols, standards, quality indicators, and best practice guidelines for adults (but not yet for children) (Downing et al. 2014b). The model explores issues related to both children's and adult palliative care provision and is based on the vision for palliative care in Servia such that all who need it will have access to high-quality, person-centered, holistic, and reliable palliative care regardless of age, diagnosis, stage of illness, or care setting (Milicevic et al. 2015). It looks at an integrated model of service development and addresses the integration of palliative care as outlined in the WHA resolution (World Health Assembly 2014).

5 Conclusion

Thus, there are different pathways that have led to the development of policy on children's palliative care in different countries, whether that be within policies specific for children, integrated with those for adults, within disease-specific policies, etc. However, children's palliative care remains a fairly new concept and is still not understood or well known in many countries; thus there is a need for ongoing advocacy to governments both nationally and through the support of organizations such as the International Children's Palliative Care Network (ICPCN) (Downing et al. 2014a) in order to support the development of appropriate policy. Regardless of the route to development or whether it is child specific or includes adults, the main emphasis is that there is some form of policy, strategy, or framework that will help to shape the development and implementation of children's palliative care within different countries and globally.

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Palliative Care, Toward a More Responsive Definition

7

Eric L. Krakauer

Contents

Abstract

The World Health Organization (WHO) definition of palliative care requires clarification. While it has been interpreted as limiting its purview to people facing life-threatening illness, this definition makes little sense in low- and middle-income countries where the means to prevent and relieve any suffering are limited, including in people without a life-threatening illness. The most basic principle of palliative care, prevention and relief of suffering, requires that palliative care conform to the needs of the people it serves.

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1 Introduction

The World Health Organization (WHO) definition of palliative care (Box 1) inadvertently has generated confusion (WHO 2002; Fallon and Smyth 2008; Pastrana and Jünger 2008; Van Mechelen et al. 2012; Hui et al. 2013). What is palliative care? Is it exclusively for people with a "life-threatening illness?" Or is it for any patient or family facing the types of **problems** "associated with life-threatening illness?" Many people who do not have clearly a life-threatening illness have problems like pain, dyspnea, anxiety, depression, impoverishment, or spiritual crisis that are "associated with life-threatening illness." The WHO definition also states that palliative care "improves the quality of life of patients and their families . . . through **prevention and relief of suffering**." It states further that "palliative care provides relief from pain and other distressing symptoms." These passages should resolve the confusion. Wherever pain and other distressing symptoms of people **without** a life-threatening illness are not

R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_1

adequately addressed, palliative care has a role. Hospices – organizations devoted entirely to inpatient or outpatient palliative care for patients near the end of life – provide a crucial service in many settings. But it is neither medically sensible nor morally defensible to assert that clinicians trained to prevent and relieve suffering should do so only for one population in need (those with life-threatening illnesses) and not for others (Fallon and Smyth 2008; MacMahon 2011). This chapter will provide a definition of palliative care based on the most basic principle of the current definition: prevention and relief of suffering.

Box 1

WHO Definition of Palliative Care

Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual. Palliative care:

- Provides relief from pain and other distressing symptoms
- Affirms life and regards dying as a normal process
- Intends neither to hasten nor postpone death
- Integrates the psychological and spiritual aspects of patient care
- Offers a support system to help patients live as actively as possible until death
- Offers a support system to help the family cope during the patient's illness and in their own bereavement
- Uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated
- Will enhance quality of life and may also positively influence the course of illness
- Is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications

WHO Definition of Palliative Care for Children

Palliative care for children represents a special, albeit closely related field to adult, palliative care. WHO's definition of palliative care appropriate for children and their families is as follows; the principles apply to other pediatric chronic disorders:

- Palliative care for children is the active total care of the child's body, mind, and spirit and also involves giving support to the family.
- It begins when illness is diagnosed and continues regardless of whether or not a child receives treatment directed at the disease.
- Health providers must evaluate and alleviate a child's physical, psychological, and social distress.
- Effective palliative care requires a broad multidisciplinary approach that includes the family and makes use of available community resources; it can be successfully implemented even if resources are limited.
- It can be provided in tertiary care facilities, in community health centers and even in children's homes.

2 A Responsive Definition: Letting the Need Define the Field

A palliative care more responsive to the full variety of peoples' suffering, and thus more people-centred, could be defined as follows: Palliative

care is the prevention and relief of suffering of adult and pediatric patients – whether physical, psychological, social, or spiritual – and of the psychological, social, and spiritual suffering of family members. It:

- Entails early identification and impeccable assessment and treatment of any type of inadequately relieved suffering
- Enhances quality of life, promotes dignity and comfort, and may also positively influence the course of illness
- Provides accompaniment for the patient and family throughout the course of illness
- Should be integrated with and complement prevention, early diagnosis, and treatment of serious or life-limiting health problems
- Is applicable early in the course of serious illness in conjunction with disease-modifying and life-sustaining treatment
- Provides an alternative to disease-modifying and life-sustaining treatment of questionable value near the end of life
- Is applicable to those living with long-term physical, psychological, social, or spiritual sequelae of serious or life-limiting illnesses or of their treatment
- Accompanies bereaved family members after the patient's death
- Seeks to mitigate the pathogenic effects of poverty on patients and families and to protect them from suffering financial hardship due to illness or disability
- Does not intentionally hasten death but also provides whatever treatment is necessary to achieve an adequate level of comfort for the patient in the context of the patient's values. In keeping with the ethical principle of double effect (Krakauer et al. 2000), there may be rare cases of severe, refractory symptoms in a patient with a terminal illness or mortal injury when the intention of assuring comfort may result in unintentional but foreseeable hastening of death
- Should be applied by healthcare workers of various kinds, including primary care providers, generalists, and specialists in many disciplines and with various levels of palliative care training and skill, from basic to intermediate to specialist
- Encourages active involvement by communities and community members
- Should be accessible at all levels of healthcare systems and in patients' homes
- Improves continuity of care, strengthens health systems, and promotes universal health coverage (Gwyther and Krakauer 2011; Krakauer 2008; Krakauer et al. 2018)

In 2014, the World Health Assembly resolved that "it is the ethical duty of health care professionals to alleviate pain and suffering, whether physical, psychosocial or spiritual, irrespective of whether the disease or condition can be cured . . ."(WHO 2014). The same resolution states that "palliative care is an ethical responsibility of health systems . . ." and that integration of palliative care into public healthcare systems is essential for achievement of Sustainable Development Goal 3.8: universal health coverage. Thus, palliative care is not optional but a medical and ethical necessity that should be accessible by anyone in need at all levels of healthcare systems.

The specific types and severity of suffering vary by geopolitical situation, socioeconomic conditions, and culture. People in low- and middle-income countries (LMICs) often endure less healthy social conditions than people in high-income countries (HICs). They also typically have less access to disease prevention, diagnosis, and treatment, to social supports, and to specialists and specialized services of many kinds. For example, many people have limited or no access to cancer chemotherapy, radiation therapy, or surgery or to effective chemotherapy for multidrug-resistant tuberculosis. Palliative care should never be considered a substitute for disease prevention and treatment, and palliative care workers have a responsibility to advocate for them wherever they are not yet accessible (Gwyther and Krakauer 2011; Shulman et al. 2014). But palliative care also should be universally accessible (WHO 2014).

Many countries also lack rehabilitation medicine specialists and services and long-term care facilities to care for people with non-life-threatening but

Table 1 Comparison of palliative care needs of specific patient populations in different economic settings

Patient population	HICs palliative care need	LMICs palliative care need
Advanced chronic noncommunicable diseases	High	High
HIV/AIDS	Moderate	Very high
Drug-resistant tuberculosis	Very low	High in some regions
Critical illness	High	High
Older people with frailty or multi-morbidity	High	Very high
Neonates with severe prematurity, birth trauma, or congenital anomaly	High	Very high
Severe nonprogressive disabilities such as paraplegia and quadriplegia	Low	High
Severe social distress such as extreme poverty or stigmatization	Low	High
Acute symptoms related to illness, injuries, or surgery	Not applicable	High
Health emergencies and crises	Very low	High in some areas

HICs high-income countries, *LMICs* low- and middle-income countries

serious disabilities such as paraplegia or quadriplegia or those due to brain injuries or congenital anomalies. In addition, mental health services and social welfare programs may be of limited capacity, difficult to access, or unavailable. Palliative care can help to fill these needs (Table 1). Further, the types of suffering typically associated with life-threatening illness – pain, other physical symptoms, and psychological symptoms – also occur acutely or in association with non-life-threatening conditions. But in low-resource settings, prevention and relief of acute or non-life-threatening suffering is inadequate or unavailable. For example, in countries where pain medicine does not yet exist as a specialty, prevention and relief of pain from trauma or burns or surgery typically is inadequate, and clinicians trained in palliative care should help to fill this therapeutic void. Thus, in these settings, clinicians trained in palliative care should intervene either by training colleagues in symptom control, by providing direct symptom relief, or both. Planning and implementing palliative care services must be based on assessment of the types and extent of inadequately prevented or relieved physical, psychological, social, or spiritual suffering. This attention to local needs is necessary for palliative care services to be people-centered: tailored to local need and to the needs of individual patients and families (WHO 2016a, b; Knaul et al. 2017).

3 Conclusion and Summary

The definition of palliative care entails responsiveness to local need. The most basic principle of palliative care, prevention and relief of suffering, requires that palliative care conform to the needs of the people it serves. Patient and families facing life-threatening illnesses suffer everywhere, and palliative care always must address this suffering. However, pain and other types of suffering are common in many other patient populations. Where pain specialists are available and adequately address trauma pain and postoperative pain, involvement of clinicians trained in palliative care is not needed. Where rehabilitation specialists are available and adequately address the needs of disabled people, involvement of clinicians trained in palliative care is not needed. Where pain specialist or rehabilitation specialists or psychiatrists or social supports are not available and patients without life-threatening illnesses suffer unnecessarily as a result, palliative care must respond.

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Challenges and Future Directions of Palliative Care

8

Jane L. Phillips and David Currow

Contents

Abstract

The unprecedented global development of palliative care over the past 50 years, originating in a counterculture and evolving through to an integral element of the health-care system, has enabled many more of the world's population to have access to quality palliative care. More of the world's population, particularly those living in high-income countries, such as Europe, North America, Australia, and parts of Asia, now die at an older age of, or with, noncommunicable diseases. The need for palliative care is also significant and largely unmet in low- and middle-income countries such as sub-Saharan Africa where communicable diseases such as

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_5

HIV/AIDS, tuberculosis, and malaria continue to lead to expected deaths for many people.

These new patterns of dying have implications for the configuration of international, national, and local palliative care policies, health-care service delivery models, palliative care delivery, engagement with primary and specialist clinical streams, workforce education, and the focus of future research.

This chapter will describe the current and future challenges to palliative care development in low-, middle-, and high-income countries and the opportunities offered by adopting a public health approach, novel technologies, and remote monitoring and better engaging communities to increase palliative care access globally.

1 Introduction

Globally, differing political, economic, and social drivers have shaped each country's response to their population's palliative care needs (Human Rights Watch 2011; The Economist Intelligence Unit 2015). The original genetic coding of many palliative care services can be traced back to the traditional hospice model introduced by various religious orders over a century ago to provide care for the dying and destitute (Clark 2007). These religious order models of hospice care dominated until the 1960s when modern palliative care emerged largely as a counterculture to the unrealistic optimism of mainstream clinical care in the years immediately after the Second World War. Led by a number of visionary clinicians in England, Italy, and North America, this movement was successful in mobilizing funds to support the development of new models of care for the dying (Clark 2007). These new funding streams fuelled the establishment of specialist inpatient palliative care services initially in the UK and Canada, with similar models being subsequently adapted and implemented in other high-income countries and extended to include community-based services (Clark 2007). Establishing these specialist palliative care services has enabled palliative medicine to be recognized as a speciality in its own right in many jurisdictions.

Despite the rapid evolution of this clinical speciality, there continue to be significant barriers to many people accessing evidence-based palliative care. Disparities in access are now one of the greatest challenges faced by the 40 million patients and their families globally who currently require palliative care each year (Connor and Bermedo 2014). The large majority of these patients (80%) live in low- and middle-income countries and are older people ($\geq$60 years of age), while a smaller proportion are children (6%) (World Health Assembly 2014). Unfortunately, less than 8% of the world's population in need of this type of care have access to it (Connor and Bermedo 2014). However, limited access to palliative care is not just confined to people living in low- and middle-income countries; it is also experienced by many people in some of the world's most prosperous economies who often struggle to access the palliative care they need (The Economist Intelligence Unit 2015).

There are many factors that contribute to these disparities in accessing palliative care including inadequate integration, especially at the primary care level, ambiguity about which patients to refer to specialist palliative care services and when referral should be initiated, a very limited workforce globally, lack of access to universal health-care coverage (especially where fee-for-service models predominate in health-care delivery), and poor or absent access to essential medicines as listed by the World Health Organization (WHO) for palliative care, including opioids (World Health Assembly 2014; World Health Organization 2015). These factors impact adversely on patients' ability to receive timely and appropriate evidence-based palliative care and currently pose some of the biggest challenges facing people late in life internationally. Whereas once people predominately died suddenly, the majority of the world's population, especially those living in high-income countries, now have an "expected" death, at an advanced age having lived for some time with one or more noncommunicable diseases, increasing levels of disability, fragility, and symptom burden (World Health Organization et al. 2011), many of whom are older women aged over 85 years, living alone without the regular support of a carer (Local Government Association, NHS Confederation et al. 2012). This changing epidemiology of dying has significant implications for the future configuration, funding, and

integration of palliative care into the existing acute, community, and aged health-care systems. Without adequate health-care reform, the challenges associated with accessing palliative care are expected to increase in line with global population growth and ageing and the rapidly rising burden of noncommunicable diseases. Addressing this growing demand for palliative care in an environment of fiscal restraints and changing epidemiology of dying will only be possible through the widespread adoption of a sustainable public health approach (World Health Assembly 2014).

At the macro level, the focus for addressing the global disparities impacting on access to palliative care ought to be focused on the policy environment in which the values, principles, and strategies for palliative care services are developed and the decisions about resource allocation are determined (World Health Organization 2002). Since the start of the new millennium, a public health strategy has been at the core of all global palliative care policies, primarily because this approach offers the greatest potential to address these access disparities (Stjernsward et al. 1996, 2007). Strengthening global palliative care is a World Health Organization (WHO)(World Health Organization 2007) priority, and the action required to achieve this vision was endorsed at the 67th World Health Assembly in 2014 (World Health Assembly 2014). Positive public policy integrated across all levels of government and the health-care system and engagement and ownership by the community through collective and social action are the cornerstones for strengthening palliative care globally (Stjernswärd et al. 2007). However, realizing this vision requires each and every country to adopt the WHO advice and guidelines on how best to:

(i) Integrate palliative care into the existing health-care system, as one of the four pillars of a noncommunicable diseases program and with inclusion in all relevant health-care policies.
(ii) Implement appropriate policies to ensure essential medicine availability.
(iii) Invest in education of policymakers, health workforce (including volunteers), and community to embed palliative care services at all levels throughout the society (Fig. 1) (Stjernswärd et al. 2007).

This chapter will examine the ten top current and future challenges that palliative care faces globally and outline potential strategies to address each challenge.

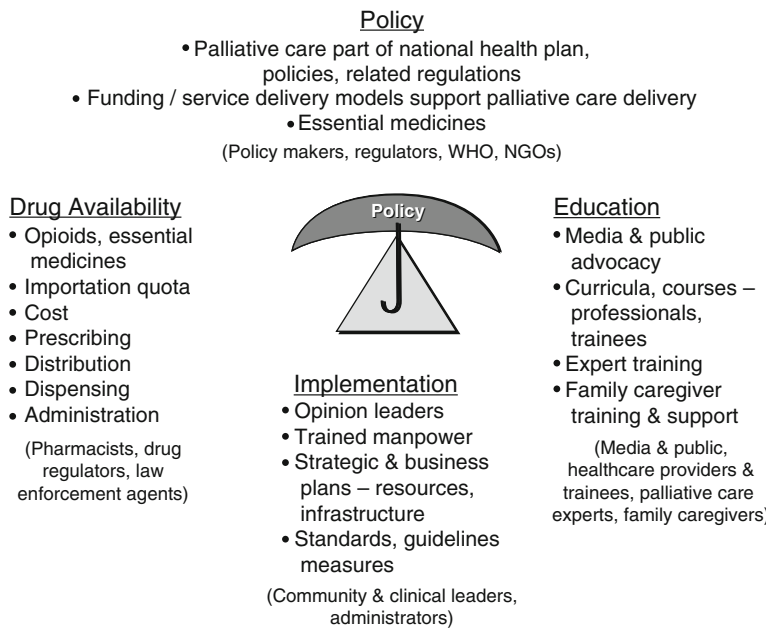

Fig. 1 WHO public health model applied to palliative care (Worldwide Hospice and Palliative Care Alliance and World Health Organisation 2014, p. 30)

2 The Ten Top Current and Future Challenges

Global policies provide governments with a framework for strengthening access to palliative care. However, operationalizing these global frameworks is left to each jurisdiction. As a result, one of the greatest and most immediate global policy challenges is the integration and financing of palliative care as part of usual clinical care irrespective of diagnosis, prognosis, or setting of care. The WHO also acknowledges the need to extend palliative care to other noncommunicable diseases in order to reduce unnecessary suffering (World Health Organization 2007). It positions palliative care as a humanitarian need and as an approach that should be integrated into the existing health-care system where active treatment(s), such as chemotherapy and radiotherapy, are offered in parallel to palliative care in order to improve patients' outcomes (World Health Organization 2007). While this approach is particularly important for low- and middle-income countries, it equally applies to high-income countries. The WHO has an aspirational goal that 80% of all people who die from cancer and 60–80% of people dying from HIV/AIDS should be seen by a palliative care service, but this is rarely achieved, regardless of the country's economic status (Palliative Care Australia 2017). Even in a high-income country like Australia, with universal health coverage and where palliative care services are well developed, many people who would benefit from this type of care do not have access to it. A recent report has found that of the 76,856 Australian inpatients who died in the hospital during 2014–2015, less than half had received palliative care during their final hospitalization; only 4% of aged care residents had a formal appraisal to indicate whether they required palliative care; and only 1 in 1000 patient encounters with GPs was palliative care-related (Palliative Care Australia 2017). Such data confirm that even within high-income countries with universal health coverage, there are significant opportunities to improve disparities in access to palliative care. Without significant positive public policy reforms, reorientation of health-care services, and additional incentives to address the unmet palliative care needs of underserved populations, the situation will rapidly worsen. We contend that there are ten major challenges that need to be addressed to ensure that more of the world's population has access to care based on the best available evidence.

2.1 Access to Essential Medications, Including Opioids

Ensuring timely access to opioids, preventing inappropriate use or diversion (Masman et al. 2015), and making essential medications affordable (United Nations 2016) are potentially the most pressing global palliative care challenges. Timely access to essential palliative care medications, especially opioids, continues to be a major challenge in many countries. While pain is omnipresent in palliative care and almost universally experienced by people with palliative care needs, this distressing symptom can largely be effectively managed with opioids. Yet 80% of the world's population, mostly people living in low-, middle-, and a small number of high-income countries, lack timely or, in many cases, any access to the essential palliative care medications they need, including opioids (World Health Assembly 2014), and at a price they can afford (United Nations 2016).

Currently, less than 10% of the globally manufactured morphine is used for palliative care needs, and its global use is unevenly distributed (United Nations Narcotics Control Board 2017). "Very inadequate" consumption is noted to occur in more than 100 countries, and "inadequate" access is evident across a further 21 countries (International Narcotics Control Board 2011). This reality contributes to some 6.5 million people with palliative care needs not having access to effective analgesia with patients forced to live with moderate to severe pain as a result of their advanced cancer and/or HIV-related disease (s) (World Health Organization 2012). Many of these opioid access issues stem from jurisdictional

efforts to prevent the illicit diversion and abuse of narcotics and psychotropic drugs. Balancing each country's needs to minimize opioid abuse while ensuring those who need opioids have affordable access presents a myriad of humanitarian, ethical, legal, and practical challenges. The United Nations (UN) guidance statements are designed to assist countries where access to opioids is severely restricted or not available in order to move to a more balanced approach by calculating the amount of controlled medications they need to meet their population's essential requirements and to obtain relevant licenses (International Narcotics Control Board 2011; World Health Assembly 2014). Despite this international policy guidance, the limited access to opioids is one of the most urgent global challenges that demands immediate attention.

The WHO Model List of Essential Medicines for adults and pediatric populations prioritizes the core medications required to manage common palliative care symptoms that ought to be available for all globally (United Nations 2016). The challenge is ensuring that all countries have a medicines policy that guarantees the availability of essential medicines, including opioids for the management of pain and chronic breathlessness (World Health Assembly 2014).

Access to medications across high-, middle-, and low-income countries is likely to be an ongoing affordability challenge that will impact on palliative care delivery globally. It is highly likely that as new advanced disease and/or symptom management medications are developed, they will be unaffordable for the majority of the world's population with palliative care needs. Affordability, therefore, poses a significant threat to the provision of evidence-based palliative care. The UN has identified that unaffordable medicines pose a significant threat to global health, largely as a result of a misalignment and tension between diverse drivers such as balancing human rights, public health objectives, intellectual property, and free-trade agreements (United Nations 2016). Addressing these anomalies requires transparency, accountability, and better governance arrangements as well as greater investment by governments in the creation of new research and development incentives (United Nations 2016). However, the real power in the UN's recommendation for affordable medications may lie in inspiring the public debate about options for reforming the research and development system to better serve the global public interest (Moon 2017).

2.2 Access to Universal Health Coverage

Access to universal health-care coverage fundamentally affects patients' and families' ability to access the care they need, including palliative care. The WHO policy imperative promoting universal health coverage is one of the most powerful drivers for increasing access to global health care, including palliative care (World Health Organization 2010; O'Connell et al. 2014; Worldwide Hospice and Palliative Care Alliance 2014). Universal health-care coverage is essential to improve palliative care outcomes globally. This level of coverage ensures that all people (children as well as adults) can use the promotive, preventive, curative, rehabilitative, and palliative health services they need, access health care that is of sufficient quality to be effective, and be protected from unnecessary financial hardship as a result of health-care costs (World Health Organization 2017).

At the macro level, there is an expectation that palliative care is integrated into all aspects of a country's national health-care financing and health system's structures (i.e., primary and community care, aged and acute care) (World Health Assembly 2014). However, this requires all countries to fund the delivery of palliative care and ensure that everyone who requires it has access. Universal health coverage is firmly grounded in addressing inequity and should distribute resources to meet population needs and targets (World Health Organization 2010; O'Connell et al. 2014; Quick et al. 2014) by providing financial risk protection, access to quality essential health-care services, and safe, effective, quality, and affordable medicines (Worldwide Hospice

and Palliative Care Alliance 2015). In the context of palliative care, in addition to improving quality of life, it may also reduce household poverty by minimizing unnecessary expenditure on medical care while enabling those affected (including carers) to continue to work (Worldwide Hospice and Palliative Care Alliance 2014). Further, by optimizing a person's function for as long as possible, it can also reduce reliance on family caregivers, many of whom would have to forego paid work for longer, and potentially reduce the quantum of paid community workers. However, for these advantages to be realized, palliative care needs to be an integral element of universal health coverage, that is, coverage that includes the costs of essential medicines; all inpatient and community palliative care; all necessary medical, nursing, and allied health care as part of the national health plan; and ongoing monitoring of the net effects of palliative care (Worldwide Hospice and Palliative Care Alliance 2014).

The power of driving change through universal health care is best illustrated in an example from Norway, a high-income country where all health care is fully funded by the government. The development of a Diagnosis-Related Group for palliative care paved the way for Norwegian hospitals to establish integrated palliative care teams within the acute care and community sectors, enabling palliative care to be rapidly developed across Norway and in the process reducing access disparities (Currow and Kaasa 2015). Similarly in the USA, the introduction of the Medicare Hospice Benefit in 1983 paved the way for establishing hospices for Medicare, Medicaid, and private insurance beneficiaries with a life expectancy of less than 6 months, who were prepared to forego curative treatment(s) (Meier 2011). Medicare-certified hospices now provide palliative care to more than 1.5 million Americans annually, helping to reduce health-care costs and improve patient outcomes (Meier 2011; National Hospice and Palliative Care Organisation 2015). However, in 2014, more than a third (35.5%) of hospice patients only received care for less than a week (National Hospice and Palliative Care Organisation 2015). These short admission periods reflect poor referral pathways, that most hospices provide limited resources, and that the past practices of linking hospice access to foregoing treatments with curative intent directly limited access to this key resource.

2.3 Integration of Palliative Care into Usual Care

Globally, each country has been largely left to determine how best to address their growing needs for palliative care. There is already wide variability in how palliative care is currently integrated into the existing health-care system. The diversity in global commitment to palliative care is evident in the 2015 study funded by the Lien Foundation in Singapore and led by the Economist Intelligence Unit Report (The Economist Intelligence Unit 2015). This report ranked palliative care development across 80 countries in the following five categories: the palliative and health-care environment, human resources, the affordability of care, the quality of care, and the level of human engagement. This ranking process revealed that 10 of the top 15 countries providing the highest quality of palliative care, including many high-income countries with very sophisticated health-care systems, do not have a national palliative care policy (The Economist Intelligence Unit 2015). Ensuring that all countries have a robust high-level national palliative care policy, backed by funding and agreed standards, is critical to increasing access to palliative care and addressing the unmet needs of underserved populations. Measuring and publicly reporting the impact of these policy initiatives is equally important to help optimize the number of countries which implement palliative care policies (World Health Assembly 2014). While the WHO guidance statements may provide the imprimatur for change, the strategies adopted to increase palliative care access need to be congruent with the country's cultural, social, ethical, and economic milieu. Positive public policy works best when policymakers understand the current context for palliative care, determine what the program aims to achieve in 3 years, and detail the strategies to achieve these outcomes (World Health Organization 2007).

Canada is a good example of a high-income country where palliative care has been well integrated into the existing health-care system (Currow and Kaasa 2015). This integration is largely because of having a strong policy framework, a national palliative care strategy, funding to support palliative care service development, and a commitment to evaluation. Canada has also established a surveillance working group who is seeking to better understand who is accessing palliative care services and how the quality of these services can be systematically measured (Currow and Kaasa 2015). Kerala, India, is an example of a state in a low-income, highly populous country that has developed palliative care services over three decades through strong local policy that emphasizes the importance of primary care and cross-sectoral support and cooperation (Worldwide Hospice and Palliative Care Alliance and World Health Organisation 2014; Currow and Kaasa 2015). Affording palliative care priority status within a public health and disease control program has enabled Kerala to effectively integrate palliative care into the existing health-care system, with a major focus on primary care delivery (Worldwide Hospice and Palliative Care Alliance and World Health Organisation 2014; Currow and Kaasa 2015). The provision of palliative care to those in need would not have been possible without the addition of a trained palliative care volunteer workforce working in partnership with clinicians to provide much-needed care and support in the community (Worldwide Hospice and Palliative Care Alliance and World Health Organisation 2014).

While Canada and Kerala exemplify how high-level WHO policy imperatives and guidance can be adopted to establish and strengthen palliative care services, there are many countries and jurisdictions which continue to struggle to do so (The Economist Intelligence Unit 2015). For example, currently no Caribbean country has successfully integrated palliative care into their health-care system (Spence and Greaves 2017), and in the USA, few hospitals currently meet national palliative care staffing requirements. Current US non-hospice palliative care programs reach very few inpatients (median of 3.4%), and half of all smaller services are nurse-only palliative care programs (Spetz et al. 2016). Of the 1.3 M US Medicare beneficiaries who received hospice care for 1 day or more in 2015, the median length of stay was 23 days, with 30% enrolled for less than 7 days (National Hospice and Palliative Care Organization 2016). Only a quarter of the programs surveyed meet the US Joint Commission interdisciplinary staffing requirements. As a result, few US patients in need of specialist palliative care actually currently receive it, which contributes to some patients being undertreated, while others are overtreated (Meier 2016). In part, this may be attributed to the lead American hospital accreditation authority, "The Joint Commission," not requiring hospitals to provide palliative care or to ensure that the care provided meets national palliative care quality guidelines. As a result, individual hospitals each determine whether or not they will seek palliative care certification (Meier 2016). Likewise, in Australia, the national accrediting body does not require palliative care to be available for a hospital to be fully accredited.

The challenges of integrating palliative care into the usual health-care system are not associated only with resourcing but rather reflect the value each country places on the provision of compassionate, affordable, and evidenced-based palliative care. Unfortunately, across the globe, the barriers that limit the integration of palliative care into existing health-care systems, even when curative care is unavailable, are much greater than the rewards for doing so. At a global macro level, there are few penalties for countries not funding palliative care delivery. As a consequence, too few health-care systems are designed to meet their country's current palliative care needs, leaving many patients with noncommunicable diseases to fall between the gaps or receive inappropriate and ineffective care, which contributes to increased health-care costs and needless suffering. This failure to implement the care required causes unnecessary suffering, especially when medically futile treatments are administered often at great cost to patients and families or symptoms are poorly managed (Davidson and Phillips 2010).

The lack of drivers to integrate palliative care into the existing health-care system, plus geopolitical issues, conflict, and economic instability, all poses significant threats to the future development and sustainability of palliative care globally. These threats also impact adversely on current funding for services, salaries, medicines, and transport. As the world becomes more uncertain, all of these factors have the potential to increase the demand for palliative care, as a humanitarian response (Powell et al. 2017), and to impact on a country's capacity to provide evidence-based palliative care. These factors, combined with changing epidemiological trends (ageing and the increasing prevalence of noncommunicable diseases), demand consideration of new models of palliative care (Connolly 2000; Franks et al. 2000; Wasson 2000). New models of palliative care are also needed to address consumers' growing health-care expectations and access disparities and to better meet the unmet needs of people who are financially disadvantaged around the world (World Health Assembly 2014). There are real opportunities to better integrate community-based nongovernment organizations in the delivery of palliative care, especially in the delivery of generalist palliative care, as educators and as advocates for better palliative care systems.

Any new palliative care models need to support the delivery and integration of generalist and specialist palliative care across health-care systems (Connor and Bermedo 2014; Gómez-Batiste and Connor 2017). For these models to be effective, all health professionals, regardless of speciality, discipline, or care setting, at a minimum need the capabilities to provide a palliative approach to care (Connor and Bermedo 2014). Increasing the capabilities of these generalist providers is essential as palliative care is not their substantive role. Adopting a public health model also ensures that specialist palliative care is care reserved for patients and families with the most complex needs and provided by health professionals whose substantive role is palliative care (Palliative Care Australia 2005). It also enables specialist palliative care providers to partner with and/or support their generalist colleagues to deliver best evidence-based palliative care.

Any new funding models will also need to reconcile the need for palliative care across care settings, in order to strengthen the coordination and integration required to reduce unnecessary fragmentation and to better reflect individual care inputs for patients' needs (Groeneveld et al. 2017). Current service-level funding is rarely linked to local population needs, which inadvertently perpetuates existing inequitable patterns in service provision and access (Groeneveld et al. 2017). New models of palliative care are urgently needed to foster and strengthen community partnerships to increase underserved populations' access to palliative care. Supporting the establishment and maintenance of effective partnerships between consumers (patients, families, and carers), health professionals (medicine, nursing, and allied health), organizations (health-care services and institutions), and communities (nongovernment organizations, volunteers, and friends and colleagues) will also be critical. The success of future palliative care models will be dependent upon them: being aligned with national policy (and often developing a national policy in the first place) and funding, having good systematic processes to identify and address unmet palliative care needs (Weissman and Meier 2011), and adopting dynamic and iterative practice improvement and policy review processes so that the models remain responsive to the needs of the population they serve.

Until recently, palliative care has largely been omitted from global efforts to manage mass causality events, communicable disease outbreaks, and the needs of displaced people living in refugee camps (Powell et al. 2017). Recent humanitarian crises, such as the *Ebola virus* outbreak in West Africa, highlighted the need for a palliative approach to be integrated into active treatment, especially given the virus's high mortality rate. Similarly, the 2010 Haiti earthquake left thousands of people with crush injuries, with many dying of acute renal failure in the weeks that followed without access to palliative care. As a society, we need to think about the minimal palliative care that needs to be provided as part of a humanitarian response and how we ensure essential medications, treatments, and care are provided

to those who need them (Powell et al. 2017). New nimble models of palliative care are needed that can respond quickly to better support families and communities and to effectively contribute to these humanitarian efforts.

2.4 Building Health Workforce Capabilities

Building the palliative care capabilities of each community, health workforce, and policymakers will continue to be a challenge into the foreseeable future. Primarily, this is because the vast majority of people who die expected deaths will be cared for by health professionals for whom managing dying is not their primary area of expertise and was often not part of their training (Al-Qurainy et al. 2009) and supported by family and friends who may not have been adequately prepared or appropriately supported for the roles they find themselves undertaking. This makes education of policymakers, health workforce, and the public an urgent and ongoing priority.

Strengthening and expanding human resources, including education and training of the existing and emerging health-care workforce, is required to ensure greater diffusion of a palliative approach to care. Enhancing palliative care delivery not only requires building the palliative care capacity of health professionals but also acknowledges the importance of having trained palliative care volunteers and an educated community (World Health Assembly 2014). The provision of a palliative approach requires that all health disciplines are able to provide primary palliative care (Quill and Abernethy 2013) and have an understanding of interdisciplinary practice (Hegarty et al. 2010). Having palliative care capabilities is essential, as the majority of people with palliative care needs will be cared for by their usual health-care providers, most probably their general practitioner and community or aged care nurses (primary providers) (Palliative Care Australia 2005; Quill and Abernethy 2013). At the same time, people with complex palliative care needs will be cared for by their specialist palliative care team (specialist providers). At a minimum, health professionals need to be able to respond to their patients' and families' palliative care needs, reflect on the interaction, understand what is not being said, identify and address any conflict, and effectively answer any questions patients or their families may have (Fisher 2002).

Despite the recognized importance of palliative care capabilities, there is wide variability in the level and quality of palliative care content taught to undergraduate health professionals (Field and Wee 2002; Oneschuk et al. 2004; Van Aalst-Cohen et al. 2008). Efforts to make palliative care content mandatory in European medical courses and to embed palliative care content into other health professional courses in the UK and Australia have been initiated. In addition to access to short palliative care courses, accreditation and inclusion of palliative care content in medical and nursing curricula is also required.

There are numerous examples of innovative approaches to building workforce capabilities including the US-based End-of-Life Nursing Education Consortium (ELNEC) Program (End-of-Life Nursing Education Consortium 2016) and the Australian Government (2005)-funded "Palliative Care Curriculum for Undergraduates" (PCC4U) Program. Since commencing in 2001, the reach of the ELNEC palliative care train the trainer program has been extensive, with some 21,400 nurses and other health-care professionals, representing all 50 US states and a further 90 countries participating in the program. It is estimated that over 25,000 nurses and other health-care providers have received ELNEC training internationally (End-of-Life Nursing Education Consortium 2016).

Similarly, PCC4U Program is designed to improve the palliative care capabilities of the emerging Australian health-care workforce using a suite of learning resources focused on the principles of palliative care, communicating with people with a life-limiting illness, palliative assessment and intervention, and optimizing function in palliative care (Australian Government Department of Health and Ageing 2005). In addition to these online resources, the program provides practical support to enable Australian universities to seamlessly integrate this learning content into their

medical, nursing, and allied health curricula (Phillips et al. 2010). The PCC4U curricula are used in 78.5% of the 205 Australian universities' courses preparing health professionals for entry into clinical practice (Australian Department of Health 2017). For the existing Australian health workforce, the Program of Experience in the Palliative Approach (PEPA) has funded a range of health workers (doctors, nurses, allied health professionals, and Aboriginal health workers) to gain short-term palliative care experience in a range of care settings and build a mentoring network between the specialist and nonspecialist workforce (Department of Health and Ageing 2012). Despite these exemplars, there continues to be wide variability in the degree to which palliative care has been integrated into medical, nursing, and allied health courses globally.

There will be an ongoing need to provide palliative care learning content to the future health workforce and for greater utilization of mobile technology and to increase the availability of learning content to health professionals, especially for those working in low- and middle-income countries and/or in remote communities in high-income countries. In addition to being adequately prepared to optimize symptom management, communicate effectively, and provide integrated palliative care, the global health workforce also needs to be able to respond effectively to future palliative care challenges such as promoting shared decision-making, managing medical dilemmas, and responding to a rapidly changing environment as physician-assisted suicide and euthanasia legislation changes around the world.

2.5 Promoting Shared Decision-Making and Preventing Medically Futile Care

As more people live longer with one or more noncommunicable diseases, the ethical and moral debates associated with withdrawing and withholding treatment are likely to become more complex. This is especially the case for some older people who may have reduced decision-making capacity as a result of cognitive impairment, and their nominated proxy may feel burdened by their inherited decision-making responsibilities (Miller et al. 2016). Having the capabilities to confidently assess older people's decision-making capacity and to tailor a supportive decision-making approach will become a core requirement for all health professionals. A supportive decision-making approach will be increasingly required to enable more people with a disability, including cognitive impairment, to have an opportunity to make their wishes and values known, develop and pursue their own goals, make choices about their life, and exercise some control over the things that are important to them (Legare et al. 2010). Improving the quality of shared decision-making and communication will be an ongoing challenge as it requires health professionals to be provided with intensive clinician training, use structured interpersonal communication interventions, and employ evidence-based decision aids (Hanson and Winzelberg 2013). Thinking creatively about how this learning content is delivered requires new models of learning that are underpinned by evidence and embrace novel approaches to building knowledge and skills while changing beliefs and practice.

Preventing clinically futile care from being offered to palliative care patients will also become more complex in the future, especially in an environment of scientific advances, new technologies, and health-care rationing. In the context of advancing noncommunicable and communicable diseases, having internationally agreed palliative care referral criteria is crucial to preventing clinically futile care from being initiated or pursued. Regularly reviewing life-prolonging interventions, such as renal dialysis and external ventricular assist devices (VADs) implemented to manage symptoms and prolong life, is critical to ensuring that these interventions do not, at some point, become unnecessarily burdensome for the patient. For example, the introduction of ventricular assist devices was initially used as a "bridge" to the definitive therapy of heart transplantation. It is now used in some clinical settings for high-technology palliation as a "destination" therapy. The use of targeted therapies late into the course of cancer has not been well studied, yet the practice is widespread with few data on the

attributable toxicities and burdens that this engenders. Failure to regularly review and clarify the role of these interventions in the context of the goals of care contributes to people receiving clinically futile, unnecessary, and potentially distressing and costly care (Hillman 2009). Such care is often not congruent with palliative care patients' wishes and values as the disease progresses (Belanger et al. 2011). Engaging in advance care planning conversations may not only help to improve communication between the patient-family-health professional triad, but these conversations are also likely to assist in preserving and promoting patient autonomy (Radbruch et al. 2016). Future technological and pharmaceutical advances guarantee that health professionals globally will be contemplating these dilemmas on a more frequent basis.

2.6 Responding to Calls for Physician-Assisted Suicide and Euthanasia

Since the first enactment by a democratic government in 1996 that made physician-assisted suicide and euthanasia legal acts, there have been growing societal debates across many jurisdictions about the need for such legislation (Radbruch et al. 2016). While palliative care does not include either of these approaches (Radbruch et al. 2016), there is an increasing expectation that palliative care leaders will contribute to the community debate. The challenge of responding to the calls for these legislative changes is unlikely to go away especially given population ageing and fears of loss of autonomy (Radbruch et al. 2016). As a society, we need to understand that individual requests for euthanasia and physician-assisted suicide are complex, and these requests are shaped by various personal, psychological, spiritual, social, cultural, economic, and demographic factors (Radbruch et al. 2016). Further, when studied prospectively, these requests are often not sustained over time. We need to ensure that any calls for euthanasia and physician-assisted suicide, especially in high-income countries, do not inadvertently sabotage global efforts to convince governments that pain relief and good end-of-life care are basic human rights (Asia Pacific Hospice and Palliative Care Network 2017). Licensing doctors to provide or administer lethal drugs to palliative patients poses serious risks for low- and middle-income countries as they work to establish better systems to address their populations' unmet palliative care needs (Asia Pacific Hospice and Palliative Care Network 2017). If physician-assisted suicide and euthanasia are legalized, it will change many doctor-patient relationships in end-of-life care. Within such a change, the impact on clinicians needs to be considered carefully.

2.7 Reducing Access Disparities Through Greater Use of Technology

As the majority of palliative care will continue to be provided in the community, consideration of technology-enabled care (TEC) will become increasingly important. Patients and carers are increasingly researching information, sharing care experiences, and identifying treatment options in an online environment. TEC represents the convergence of health technology, digital health, media, and mobile telecommunications. This type of technology is increasingly seen as an integral part of the solution to many of the challenges facing the health, social care, and wellness sectors (Taylor 2015). TEC offers the potential to enable more effective integration of care, including palliative care across the care continuum (Taylor 2015). As digital technology is advancing exponentially and its costs are rapidly falling, there are real opportunities to deliver safer, more efficient, and cost-effective care (Taylor 2015). For example, in one study, TEC solutions reduced community nurses' paperwork by 60% and increased their face-to-face time with patients by 29%, which enabled community nurses to see two additional patients per day (Taylor 2015). The right TEC solutions can also empower patients and carers by giving them more control of their health, making them less dependent on health professionals for information (Taylor 2015). The development of health-care biosensing wearables, such as digital blood pressure monitors

and glucose sensors, provides patients and their health professionals with real-time health-care data (Taylor 2015). Many of these features are now being incorporated into smart phone technology (Taylor 2015). However, this disruptive technology requires health-care professionals to work differently and to exploit such capabilities fully to improve care outcomes.

Telehealth enables clinicians to assess or monitor patients remotely from another health-care setting using videoconferencing or other technologies. A recent Australian pilot study demonstrated the feasibility of using a telehealth-based model of palliative care, which included patients entering self-reported data into the telehealth system (Tieman et al. 2016). Any changes in the patient's performance or symptom distress can trigger a service alert and prompt the service provider to contact the patient using videoconference, phone, or a face-to-face visit (Tieman et al. 2016). However further research is needed to identify the optimal time to introduce telehealth for community-based palliative care patients and whether a reduction on data entry ought to be considered as a proxy measure alerting clinicians that the patient may be deteriorating, prompting contact (Tieman et al. 2016). Despite these challenges, telehealth offers real opportunities to reduce disparities in access by thinking creatively about how to use existing services and resources to better support patients and families with palliative care needs living in the community.

2.8 Building Community Palliative Care Capacity

Involving consumers in the planning, co-creation, and delivery of health-care policy has long been advocated by the WHO (1978). This advocacy is primarily because community engagement enables communities and services to collaborate to understand local needs, to build capacity, and to address local palliative care issues (Sallnow and Paul 2015). At a minimum, it involves informing and consulting through to more active engagement such as co-production, collaboration, and empowerment which occurs when there is a desire for individual or collective change, signalling a transition to community development (Sallnow and Paul 2015; Noonan et al. 2016). As the demand for palliative care increases, there are opportunities to better engage communities and informal caregiving networks in the provision of palliative care. Consumer advocacy is required to ensure that the funding, availability, and accessibility of palliative care services are guaranteed, regardless of whether care is provided in primary, acute, or aged care settings. However, there are many barriers to effectively engaging consumers, ranging from managing stigma, language, and cultural differences. Acknowledging these barriers is essential to ensure successful consumer engagement and requires the employment of targeted strategies that address the lack of infrastructure support of organizations, lack of organizational skills or confidence, consumer skills deficits, limited opportunities for input from disadvantaged groups, weak links between providers of health information and recipients, and dissemination of information without consumer input (National Health and Medical Research Council 2006). Despite these challenges, authentically engaging consumers in palliative care reforms and initiatives offers the potential of determining the best use of scarce resources and creating services that best serve the population's unmet palliative care needs.

Engaging community members in palliative care delivery also helps foster death literacy, which is considered to be the net result of people's experiences of, and learnings about, death and dying making it an essential for a public health approach to palliative care (Noonan et al. 2016). Death literacy marks a shift away from relying solely on resource-intensive service delivery models toward more integrated models of care, where communities are engaged and reorientated to becoming more responsive to death, dying, loss, and bereavement (Noonan et al. 2016). Death literacy enables community members to more effectively manage the death of a close family member or friend at home in a way that is not entirely dependent upon the traditional palliative care model (Noonan et al. 2016). Community members with death literacy are able to build their

knowledge and skills and activate community resources in a timely and appropriate way to meet the dying person's and their family's needs.

There will be few general practitioners and community-based palliative care clinicians, especially nurses, who have not contributed to death literacy, as they walk with a patient and family, and provide practical suggestions to enable them to manage to spend as many days as possible at home. In many communities, a lack of resources but strong social cohesion facilitates greater involvement of community members in informal carer networks. This network of informal carers often provide additional physical, emotional, or spiritual care and often take on important practical tasks such as picking up children from school, taking them to before or after school activities, cooking meals, helping with laundry, shopping, and driving. A home death may be a community event where each person within the patient's carer network has an important role to play and is valued for their unique contribution (Noonan et al. 2016).

Death literacy provides a framework for effectively engaging communities in the planning and delivery of a palliative approach to care, through the acquisition of knowledge and skill from experiential learning, which often leads to social action (Noonan et al. 2016). However, the effective engagement of informal care networks will require many palliative care services to reevaluate their organizational values, recognize and value the primacy of caring networks, and address any inherent paternalism in health-care provision (Rosenberg et al. 2017).

Access to palliative care is also shaped by a range of cultural and social barriers, which makes addressing death and dying misconceptions a global concern (World Health Assembly 2014). Understanding cultural differences and responding appropriately will become increasingly relevant given global mobility. This is especially the case as end-of-life communication, preferences, and palliative care knowledge among first nation people and cultural and linguistically diverse populations are likely to differ from the majority of views reported from largely white English-speaking populations (Eneanya et al. 2016).

China is the most populous country in the world with a population of 1.3 billion and has one of the most rapidly expanding global economies. Despite its rapidly ageing population and cancer being the leading cause of death, there are few established palliative care services in mainland China (Li et al. 2011). Many of the 4.3 million mainland Chinese diagnosed with cancer in 2015 presented with very advanced disease and had significant palliative care needs, yet only 0.7% (146/22,000) of hospitals offer palliative care (Li et al. 2011; Wei and Ping 2017; Yin et al. 2017). Mainland China's slow adoption of palliative care has been shaped by a combination of factors including the country's focus on strengthening acute care services and the communities deeply held cultural beliefs about death and dying, filial duty, and social biases (Li et al. 2011; Wei and Ping 2017; Yin et al. 2017). Collectively, these factors have contributed to China being ranked 71 out of 80 countries in a recent global quality of palliative care study (The Economist Intelligence Unit 2015). A lack of national policy, guidelines, and financial support and limited professional opportunities to build health workforce capabilities have been identified as major barriers to developing palliative care in China (Hu and Feng), which the country is endeavoring to address (Hu and Feng). However, an even larger hurdle is addressing the public's misunderstanding about palliative care, dying, and death (Wei and Ping 2017). The intangible cultural factors surrounding the need to talk about and build service models designed to address unmet palliative care needs are one of the greatest palliative care challenges currently facing China (Health Intelasia 2013). Initiating death and dying conversations is difficult, and China's challenge is not that different to those experienced in other parts of world where individual autonomy is highly valued and death is feared. However, there are real opportunities to address these significant challenges by raising public awareness about the role of palliative care in minimizing suffering and maximizing function and well-being (Wei and Ping 2017) and through targeted policy, funding, and education initiatives (Hu and Feng).

2.9 Implementation of Best Evidence-Based Palliative Care

Good policy is underpinned by the best available evidence, program management experience, and political judgment (Head 2007). Yet, all too often, policy is implemented without being informed by evidence or consideration of how it will be operationalized or for political expediency. A recent example of palliative care policy that was implemented in an evidence void is the rapid rollout of the Liverpool Care Pathway firstly in the UK and its subsequent adoption in other parts of the world, prior to it having been adequately evaluated (Chan et al. 2014). Conversely, the lack of availability of opioids for palliative care patients in many parts of the world is an example of another evidence-based policy gap (Human Rights Watch 2011; Saini and Bhatnagar 2016). Despite there being abundant evidence of opioids being highly effective for cancer-related pain (Wiffen et al. 2016) and other symptoms (Ekstrom et al. 2017), it is not yet universally available for those in need (Human Rights Watch 2011; Saini and Bhatnagar 2016). However, there is too little evidence about how best to address community concerns about the illicit use of opioids and the wider ramifications for society or how a rapid opioid access program for palliative care could be feasibly established within the constraints of the existing social and health legislative and policy frameworks (Human Rights Watch 2011). Failure to consider and address these additional elements will continue to challenge the ability of countries to make opioids more widely available for those in most need of strong analgesics – palliative populations. The resulting suffering is unacceptable in a compassionate world.

Another policy failure is allowing palliative care patients to be ordered off-label medications for which there are no known optimal doses or no evidence supporting their use (To et al. 2013; Masman et al. 2015). This is especially the case when little is known about the adverse effects of these medications in this population, how they interact with other medications for chronic illnesses that the patient may be taking, or their functional impact on patients (To et al. 2013). As palliative care patients are at high risk of adverse effects from drugs, more prospective trials and pharmacokinetic and pharmacodynamics studies are needed to understand the place of various off-label medications that are often cited in consensus-based symptom management guidelines and frequently prescribed. Of the recent adequately powered, well-designed randomized controlled trials that have been completed on medications commonly prescribed for the management of common palliative care symptoms, several have been found to be ineffective and were actually noted to cause clinically significant harms (Hardy et al. 2012; Agar et al. 2015). Implementing this evidence into practice is essential to ensure that patients are not harmed unnecessarily.

In Australia over the past decade, the Palliative Care Clinical Studies Collaborative (PaCCSC) exemplifies the importance of both building and implementing the palliative care evidence. Over the past decade, this collaborative has completed nine phase III clinical trials. A need to encourage the reporting of adverse drug events prompted the development of the PaCCSC Rapid Pharmacovigilance studies, with more than 90 centers in 18 countries now participating (Currow et al. 2011). Collectively, the outcomes of the PaCCSC palliative care trials are improving the well-being of people with life-limiting illnesses, changing clinical practice as well as advancing health professionals' practices, influencing global policy, and helping to reduce unnecessary harm and waste within the global health-care system. Despite this incredible progress in such a short period of time, there is still much to be done in terms of building the evidence and preventing the inappropriate prescribing and administration of medications at the end of life. While this collaborative research model now exists in the USA and Japan, there are opportunities for this model to be replicated elsewhere to help accelerate the development of new palliative care evidence and to implement existing evidence into practice.

Just as there is an urgent need for all palliative care policy to be underpinned by robust evidence, sound program management, and informed political judgment (WHO and World Bank 2013), a greater investment in developing the evidence

base that will positively influence and inform appropriate policies globally is also required. Access to evidence-based treatments is dependent upon the generation of evidence backed by policy, creating an environment where the implementation of the best available evidence is expected (Rowett et al. 2009). As the palliative care evidence base increases (Tieman et al. 2008), there is mounting pressure for policymakers to integrate this evidence into policy that will inform clinical behavior. For example, policy at the national and local levels is required to halt the widespread practice of off-label prescribing of medications for palliative care symptoms where robust evidence now exists. The development of the evidence base for the use of off-label medications is required so that more patients have access to these medications if deemed effective or are not exposed to unnecessary harms if found to be ineffective for the symptoms they are prescribed for (Rowett et al. 2009). Funding these studies will most likely need to come from government or philanthropic sources as they are unlikely to appeal to the pharmaceutical industry, especially if the medication of interest is off-patent.

2.10 Measuring What Matters Most to Patients and Their Families

For the past 25 years, people with palliative care needs and their families have consistently reported what matters most to them in terms of end-of-life care: effective communication and shared decision-making, expert care, respectful and compassionate care, and trust and confidence in clinicians (Virdun et al. 2015). The final domains differed between patients and families, with financial affairs being important to families, while an adequate environment for care and minimizing burden are ranked equal fifth as being important to patients (Virdun et al. 2015). "Not being a burden" requires that palliative care services focus much more on maintaining a person's physical function and physical independence for bathing, toileting, dressing, and preparing food for as long as possible as a specific goal of care.

A recent review of available evidence highlights the varied approaches used globally for quality measurement of end-of-life care and noted that the care domains rated most important by patients and families are rarely covered (Zwerink et al. 2014). It also identified that only 5 out of the top 10 countries ranked in the "quality of care" category of the 2015 Quality of Death Index study (The Economist Intelligence Unit 2015) have national indicator sets, with only two indicator sets suitable for use by all service providers. No countries currently mandate indicator use, and there is limited evidence of consumer engagement in the development of indicators (Virdin, Luckett et al. under consideration – 5 August 2018). Two thirds of the 128 identified indicators were outcome measures (62%) with the remainder being process measures. Most indicators focus on symptom management (38%), social care (32%), or care delivery (27%) (Virdin, Luckett et al. under consideration – 5 August 2018).

A better understanding of who is missing out on palliative care and who most would benefit from accessing this type of specialist care is crucial to improving care outcomes (Currow et al. 2008a). However, until recently, few health-care services globally have endeavored to measure the degree to which their services are meeting their palliative care patients' and families' needs. Integration of quality palliative care indicators and measures across the health-care system that are relevant for use in low-, middle-, and high-income countries is required to demonstrate the value of this type of care. Without robust measures and agreed use, it will be difficult to demonstrate the impact palliative care has on patients and families, which has been a major driver for several outcome-related initiatives, like the development of the Palliative Outcome Scale (POS) (Collins et al. 2015) in the UK and the establishment of the Palliative Care Outcomes Collaborative (PCOC) in Australia (Currow et al. 2008b).

The POS has more than 8000 registered users in 126 countries and is an example of an instrument that is able to compare palliative care needs and quality of care across diverse contexts and patient groups (Collins et al. 2015). The Palliative Care Outcomes Collaborative (PCOC) is the first

national voluntary benchmarking system, funded since 2006 by the Australian government (Currow et al. 2008b). The rollout of the PCOC program over the past decade has enabled 80% of Australians seen by specialist palliative care services to have point-of-care service delivery data collected from their initial referral until their death (Currow et al. 2012). The use of PCOC's suite of standardized clinical assessment tools enables palliative care patients' outcomes to be measured and benchmarked, allowing services to reflect on their practice and to strengthen care practices in areas of need.

Perhaps one of the final great challenges facing palliative care globally is to be able to demonstrate that this type of care makes good economic sense. Research across high-income countries has consistently demonstrated that people who receive palliative care compared with those receiving usual care have less hospitalizations, shorter lengths of hospital stay, reduced use of intensive care units, and fewer emergency department visits (Smith et al. 2014; Palliative Care Australia 2017). Cost savings from palliative care interventions occur across a number of settings including delivery at home, in hospital, and in residential aged care, for cancer and non-cancer life-limiting illnesses and early versus late delivery of care (Palliative Care Australia 2017). However, it is imperative to expand the scope of economic evaluations to more fully understand and recognize the role palliative care plays in enhancing value in health care and improving the quality of life for people accessing this type of care (McNamara et al. 2013). However, a notable gap is our understanding how cost shifting from the health-care setting to the community impacts on family finances, especially given the financial toxicity of living with an advanced progressive illness (Zafar and Abernethy 2013).

In considering the net effects of palliative care on the health of the population, consideration needs to be given to the health and well-being of caregivers while providing care for a family member or friend and after having completed the caregiving role. The long-term health outcomes for caregivers need to be demonstrated to be better as a result of the involvement of palliative care. Without this broader benefit, palliative care will not realize its full potential (Abernethy et al. 2008; Burns et al. 2017).

3 Conclusion

Addressing the top 10 challenges facing palliative care is critical to improving global palliative care outcomes. A combination of scientific, technological, and pharmacological advances, population ageing, and growing community expectations will continue to challenge access to palliative care globally. The challenges that need to be immediately addressed if more of the world's population are to have access to evidence-based care are to:

- Ensure everyone has access to essential medications, including opioids for the management of pain and breathlessness.
- Implement universal health-care coverage in all countries without this coverage.
- Build the palliative care capacity of the existing health workforce.

Enhanced and expanded access to palliative care requires greater attention to ensuring all future models of palliative care are underpinned by a public health approach to care and embedded into a country's existing health-care delivery and accreditation systems. This includes a very specific focus on upskilling the primary care workforce. Rapid and sustained efforts in education, financing, and health systems management are required to prepare the health workforce to meet the palliative care needs of a growing and ageing population living with serious and complex chronic illnesses. Palliative care leaders need to work collaboratively to identify the areas of greatest need and evaluate the impact of policies intended to support palliative care. Adopting a public health approach, embracing novel technologies, and better engaging communities offer real opportunities to increase palliative care access globally.

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Part II

Symptom Assessment and Management

9 Physical, Psychological/Psychiatric, Social, and Spiritual Problems and Symptoms

Philip J. Siddall and Roderick D. MacLeod

Contents

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_9

Abstract

The person who presents to the clinician in the palliative care setting is not only afflicted by physical symptoms. They bring with them a complex, rich but often disabling tapestry of psychological symptoms as well as social disruption and existential or spiritual symptoms, such as loss of identity, meaning, and purpose. Exploring these various aspects that are framed within the biopsychosocial-spiritual model seeks to address all potential interests, worries, and questions of the person and provide a full "scientific" picture of each individual. This is a fundamental aspect of palliative care, to enable and support the whole person to be supported in living with a terminal illness.

1 The Biopsychosocial Model

In the late 1970s, George Engel (1977, 1981), a New York psychiatrist, proposed an alternative, hypothesized model of healthcare that acknowledged and inquired about more than the biological symptoms of the patient: the landmark biopsychosocial paradigm hinted at what we now identify as holism, which includes the psychological and social perspectives alongside the biological (Smith 2002; Sulmasy 2002; Weiss 1980).

In a response to what Engel saw as the paternalistic, somewhat cold, technical, biomedical approach of doctors toward patients, he proposed a more empathetic view accentuating human warmth, understanding, generosity, and caring, all based on the subjective experience of the patient. This biopsychosocial model encouraged an individually tailored approach toward individual patient care, linking science and a humanistic approach (Smith 2002).

2 The Biopsychosocial-Spiritual Model

In the 1990s, spirituality was cautiously added to the model, therefore becoming the biopsychosocial-spiritual model (Borrell-Carrió et al. 2004; McSherry and Jamieson 2011; Sulmasy 2002). This holistic model acknowledges that a person is made up of biological, psychological, social, and spiritual aspects: each facet relationally interacting and affecting the other (McSherry and Jamieson 2011; Sulmasy 2002). The biopsychosocial-spiritual model of health helped to articulate that well-being was associated with health across all of those dimensions. Conversely, suffering occurred when any of these domains are affected.

The term spirituality has its historical roots within a religious context (Muldoon and King 1995). For many people, this link with religion is maintained, and many use terms such as spirituality and religion almost interchangeably (Sloan et al. 1999). In more recent times, this view of spirituality as the domain of one or even any religion has been increasingly challenged. Many people now take the view that religion and spirituality are related but separate concepts (Sulmasy 2002; Edwards et al. 2010; Selman et al. 2011; Chochinov and Cann 2005). In this view, a person's spirituality can be expressed in many contexts outside a formal or even informal religion and acknowledges that spirituality means different things to different people (Egan et al. 2011).

A review of publications dealing with spirituality and end-of-life care has identified several dominant themes including transcendence both in relation to self and a higher being, a sense of communion or connection, faith or beliefs, and hope (Vachon et al. 2009). Transcendence is

defined variously, but the central issue is of "going beyond" our physical selves (Zinnbauer et al. 1999). Although it may be expressed within the context of a relationship with God or the sacred, it may also be about nature, art, music, family, or community (Puchalski and Romer 2000). In this broader view of spirituality, it is most commonly conceptualized in terms of those aspects of life that lie at the core of a person's identity and direction and may be understood at an individual or a population level. These aspects include the beliefs, values, activities, and relationships that provide meaning and purpose for life (Egan et al. 2011).

These issues of meaning and purpose have long been regarded as central to the concept of spirituality. Early proponents of the importance of existential or spiritual issues in suffering and resilience such as Viktor Frankl suggested that meaning and purpose lie at the heart of spirituality (Frankl 2006; Muldoon and King 1995).

What emerges from this literature is that while it is very difficult to reach consensus, spirituality can be broadly defined as an experience that incorporates a relationship with the transcendent or sacred that provides a strong sense of identity or direction which not only has a strong influence on a person's beliefs, attitudes, emotions, and behavior but is integral to a sense of meaning and purpose in life.

3 Symptoms and the Biopsychosocial-Spiritual Model

Therefore, the person who presents to the clinician is not only afflicted by physical symptoms such as intractable pain or breathlessness but brings with them a complex, rich, but often disabling tapestry of psychological symptoms such as anxiety, depression, hopelessness, guilt or fear, social disruption, and existential or spiritual symptoms such as loss of identity, meaning, and purpose (Beng 2004; Ellis and Lloyd-Williams 2012; Sulmasy 2002).

This biopsychosocial-spiritual model, with all aspects interacting equally, accommodates all potential interests, worries, and questions of the patient, providing a full "scientific" picture of each individual (Kelly 2012; Smith 2002). This is a fundamental aspect of palliative care, to enable and support the whole person to be supported in living with a terminal illness. Accompanying this is the need to ensure effective communication with all concerned.

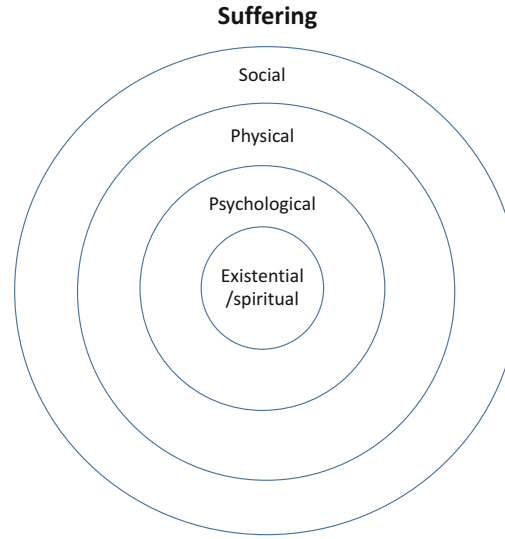

Fig. 1 The totality of suffering

Any existential crisis of being, meaning, and purpose brings spiritual pain and disconnectedness to the forefront within palliative care trauma (Burke and Neimeyer 2012; Puchalski 2002). The hearing of a terminal prognosis can confront an individual with the reality of nonexistence. It is therefore not surprising that some consider this the essence of spiritual pain.

4 Symptoms: Looking Before and After

Symptoms of course do not occur in isolation. By nature, symptoms are indicative of disease. Much of medical training is devoted to recognizing symptom clusters that indicate the presence of a specific disease that can then be treated. By definition, a primary focus of palliative care is palliation – symptom management. In fact, there can often be frustration at other professionals who, for a variety of reasons, encourage ongoing treatment when cure is no longer likely and

palliation and support are more appropriate. The transition from cure to palliation is not an easy one for the health practitioner or the person affected.

Although this transition is an important one, it is also important to not let go completely of that model which relies on symptoms to identify a treatable cause. Although the symptoms may be generally due to a cancer or another disease which is no longer treatable, they may be due to a specific pathology that is. For example, with someone with cancer and back pain, identifying the fact that the pain is due to vertebral metastases may have very specific implications for how it is managed. Therefore, although in some circumstances a decision may still be made against providing treatment, the first step in symptom management is to identify the underlying cause of the symptom.

Having done that, if it is decided that the focus of treatment is symptom management, then the next step is appropriate and skilled management of the presenting symptom. As described in the following chapters, there are evidence-based approaches and guidelines that can be applied to assist the person with these particular symptoms.

However, it is to be hoped that assessment and treatment do not stop with that specific symptom no matter how successful. Symptoms not only have a cause; they also have an impact. The impact affects the whole person: (a) physically through specific symptoms and general debilitation; (b) psychologically through depression, anxiety, fear, anger, hopelessness, etc.; (c) existentially or spiritually through the impact on identity, meaning, and life purpose, and (d) socially through the impact on relationships.

In the case of pain, this means not just identifying and assessing the cause and intensity of the pain and prescribing an analgesic but exploring the psychological, social, and spiritual/existential issues associated with the pain. All of these together make up potential suffering or, as Cicely Saunders termed it, "total pain."

Robert Twycross (1995) wrote descriptively about aspects of what had earlier been identified as the components of total pain. In illustrating the four principal dimensions of this symptom, he wrote about anger at delays in diagnosis and treatment, at therapeutic failure, at disfigurement, and at feelings of helplessness (psychological). He described worries about family, finances, job prestige, and income and feelings of abandonment and isolation (social). He described physical symptoms relating to illness, adverse effects of treatments, and the fatigue that follows the debility associated with disease progression (physical). Finally, he suggests that people ask: Why is this happening to me? Why now? What's the point of it all?" - in other words, spiritual distress.

Eric Cassell (1991) writes about suffering in similar terms – that is, in having many dimensions – although all may be viewed as making a whole person and any impending destruction or disintegration of the person may lead to suffering.

He writes of our inability to reduce a person to their parts in order to better understand them but to acknowledge that we all have certain features which define us. We have personality and character. We have a past, life experiences, a family, and a cultural background. Each person has roles, and none of those roles really exist without others; we have relationships that allow expression of happiness, anger, gratitude, and many other emotions. It is within relationships that we express our sexuality. We have relationships with ourselves and with others; we are political; we do things; we have behaviors; we have a secret life and a perceived future; and every person has a body, and everybody has a transcendent dimension. When one or another of these parts begins to peel away from the whole – disintegration – then perhaps that is when we begin to suffer. So, it is really impossible to reduce suffering without at least identifying and acknowledging these many facets of what it is to be human.

When looking at the management of symptoms, we need to at least try to envisage who this person is – in all their dimensions. Is there anything to suggest loneliness? How will this affect each symptom? The realization that one's future is

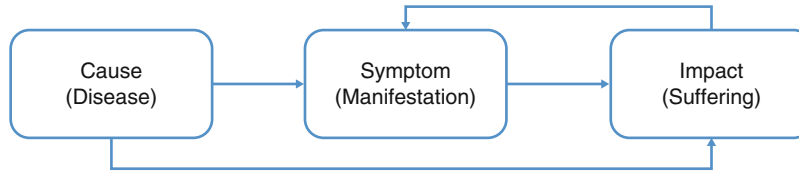

Fig. 2 Holistic view of a problem

short and is dissolving rapidly brings with it fears, anxieties, concerns, and even despair. There is often an acute awareness of the finitude of life and, with that, a sense of powerlessness and even at times a loss of meaning.

Palliative care is therefore more about moving toward the impact of the disease and its symptoms than treating its cause. It therefore calls for an approach that is holistic and that does more than merely treating symptoms but sees the impact of both the disease and its resultant symptoms on the person in their entirety. At the end of life, people present with a constellation of physical, psychological, social, existential, and spiritual issues that call for consideration on their own merits.

5 The Symptom of Pain

5.1 Pain as a Symptom

Pain is one of the most common presenting symptoms in palliative care, and the following section of this textbook contains a chapter which very thoroughly covers the management of pain as a symptom. It is not our intention to provide another overview of managing pain but rather to use pain as an example of the holistic approach that we have described so far.

5.2 Pain Is More Than a Symptom

In essence, pain has traditionally been regarded as a symptom. What this means is that pain is indicative of a disease process that needs to be fixed. While pain needs to be relieved, the main focus is identifying the cause so that the pain may be removed.

This traditional view of pain as a symptom works well in the management of acute pain. If we are working in the emergency department and someone presents with colicky abdominal pain or severe pain in a limb following a fall, it is appropriate that efforts are put toward determining the cause of the pain so appropriate treatment can be instituted. In this situation, pain as a symptom merely acts as a warning sign that something is wrong and needs to be fixed.

However, this traditional view of pain as a symptom has been questioned (Siddall and Cousins 2004). In the field of pain medicine, there has been a move to see pain not just as a symptom but as a disease in itself. This view is based on two underlying facts. One is the growing understanding and recognition of the multitude of physiological changes that accompany the sensation of pain. These changes extend from receptor changes in the periphery through to neuroplastic changes in the brain. This knowledge argues against the concept that the sensation of pain is simply due to activation of a peripheral receptor which is transmitted and then finally perceived as pain. These changes not only modify and modulate the transmission of sensory information which has a profound impact on pain, but they may also result in long-term changes that are responsible for the continued perception of pain even when there appears to be no noxious inputs.

5.3 Biopsychosocial Model

The second fact that underlines the limitations of viewing pain as a symptom is the growing incorporation of the biopsychosocial model of pain. Like palliative care, pain medicine has been a strong adopter of the biopsychosocial model, and it has become the dominant framework for

the understanding, assessment, and treatment of persistent pain (Keefe and France 1999; Loeser and Melzack 1999; Turk 1999).

Viewing pain as a symptom runs the risk of a singular focus on the physical and biomedical at the expense of the psychological and social. This approach is almost acceptable in the emergency department. However, it is hopelessly inadequate for almost any situation where pain lasts for more than 3 months or for where pain is accompanied by other issues which profoundly affect a person's psychosocial milieu, of which end of life is a prime example.

This incorporation of the biopsychosocial model means recognizing the bidirectional nature of these multidimensional interactions. Pain, as we have said, is not just a symptom that is merely registered by the brain. It has an impact. This includes the physical with increase in heart rate, blood pressure, and muscle tone. It includes the psychological with fear, anxiety, frustration, and depression. It includes the social with withdrawal or seeking help on one side and solicitousness, fear, and possibly helplessness on the other. Therefore, treating pain as a symptom means not just identifying its presence and intensity and relieving it but identifying and managing the secondary issues that almost invariably accompany pain in a myriad forms. This is a challenge, but treatment that does not recognize and address the impact on all these areas is likely to be incomplete.

5.4 The Addition of the Existential/Spiritual

The biopsychosocial model has been a major advance in many fields including the management of pain. However, as mentioned above, there has been a move to incorporating the existential and spiritual as an addition to this model. In the palliative care field, Cicely Saunders was an early advocate for the inclusion of the spiritual and the concept of "total pain."

So much has been written about Cicely Saunders and the concept of total pain that it is worth reviewing how that concept came about. Saunders was a meticulous keeper of records and recordings that give us insight into the ideas that she developed over time. As early as 1959, she wrote "Much of our total pain experience is composed of our mental reaction. . .." Saunders developed her ideas and published continually in order that the general readership could be alert to her findings. By 1964a she had more clearly articulated what later became the notion of "total pain" by describing an encounter with a patient. ". . .She said, 'Well doctor, the pain began in my back, but now it seems that all of me is wrong.'. . .And then she paused before she said, 'But it's so wonderful to begin to feel safe again.' Without any further questioning she had talked of her mental as well as physical distress, of her social problems and of her spiritual need for security." That phrase "all of me is wrong" is used later to introduce the concept of "total pain" that has become one of the hallmarks of palliative care practice (1964b) (All of this information comes from David Clark's manuscript "Total pain," disciplinary power and the body in the work of Cicely Saunders, 1958–1967. *Social Science & Medicine* 49 (1999) 727–736.).

5.5 The Biopsychospiritual Model and Pain

Although the field of palliative care has been a leader in advocating and using a biopsychospiritual model, it is increasingly recognized that it is a helpful approach in managing pain (Wachholtz and Keefe 2006; Büssing et al. 2009; Rippentrop 2005; Wachholtz et al. 2007). One of the possible reasons for its strong adoption in the palliative care field is the awareness of the importance of existential issues such as meaning and purpose which can loom larger in those facing death. Not surprisingly, studies that have examined these issues have found that spiritual well-being is profoundly impacted in people with cancer or HIV/AIDS (Boston et al. 2011).

While there are a large number of studies going back some time in the palliative care field that look at spiritual and existential factors, there are relatively few in the field of pain medicine. However, there are now several studies that indicate that spiritual or existential well-being in people

with chronic pain is impacted to the same extent as those who have cancer and are facing the end of life (Siddall et al. 2017).

These findings indicate that not only does pain have an impact physically, emotionally, and socially but it also has a profound impact on existential issues such as meaning and purpose. This highlights more strongly the importance of identifying and assessing these issues as part of the assessment of pain.

5.6 Addressing the Existential and Spiritual

It has been demonstrated that those with higher levels of spiritual well-being are more optimistic and have higher levels of self-esteem and higher levels of function (Cotton et al. 2006). This research in the palliative care field now overwhelmingly supports the importance of addressing spiritual issues in people facing a terminal illness (Cotton et al. 2006). This has led to the exploration, trial, and use of treatments that specifically seek to address spiritual issues (Breitbart and Heller 2003; Breitbart et al. 2010; la Cour and Hvidt 2010).

Recent evidence suggests that the use of spirituality and religiosity can be regarded as an active and positive coping process with beneficial effects (Büssing et al. 2009). For example, those who deal with persistent pain using positive spiritual coping practices such as looking to God for strength and support adjust better to pain and have significantly better mental health (Bush et al. 1994; Rippentrop 2005).

Religious and spiritual coping strategies are associated with feelings of spiritual support and connection as well reduced depression and anxiety and a greater sense of peace and calm. This may be due to a number of factors including the ability to ascribe meaning to the suffering, increased self-efficacy, spiritual and social support, distraction, relaxation, and positive reappraisal (Wachholtz et al. 2007; Dezutter et al. 2011).

The overall evidence suggests that spiritual well-being has a stronger link with higher pain tolerance and higher levels of psychological well-being including satisfaction with life (Moreira-Almeida and Koenig 2008; Dezutter et al. 2010).

5.7 Suffering

In talking about these issues, it can also be seen that the further we get from the symptom, the more general the impact. This total impact is what we often refer to as suffering. While pain and suffering are often linked, most physical symptoms will be associated with suffering. This combination of symptoms leads to suffering, and in the end, the relief of suffering – in all its dimensions – is the primary goal of the health professional caring for those at the end of life.

Although the relief of suffering has always been a goal of physicians, Eric Cassell brought suffering to the fore in medicine with his landmark paper (1982) and subsequent book (1991). He writes eloquently about the disintegration of the self and injuries to the integrity of the person that can be manifest as sadness, anger, grief, and withdrawal. However, he points out that these are merely outward expressions of injury, pain, and disintegration and if the injury is sufficient, then the person suffers. By attending to the meaning of such suffering and perhaps assisting patients to transcend it, Cassell suggests that such suffering (associated with the destruction of those aspects of personhood) may be ameliorated. To quote Cassell, "Transcendence is probably the most powerful way in which one is restored to wholeness after an injury to personhood" (p. 644) (Cassell 1991).

This recognition that all symptoms result in a shared impact on our psychological, social, and existential or spiritual selves argues for a layered approach that seeks first to identify physical symptoms as a totality and then explores the psychological, existential, spiritual, and social impact. It also means identifying management strategies that address each of these secondary issues independent of the presenting symptom. For example, while there is evidence to support the use of psychological approaches in managing pain, most of these are not specific to pain and may have limited impact on the intensity of pain.

Therefore, it could be argued that we should do our best to treat the physical aspects of each symptom first and then address the other symptoms that may accompany it.

6 Management of Some Other Symptoms

6.1 Breathlessness

Another symptom that lends itself to a holistic management approach is breathlessness. Historically, the assessment of breathlessness has tended to focus on the physical attributes of that symptom and has necessarily focused on the physical or sensory features, without including psychological reactions and subjective observations.

It is often suggested that the most effective treatment for breathlessness is prevention, so attention to the detail of the nonphysical dimensions of this complex symptom is essential. Breathlessness can be seen as a global symptom, but deconstructing the symptom is often helpful in its management. Adaptive breathing patterns are built up often over months or even years, and those patterns become familiar to each individual.

For each individual, however, there can be a disjunction between the rate and depth of breathing so that the health professional can remain confused by mere observation of breathlessness. Psychosocial therapies involved in the management of breathlessness not only rely on an understanding of an intensity measurement which shows the quantity of breathlessness, but attention must be paid to the *quality* of breathlessness in order to help to recognize the most appropriate therapeutic intervention. Skevington et al. (1997) underlined the potential value of the linguistic qualities of breathlessness, designing a scale of breathlessness that was proposed to help to direct the therapy to the most appropriate quality. Those authors reinforced the understanding that breathlessness was not purely a sensation but included significant affective and evaluative features. They also showed that breathlessness included a distinctive, consistent, but relatively small component of low energy which had often been subsumed within physical sensations in other studies (Table 1). One outcome was that asking the question "How would you describe your breathlessness today?" can prove useful in helping to identify the most helpful therapeutic intervention. For example, if a person describes their breathlessness by using descriptors such as frightening or panicky, then it is proposed that adopting a more psychological approach could be beneficial.

Table 1 Structure for a scale of breathlessness

1. Physical sensations
2. Affective/evaluative
3. Low energy
4. Hyperventilation
5. Speechless

Similar observations had previously been made by Kinsman et al. (1974, 1977) when exploring breathlessness in people with asthma. Their original studies focused on two *mood* symptom categories and two *somatic* categories, and this work was elaborated in later studies identifying categories of breathlessness and congestion alongside three secondary mood categories, worry, loneliness, and anger.

6.2 Exploring the Impact of Breathlessness

The process for identifying an appropriate approach to psychosocial management of breathlessness could include a number of elements (Corner et al. 2016):

1. An exploration of the *meaning* of breathlessness for the patient and family and the feelings associated with that meaning. This includes asking how those people respond to breathlessness psychologically:
   What fears do they have?
   – One of the most commonly held fears is that the patient will choke to death or suffocate.
   What has been lost by the development of breathlessness?
   – Loss of control, independence, or physical function is often seemingly relentless.

What degree of control do those people feel they have?

– They may feel that health professionals have control with the use of medications, or they may feel that their breathing controls them rather than the other way round.

Do they feel responsible in any way for their breathlessness?

– Exploration of their lifestyle before illness and any "blame" attached to that for the development of their breathlessness.

How do they respond to feelings of panic, anger, loneliness, or worry?

– Most people have learned coping strategies for similar emotions throughout their lives that may not be relevant or effective in this situation.

What are their hopes for future management of breathlessness?

– Is their hope realistic or are they hoping for an impossible cure?

What goals do they have for their future?

– Again, goals for the future must be set in realistic terms.

How can they see themselves developing greater control of their breathlessness?

– This can be a most effective way of rebuilding hope.

6.3 Case Histories

Pat was a 28-year-old woman with a neuroendocrine tumor that progressed rapidly. Throughout her involvement with the hospice team, her predominant symptom had been severe bone pain in multiple sites. About 3 weeks prior to her death, she developed intermittent but severe breathlessness with coughing and retching. No physical cause was identified and her distress became intense. She described her breathlessness as "choking," "suffocating," and "as if I can't get my breath." Exploration of her fears revealed that she was indeed fearful of suffocation, and ultimately she was able to confide in one of the team that she had previously been in an abusive relationship where her partner had tried to strangle her. Discussion of this with reassurance that there was no reason for her to choke or suffocate led to a dramatic reduction in her perception of breathlessness. Despite the later development of a bronchopneumonia, she never expressed feelings of breathlessness in such distressing terms again and remained in control of her breathing until she became unconscious prior to death.

James was a 72-year-old clergyman with chronic obstructive pulmonary disease who was steroid dependent and required continuous oxygen therapy when he was first seen by a hospice team member. He was concerned that he was achieving nothing and had nothing to look forward to. On further inquiry it transpired that he had lost his faith and had serious doubts about his previously strongly held religious convictions. A variety of techniques for relaxation including imagery were discussed, and work with the spiritual care team helped him to make some sense of his doubts and fears. Over a period of 2 weeks, he learned the effectiveness of imagery for him and became more relaxed and confident – looking forward to participating in his family life. He was able to discontinue his use of oxygen. He talked of his feelings of guilt for some past events and achieved a sense of resolution and forgiveness for himself.

1. A process of education for both patient and family about the meanings, significance, and process of breathlessness

   This includes an explanation of how and why breathlessness has developed including possible psychosocial and behavioral risk factors (e.g., smoking). The anatomy and physiology of breathlessness can be outlined, if appropriate. An understanding of the normal mechanisms for the control of breathing can be a simple and effective way of empowering people with breathlessness. The efficiency and effectiveness of differing breathing techniques should be explained using examples of positioning, muscle groups involved in breathing, and rate and depth of respirations associated with the unlearning of any maladaptive techniques that may have already been utilized.

2. An acknowledgment that breathlessness may be a symptom that may never "come right" and therefore exploring more helpful ways of carrying out everyday tasks and activities

   This aspect of management should include a discussion about the difficulty of maintaining hope while the prospect of cure is no longer possible or likely. An acknowledgment that the professional carers have a commitment to the patient and family and the confirmation that the carers will not lose interest in them as the illness progresses.

   Other modes of therapy can be hugely influential in improving symptoms. Over 20 years ago, music therapy was identified as a useful adjunct in many aspects of palliative care. The discipline continues to develop as evidenced by international activity and development of techniques.

   Given that breathlessness has many dimensions, music therapy can be a useful adjunct in the management of this symptom. In this context, music therapy is the controlled use of music, its elements, and their influences on the human being to aid in the physiological, psychological, and emotional integration of the individual during an illness. It can act as a catalyst in mobilizing deeply held beliefs and feelings and can assist in communication. From a psychosocial point of view, it can help in identifying and reinforcing self-concept and self-worth, it can help to improve the patient's mood, it can help with recall of past significant events, and it can help in exploring fantasy and imagery. From a social point of view, it can act as a means of socially acceptable self-expression, recreating a bond and a sense of community with family members, as a link to the patient's life before illness, and as entertainment and diversion.

6.4 Art Therapy

Restoring creativity to the dying patient has been long held as an important goal of palliative care teams. As with music therapy, art can be used to help to promote a healthy and safe environment. It can be used as a diversion from pain and breathlessness. It can assist in rehabilitation and can help to build esteem. Where art therapists are not available, this role has been sometimes filled by occupational therapists and physiotherapists. An art therapist has the specific goal of helping patients express themselves with communication being the prime goal. The artist is concerned with the patient, and the artwork is the expression of that patient, nothing more. Patients can be encouraged to become actively involved in creating a picture or painting, or they can choose to watch others. Being part of a creative process can provide an escape from everyday life and can help individuals explore their creativity and have fun, which can often be a useful diversion from troublesome or distressing symptoms.

For the purposes of definition, art can include all forms of creative and interpretative expression. Other aspects of the arts, which have been used successfully in the management of symptoms near the end of life, include biography work, journaling, reminiscence therapy, and poetry. It has been suggested that we can express in written words things that we find hard to say, and so poetry and prose can have a significant part to play in the discovery of the journey toward the end of life. The arts can also provide a most effective means by which a legacy can be left for the family. During the preparation of such items, a focus on relieving symptoms such as breathlessness can be maintained.

Using some of these approaches, as part of a rehabilitative dimension to the management of pain or breathlessness, has been reported anecdotally by many as being useful in complementing a more medical approach.

6.5 Case History

Mary was a 54-year-old woman with widely metastatic breast cancer who became severely breathless toward the end of her life as a result of lymphangitis carcinomatosis. Discussion with her about discharge from the hospice in-patient unit led to a recognition that she was fearful of going home because of the severe limitations she

perceived her breathlessness would have on her activity and quality of life. She chose to express this in artwork in which she drew "her life." This work indicated to the therapist the areas of her life that she perceived as difficult, and she was able to eliminate some of these through discussion and planning. She later redrew her life with "boundaries" in place that she felt comfortable with, and her discharge was completed successfully. She was confident that she would remain in control of her breathing – this was the case until the end of her life, at home, some weeks later.

6.6 Nausea and Other GI Problems

Many other symptoms can be used to illustrate this multidimensional nature. People approaching the end of life frequently experience symptoms such as nausea, anorexia, progressive weight loss, and, in some, malnutrition. Because of the social nature of food provision and acceptance, these symptoms and signs can impact heavily on the relationship between patient and carer. Taste and smell abnormalities are reported in a majority of people with advancing cancer (Brisbois et al. 2006). People with cancer face a number of barriers to food intake that include phantom smells, persistent bad tastes, hypersensitivity to odors, and food aversions to the point of nausea. Sometimes, little if anything is done to address these issues, and yet they can have a significant adverse effect on quality of life. Merely providing medication either to reduce nausea or to attempt to stimulate appetite is often a futile gesture aimed to encourage patients and families that "something is being done." Family members may go to fairly extreme lengths to monitor food intake when someone is nearing the end of life – monitoring intake is accompanied by tempting with favorite foods and adjusting portion sizes. One study even identified force-feeding taking place (Meares 1997). Anecdotal evidence suggests that healthcare providers are frequently challenged by family members to "do something" to ensure adequate food intake. This challenge often has the spillover effect of making the patient feel uncomfortable or even guilty.

What we know however is that chemosensory changes take place when someone is dying and these may be produced by numerous micronutrient deficiencies, medications, infections, poor oral hygiene, dry mouth, etc. There is no easy answer to these problems, but acknowledging them is the first step to finding solutions. Much social and psychological disquiet and even distress can arise with seemingly simple "physical" symptoms such as nausea and anorexia, so addressing them and talking with patients and families is a first step to helping them understand. Decreased sensitivity for sweet and sour is common, but also an altered sensation for bitter has been reported (Mahmoud et al. 2011) Sensory enhancement of food may help (adding spices, flavors, herbs), but working with the family and patient to find a solution together may be the best option available (Brisbois et al. 2006). Findings from a Canadian study (McClement et al. 2003) suggest that family members' behavior regarding nutritional care is influenced by "the personal beliefs they hold regarding the patient's illness experiences." Some will "fight back" in the belief that is promoted by much mainstream media that cancer and/or death is something that needs to be "fought," "defeated," or "beaten." Such an approach (which may not be taken by all involved) can have a devastating effect on the morale of either the patient or the family. Differing beliefs between patients, family members, and healthcare providers need to be identified and worked through in order that conflicting expectations of treatment regimens do not arise which in turn may cause social and psychological distress. Such a step is important in order to develop an effective holistic plan of care.

6.7 Fatigue

Perhaps one other symptom that best illustrates multidimensional aetiology and effect is fatigue. Fatigue is ubiquitous in end-of-life care with a majority of patients experiencing it, but in some studies, it has been found that patients rarely discuss it because of a perception of doctors to offer effective interventions or patients' lack of

awareness of effective treatments (Passik et al. 2002). However, we know that fatigue is one of the most frequent symptoms that has a significant effect on quality of life, not only in people with cancer (where the fatigue may well be related to treatment) but also in nonmalignant diseases such as heart failure and neuromuscular diseases and HIV/AIDS. Physical fatigue prevents participation in many of the activities of daily living, whereas cognitive fatigue makes many activities more challenging; many fatigued people feel grumpy, irritable, listless, or depressed (Radbruch et al. 2008). The qualitative difference of cancer-related fatigue to fatigue in everyday life has been stressed; "Fatigue in cancer patients is a subjective feeling of unusual tiredness, affecting the body (physical), the emotions (affective) and the mental function persisting for several weeks and relieved only partially or not at all by rest or sleep" (Glaus et al. 1999). Correspondingly, various modalities for treatment have been suggested. Physical treatments include anti-cytokine or anti-inflammatory pharmacological approaches, but other modalities include cognitive-behavioral and psychosocial interventions including mindfulness-based approaches, yoga, acupuncture, and exercise. All of these latter modes will necessarily impact on psychosocial or spiritual dimensions of this symptom. These forms of management have not been tested in any rigorous way but may be useful in addressing the multifaceted reality of fatigue in these patients (Radbruch et al. 2008). Given that this is such a common symptom, it is necessary that research efforts are strengthened to identify the most effective forms of management for this most distressing and persistent symptom not just for people with cancer near the end of life but also for those with debilitating nonmalignant diseases. Energy must be used not just to find pharmacological interventions that are effective but also non-pharmacological modalities that will address the nonphysical dimensions of fatigue. In fact, a recent review indicates that exercise and psychosocial interventions are significantly better than pharmacological interventions in reducing cancer-related fatigue and should be regarded as first-line treatment (Mustian et al. 2017).

6.8 The Role of the Practitioner

This chapter has so far focused on the concepts underlying a multidimensional approach to the management of symptoms and how this applies to the person facing many of the common issues seen at the end of life. The chapter would not be complete without also discussing the role of the other key person in any health interaction: the health practitioner.

The health practitioner is of course the central bridge between the concepts and the patient. It is what the health practitioner brings in terms of knowledge, beliefs, values, and even capacity that determines the effectiveness of the therapeutic encounter. The practitioner who brings a singular focus on the physical symptoms of the patient's presentation may have success in treating those symptoms. However, there is a very good chance that they will leave the patient only partially treated and only partially satisfied. Even worse, it can result in depersonalization that results in the classical description of the case with breathlessness in Bed 14.

There is abundant evidence that the modern patient is left curiously underwhelmed by modern medicine. Despite the many advances in disease treatment and symptom management, there are a growing number of people who are skeptical and rejecting of what modern medicine has to offer. This applies at both ends of the life spectrum. Our media abounds with stories and debates of everything from rejection of childhood immunization to rejection of chemotherapy in favor of "traditional" or folk medicines, sometimes with tragic consequences.

It is not possible to fully discuss all the reasons for this social shift, and it is not really relevant to the topic at hand. However, many have landed at least part of this skepticism and rejection at the foot of modern medicine's ever-increasing focus on the symptom at the expense of the person. Many people come away from a health encounter feeling fully investigated but hardly heard. Much of modern healthcare appears to focus perhaps inappropriately solely on the diagnosis and management of disease rather than on the management of a *person*

who happens to be experiencing the impacts of a disease.

It is encouraging to know that in a field of disciplines that have focused more and more on the symptom and less and less on the person, palliative care often stands out as a discipline that has had its beginnings in a rich tradition of holism and continues in that tradition. It is imperative for the best possible care to continue in that same tradition. Not only is it good for the people we care for; it is good for our own selves. Palliative care more than many disciplines offers a relationship with the person that is often rich and rewarding. The particular issues faced by those who are dying offer the opportunity to interact with a person not only on the level of the physical but also the psychological, social, and even existential and spiritual. As Christina Puchalski (2002) has eloquently stated:

> It is also through that dimension that I think the compassionate, caring part of the doctor/patient relationship is enacted. . . . . What has happened over the last 30 years is that science has really led medicine, and a lot of the nontechnical aspects of medicine have been neglected. The spiritual assessment brings us back to those compassionate, caregiving roots of the patient-doctor relationship. . . . . When you get involved in a discussion with a patient about his or her spirituality, you enter the domain of what gives that person meaning and purpose.

6.9 Which Practitioner?

Discussing the role of the practitioner necessarily raises another question: which practitioner? A dominant focus on the palliation of physical symptoms can mean that the primary role of palliative care falls to medical and nursing staff with some involvement of other practitioners such as physiotherapists, occupational therapists, psychologists, social workers, and pastoral care workers depending on the needs of the person.

However, a broader focus on not just physical symptoms but also psychological and existential/spiritual (i.e., the whole person) can mean a slightly different approach. Firstly, it may mean a stronger reliance on and involvement of the multidisciplinary team. Palliative care is a leader in multidisciplinary management and has traditionally recognized the important contributions that different disciplines make to the care of the dying person. Despite this, the involvement of other health professionals can be relatively minor or only occur when other symptoms become distressing or intrusive and need to be addressed.

Although physical symptoms are often seen as primary, facing the end of life has a major impact on a person's psychological state and, for most, raises deeper existential questions. For a large proportion, there is abundant evidence that the impact is severe enough to be clinically important and require intervention. A model that recognizes the importance of all dimensions – physical, psychological, social, and existential/spiritual – means firstly a keen awareness including formal assessment that addresses all of these domains as well as early referral to an appropriate practitioner to follow through with assessment and address the problem. Given the frequency with which facing the end of life has an impact on each of these domains, it is likely that other health practitioners are currently vastly underutilized. Providing excellent palliative care requires administrators to recognize the importance of these other health professionals in caring. It also requires those who have the primary role in management to value the contribution of these other health professionals and make use of them.

A broader view that sees the contribution of physical, psychological, social, and existential/spiritual to overall suffering brings us back to our original question: which practitioner? The previous paragraph may suggest greater involvement of specialists in each of those domains, for example, bringing in a clinical psychologist or psychiatrist to address psychological issues, a social worker to address social issues, and a clinical psychologist, psychiatrist, or pastoral care worker to address existential or spiritual issues. This approach is in line with the trend in modern medicine to specialization and recognized expertise in different domains and in some quarters has been recommended as an approach to address all of these factors in a holistic fashion.

Although there is no doubt that people with expertise and training in a specific domain bring a

specific set of skills that are valuable, there may be several dangers to a move to a specialization of care. First, it can result in a very reductionist approach that breaks down the person into various interrelated but separate domains that are the province of different specialists. This means that you need the doctor or nurse to help with your body, the psychiatrist or clinical psychologist to help with your mind, and the pastoral care worker to help with your spirit. This can mean that the doctor or nurse does not see the psychological or existential as their domain and either neglects to explore them or, if they are raised, quickly moves to organize a referral to another practitioner.

This division of labor has the potential to lose an opportunity to build on the trust and connection that may have developed with this practitioner and which are crucial factors in exploring these other domains. It may also deny the practitioner the opportunity to develop a deeper relationship with the person who is dying as they explore and wrestle together not just with physical symptoms but with deeper psychological, existential, and spiritual issues.

Although it is important not to diminish the contribution of someone with specific skills, it is also important not to diminish the contribution that any member of the team can make across all of these domains. In fact, for some patients, the most significant encounter of the day may be with the cleaner or kitchen hand who through their empathy and care exhibits a compassion that touches their psychological and even spiritual needs.

Therefore, we would suggest that if we are to see physical symptoms as one small dimension of the suffering experienced by the person who is dying, it necessitates a strong reliance on the whole multidisciplinary team. In many situations, this will be because of the specific training and expertise of some disciplines who may be called in to help with different aspects of the person's suffering. However, often it will not be the training and skills but the qualities that any member of the team brings that mean an opportunity for almost any encounter to have a profound impact for the patient which can also be deeply meaningful and satisfying for the health practitioner.

6.10 The Care of the Health Practitioner

The quote by Christina Puchalski raises an issue that is perhaps an important one to close this introductory chapter. If we are to approach the person as not just someone with physical symptoms but a person who brings a whole host of other issues in the psychological, social, existential, and spiritual domains, the therapeutic encounter and relationship may be immensely satisfying and effective for both parties. However, it also brings a cost.

As Puchalski states, the roots of caregiving are grounded not just in expertise in elucidating and managing relevant symptoms but in compassion. Compassion at its heart means "to suffer with." For those who aspire to practice a holistic model of care, this means not only sharing someone's distress at physical pain, breathlessness, or fatigue but their sadness and fear, their loss of relationships with loved ones, and even their existential distress at the prospect of death.

To turn to neuroscience, brain imaging clearly demonstrates that those who are empathetic share others' pain in a very real and active sense. Visualizing another person in apparent pain results in activation of brain regions that are part of the pain network (Singer et al. 2004). Thus, if we are to work with people who are suffering and if we are to care, then we will not just figuratively but physiologically share their pain with them.

Knowing this helps us understand the relatively high rates of burnout in those caring for people who are dying. There is an option of extracting ourselves emotionally, and in fact, those with less empathy have reduced brain activation and presumably less distress. However, is this the best option for ourselves or for the people we care for? The other option is to develop ways of dealing with our own suffering that enables us to continue to deliver care with both dispassionate professionalism and compassionate support.

The way to do this is varied and each individual has their own ways of self-care. However, it is important that all health professionals recognize the impact of compassionate palliative care and ensure that they have ways to ensure their own health. This will ensure that they are able to not

only continue to practice but practice in a way that provides the best possible for the people under their care. This will mean not just surviving but practicing with the energy and resources that enable them to provide the multidimensional care they would wish.

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Pain and Pain Management

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_10

Abstract

Pain is one of the most common symptoms encountered in palliative medicine. Good pain management involves ensuring pain is screened for, adequately assessed if present and appropriately managed. This includes targeted and systemic, nonpharmacological, and pharmacological approaches. This chapter seeks to give an evidence-based overview of approaches to screening for assessing and managing a patient's pain.

1 Introduction

Pain is one of the most common symptoms experienced by people, especially those with serious illness. The prevalence of significant pain increases as patients near the time to death, from nearly a third of the general public reporting moderate to severe pain 2 years before their death, to nearly half of people in their last month of life (van den Beuken-van Everdingen et al. 2016). Pain remains common in far advanced, noncancer, life limiting illness with prevalences recorded at 63–80% of patients with Acquired Immune Deficiency Syndrome, 41–77% of patients with heart disease, 33–77% patients with Chronic Obstructive Pulmonary Disease (COPD), and 47–50% of patients with renal disease (Solano et al. 2006).

Despite pain being such a common symptom, it is often inadequately controlled (Solano et al. 2006; Deandrea et al. 2008). Field testing of the WHO Three Step Analgesic Ladder approach suggested pain control is possible in 70–90% of patients (Ventafridda et al. 1990). However, for patients admitted into acute hospice care, significant rates of moderate or severe pain were found in most patients during their first 48 hours of admission (cancer 91.5%, dementia 75%, COPD 82.4%). Adequate pain control was reached after 24 hours in 64.3% of patients with dementia, 41% of patients with cancer, and only 28.1% of patients with COPD.

This chapter will discuss screening for and assessing pain, and approaches to manage pain including nonpharmacological techniques, a review of the WHO pain ladder (Fig. 1) simple analgesics, weak and strong opioids, adjuvant analgesics, and other strategies that may be of benefit.

2 Definitions

Pain has been defined in multiple different ways from the pathologically based "unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (International Association

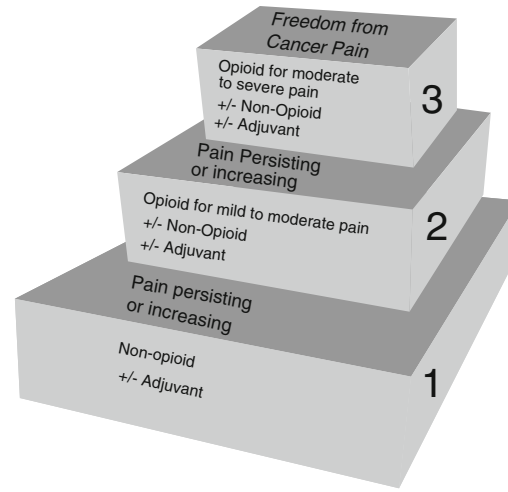


Fig. 1 WHO analgesia ladder (World Health Organisation 1987)

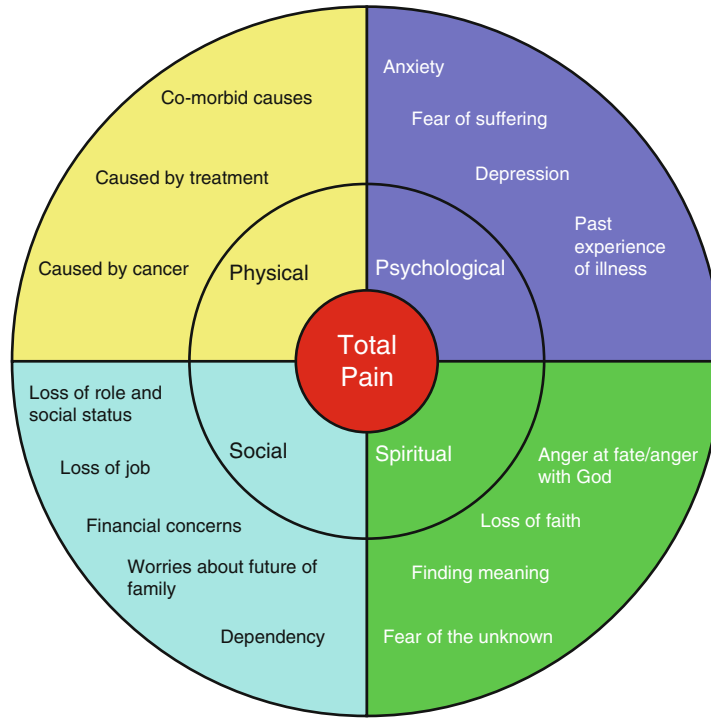


Fig. 2 Total pain (International Association for the Study of Pain 2009). This image is taken from the Total Pain Factsheet and has been reproduced with the permission of the International Association for the Study of Pain® (IASP). The image may not be reproduced for any other purpose without permission

for the Study of Pain 2017) to the more global approach by Margo McCaffery, who described pain as "whatever the patient says it is, existing whenever and wherever the patient says it does." The concept of "total pain" was very effectively defined by Dame Cicely Saunders, who wrote of hearing patients describe not just physical pain, but also associated psychological and social distress. She noted that some patients' pain did not respond to analgesia alone, but rather a holistic approach. Total pain encompasses the "division of a whole experience into physical, emotional, social and spiritual components." What we can take from this is that simply assessing patients for physical pain is likely to be inadequate (Fig. 2).

Physical pain can be due to the life limiting illness, comorbidities arising from the illness (e.g., pulmonary embolism), treatments for the illness (e.g., mucositis, post radiotherapy, chemotherapy induced peripheral neuropathy), or pre-existing disease (e.g., osteoarthritis). It is increasingly accepted that good symptom control, including pain, is linked with improved quality of life, lower levels of distress for both patients and caregivers, improved function, and indeed improved survival in patients with cancer (Davis et al. 2015). It is therefore of utmost importance that pain is assessed for, investigated, and managed appropriately.

3 Pathophysiology

The pathophysiology of pain has long been investigated. In 1664 René Descartes suggested that pain travelled along nerve fibers to the brain (Schug et al. 2015). The "Gate Theory" was first described in Melzack and Wall (1965) suggesting the involvement of both large and small diameter fibers modulating the pain response allowing pain modulation both by touch and central control mechanisms. The authors conclude in a statement still valid today "A 'modality' class such as 'pain', which is a linguistic label for a rich variety of experiences and responses, represents just such an abstraction from the information that is sequentially re-examined over long periods by the entire somesthetic system." Social and spiritual modulating factors have been included into this list in more recent time, leading to the biopsychosocial-spiritual model of pain.

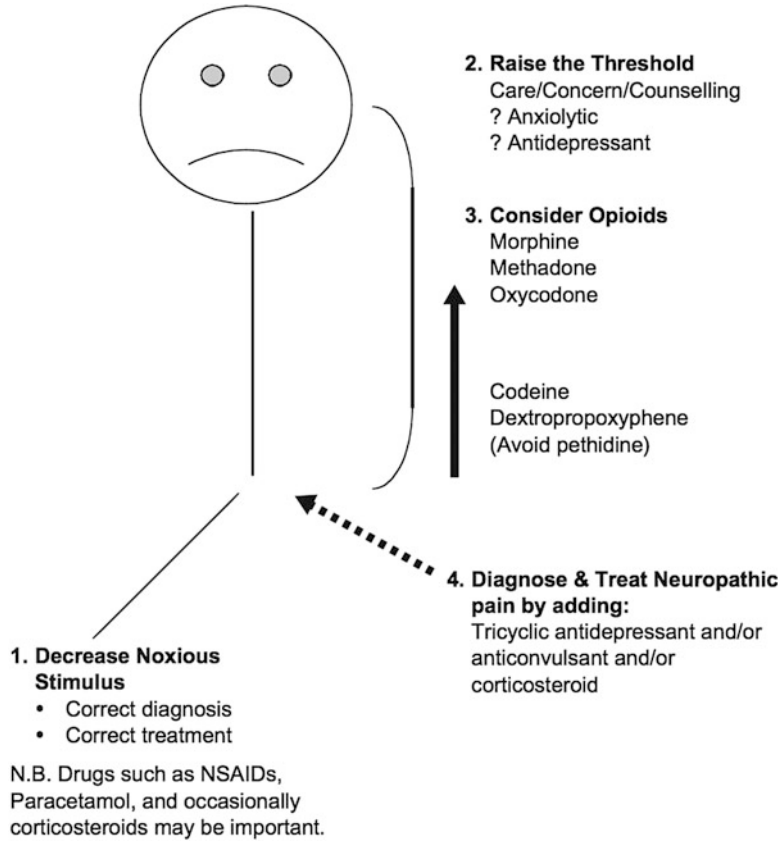


Fig. 3 The Sydney Stick Man (Lickiss 2001)

Norelle Lickiss suggested the concept of the "Sydney Stick Man" in the 1990s. It remains valid today when considering the pathophysiology of pain, as well as an approach to its management (Fig. 3).

As shown in Fig. 4, the pain pathway involves several processes: transduction, transmission, perception, and modulation. This requires interacting central and peripheral receptors as well as a group of factors unique to the individual experiencing the pain including environmental and psychological modifiers.

3.1 Transduction and Peripheral Transmission

The afferent pain receptors respond to physical (heat, cold, pressure) and chemical stimuli (the "chemical soup" e.g., COX-2, TNF-α, interleukins, prostaglandins, substance P, glutamate, proteinases, and chemokines). These receptors are widespread through the skin, muscle, joints, viscera, etc., and form part of both A-delta fiber (myelinated) and C fiber (unmyelinated) neurons.

Afferent fibers travel along the nerve (both myelinated A-delta fibers and unmyelinated C fibers), using mainly a fast sodium current, which may be blocked by local anesthetics, passing the cell bodies in either the dorsal root ganglion (for fibers coming from below the neck), or the trigeminal ganglion (for receptors based on the neck, face and oral cavity). The efferent fibers then synapse in lamina I and II of the dorsal horn or the spinal cord.

The peripheral nerve impulse can be modulated locally, NSAIDs can reduce the presence of chemical stimuli, and the presence of

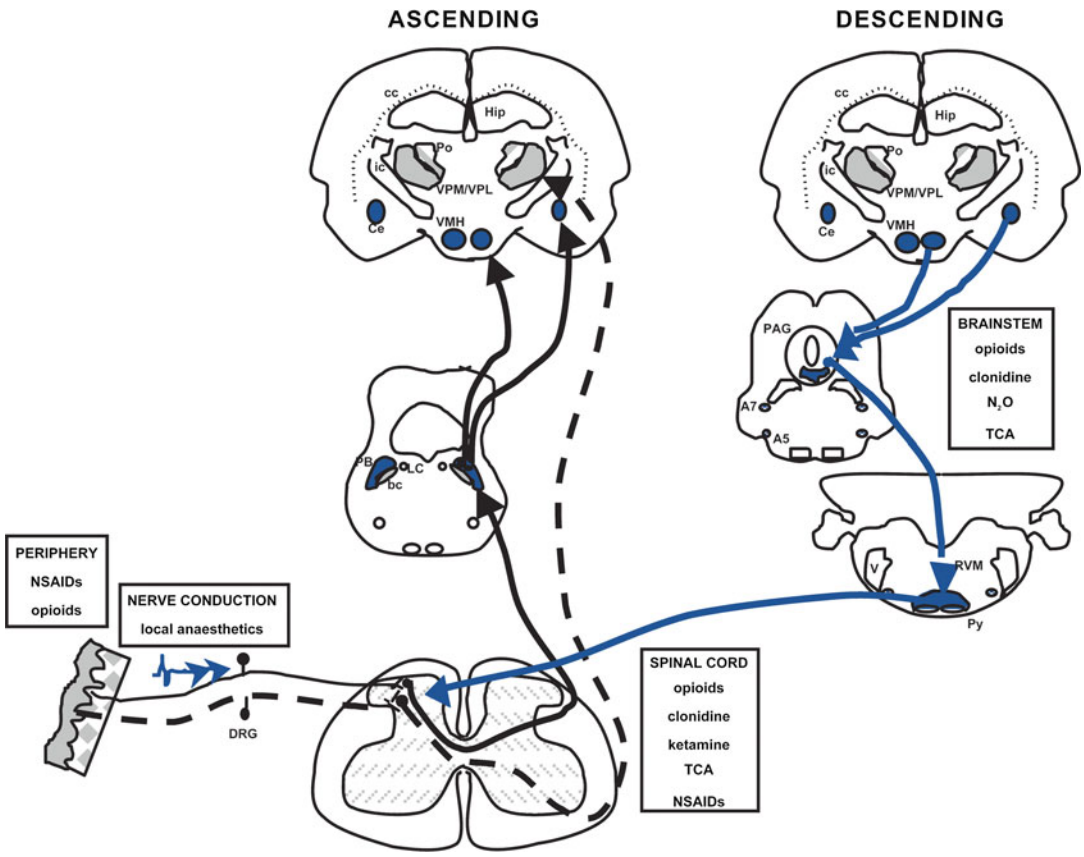


Fig. 4 The main ascending and descending spinal pain pathways (Hunt and Mantyh 2001; Schug et al. 2015). The site of action of some analgesics is included. Image courtesy of Acute Pain Management: Scientific Evidence (4th Edition) published by ANZCA and FPM. *A* adrenergic nucleus; *bc* branchium conjunctivum; *cc* corpus callosum; *Ce* central nucleus of the amygdala; *DRG* dorsal root ganglion; *Hip* hippocampus; *ic* internal capsule; *LC* locus coerulus; *PAG* periaqueductal grey; *PB* parabranchial area; *Po* posterior group of thalamic nuclei; *Py* pyramidal tract; *RVM* rostroventromedial medulla; *V* ventricle; *VMH* ventral medial nucleus of the hypothalamus; *VPL* ventral posterolateral nucleus of the thalamus; *VPM* ventral posteromedial nucleus of the thalamus. Reproduced with permission of Acute Pain Management: Scientific Evidence

inflammation stimulates the transport of opioid receptors to the periphery, allowing topical opioids to be of benefit.

3.2 Central Transmission and Perception of Pain in the Higher Centers

At the dorsal horn synapse multiple chemical messengers are involved (e.g., glutamate, NMDA, aspartate, substance P, CGRP). With each stimulus, there is an increase in the action potential from the dorsal horn cell (the concept of "wind-up"), which over the long term may be involved in hippocampal learning and memory and spinal cord sensitization. Wind up, in association with the similar phenomena of long-term potentiation and secondary hyperalgesia, may contribute to central sensitization. From the dorsal horn, second order neurones ascend through the spinothalamic tract.

The spinothalamic tract is subdivided into the neo-spinothalamic (fast, pin-prick sensation to the thalamus, and then to the sensory cortex), the paleo-spinothalamic (slow, dull pain, with

collaterals to multiple areas; also involved with stimulation of descending, inhibitory fibers), and the archi-spinothalamic tract (innervating the hypothalamus and limbic systems). It is postulated the archi-spinothalamic tract could have effects on the autonomic nervous system, emotional and behavioral responses to pain.

3.3 Modulation and the Descending Pathways

Multiple descending pathways act as modulators at the dorsal horn, with input from the amygdala and hypothalamus via the periaqueductal grey matter. The main neurotransmitters involved at inhibitory pathways are glycine, GABA, and enkephalins. The dorsolateral funiculus has specific serotonergic and noradrenergic inhibitory descending pathways.

Considering these principles of pain pathophysiology allows an approach to assessment and management to be generated.

Radiotherapy or chemotherapy are options that can directly target a lesion causing pain. Splinting may stabilize and therefore reduce pain from a lesion. Physical treatment options including heat, massage, and TENS may be of benefit. Medications can reduce the chemical soup (NSAIDs) or target receptors themselves, either locally or centrally.

Higher-level modulation options have been the focus of much research of late and have an increasing evidence base.

4 Screening for and Assessment of Pain

The WHO definition states that palliative care should include "the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual" (World Health Organisation 2016). It is therefore essential that pain is screened for at every meeting and thoroughly assessed if present. International guidelines suggest a comprehensive assessment of pain should be conducted if there is pain present, allowing an individualized pain management plan to be implemented if needed (Scottish Intercollegiate Guidelines Network 2008; National Clinical Effectiveness Committee 2016; National Comprehensive Cancer Network 2016; Australian Adult Cancer Pain Management Guideline Working Party 2016).

4.1 Screening

International guidelines suggest patients able to communicate their level of pain should be asked to rate any pain on a Numeric Rating Scale (0–10) at every clinical encounter. For patients who have communication difficulties, pictorial scales such as the Faces Pain Rating Scale for children can be used (Bieri et al. 1990). Ideally the patient should be the main assessor of the pain as health professionals have been shown to underestimate the level of pain a patient is experiencing. If the patient is unable to adequately assess their pain family members or health professionals may act as a substitute.

Example of numeric pain rating scale is "What is your current level of pain, between 0 and 10, with 0 being no pain and 10 being the worst pain you could imagine?" (Fig. 5).

For patients unable to use a scaling system (e.g., patients with dementia), an Abbey Pain Scale or PAINAD scale can be used (Abbey et al. 2004) (Fig. 7).

4.2 Pain Assessment

A comprehensive pain assessment should be undertaken in any patient scoring 2 or more on a Likert or Faces scale, three or more on an Abbey pain scale, or a patient reporting a new pain or an unexpected change in pain intensity. This should

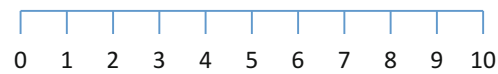


Fig. 5 Numeric Rating Scale

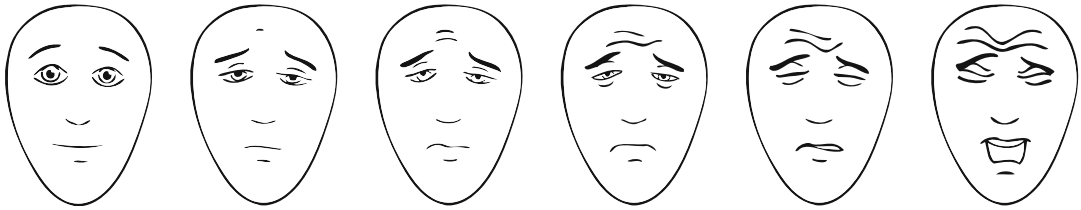


Fig. 6 The Faces Pain Scale- Revised has been reproduced with the permission of the International Association for the Study of Pain® (IASP). The figure may not be reproduced for any other purpose without permission

be tailored to the individual. It should be included as part of a full history, examination, investigation, and use of standardized assessment tools (Scottish Intercollegiate Guidelines Network 2008; Scottish Partnership for Palliative Care 2013; National Clinical Effectiveness Committee 2016; National Comprehensive Cancer Network 2016; Australian Adult Cancer Pain Management Guideline Working Party 2016):

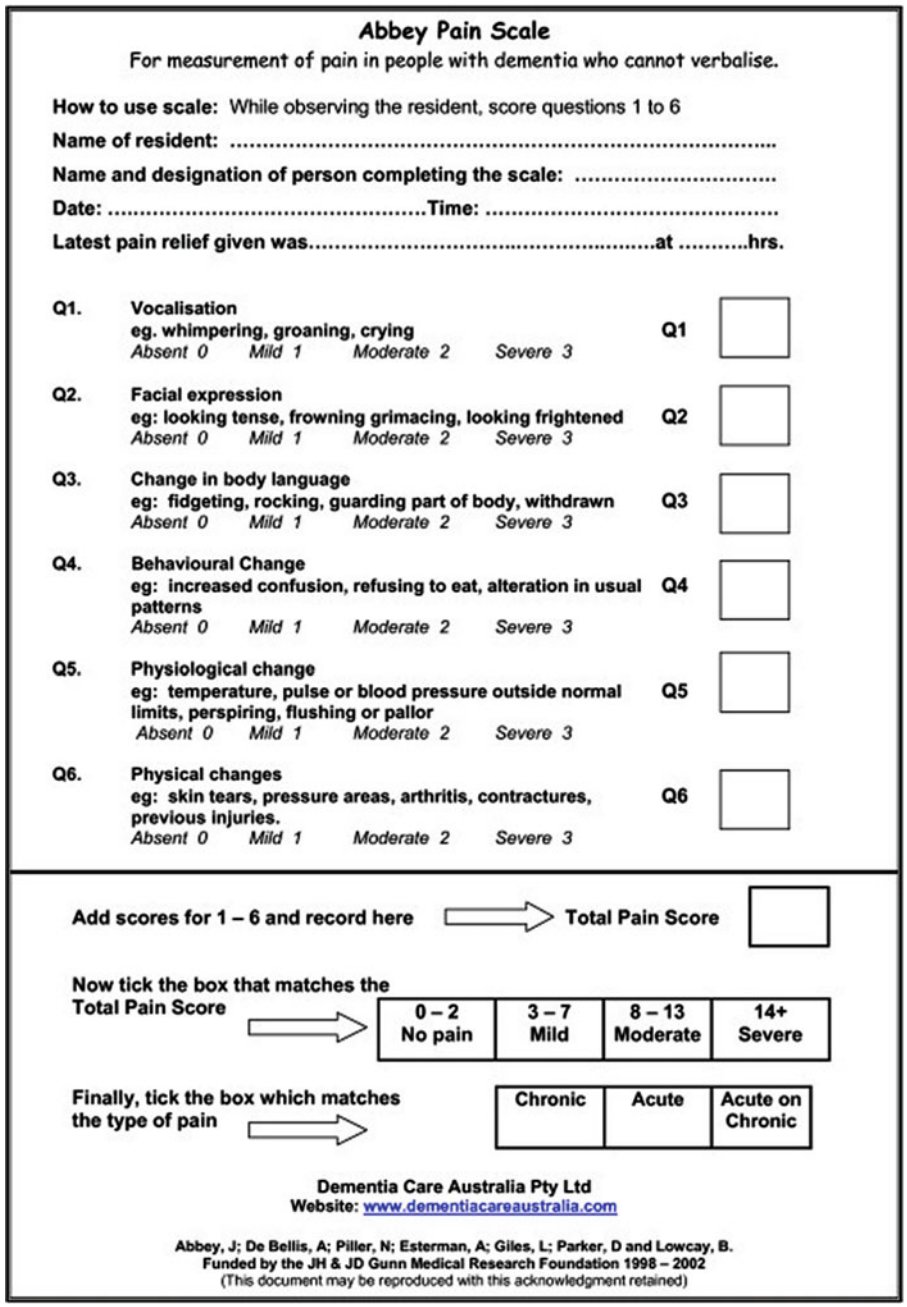
- Medical History
  - A medical history including disease status and treatment
  - Pain severity using a validated scale (e.g., Brief Pain Inventory (Cleeland 2009))
  - Pain experience (e.g., SOCRATES, PQRST see below)
  - Functional effects including interference with ADLs (including activity, walking, work, mood, sleep, relationships with people, and enjoyment of life)
  - Associated symptoms
- Medication History
  - Previous and current treatment for pain including compliance and any side effects
  - Use of any complementary and alternative medicines (approximately 40–50% of patients) (Horneber et al. 2012)
- Psychosocial history
  - Patient's fears and concerns about the pain including perceived meaning of the pain
  - Specific questioning to detect depression (e.g., the two question technique: "are you depressed? Have you experienced loss of interest in things or activities you would normally enjoy? (Mitchell 2008)),
  - Social, cultural and spiritual assessment (e.g., FICA, HOPE assessment (Puchalski et al. 2009))
  - Potential modulators such as substance abuse, alcohol and delirium
  - Any risk factors for medication misuse and abuse
- Physical examination
- Appropriate investigations
- Patient and carer preferences
- Factors suggesting a medical emergency

Pain assessment mnemonics:

SOCRATES
Site
Onset: when did the pain start, sudden or gradual?
Character: nociceptive or neuropathic features
Radiation
Associated symptoms
Time course-constant or fluctuating
Exacerbating or relieving features
Severity, e.g., using numerical-rating scale/Faces (Fig. 6)

PQRST
Provoking/precipitating factors
Quality of pain-nociceptive or neuropathic features
Region or radiation
Severity or associated Symptoms
Temporal factors

The aim of assessment is to identify the etiology and mechanism of the pain, diagnose any



Abbey Pain Scale

For measurement of pain in people with dementia who cannot verbalise.

How to use scale: While observing the resident, score questions 1 to 6

Name of resident: .....

Name and designation of person completing the scale: .....

Date: .....**Time:** .....

Latest pain relief given was.....at .....hrs.

Q1. **Vocalisation**
eg. whimpering, groaning, crying **Q1**
Absent 0 Mild 1 Moderate 2 Severe 3

Q2. **Facial expression**
eg: looking tense, frowning grimacing, looking frightened **Q2**
Absent 0 Mild 1 Moderate 2 Severe 3

Q3. **Change in body language**
eg: fidgeting, rocking, guarding part of body, withdrawn **Q3**
Absent 0 Mild 1 Moderate 2 Severe 3

Q4. **Behavioural Change**
eg: increased confusion, refusing to eat, alteration in usual patterns **Q4**
Absent 0 Mild 1 Moderate 2 Severe 3

Q5. **Physiological change**
eg: temperature, pulse or blood pressure outside normal limits, perspiring, flushing or pallor **Q5**
Absent 0 Mild 1 Moderate 2 Severe 3

Q6. **Physical changes**
eg: skin tears, pressure areas, arthritis, contractures, previous injuries. **Q6**
Absent 0 Mild 1 Moderate 2 Severe 3

Add scores for 1 – 6 and record here → **Total Pain Score**

Now tick the box that matches the Total Pain Score →

0 – 2 No pain	3 – 7 Mild	8 – 13 Moderate	14+ Severe

Finally, tick the box which matches the type of pain →

Chronic	Acute	Acute on Chronic

Dementia Care Australia Pty Ltd
Website: www.dementiacareaustralia.com

Abbey, J; De Bellis, A; Piller, N; Esterman, A; Giles, L; Parker, D and Lowcay, B.
Funded by the JH & JD Gunn Medical Research Foundation 1998 – 2002
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Fig. 7 Abbey Pain Scale

specific medical emergencies, and understand patient-specific goals of care. It should also provide an opportunity to consider specific symptom clusters. Research on symptom clusters in advanced cancer has found that dyspnea, drowsiness, and fatigue often cluster with pain (Dong et al. 2014).

5 Pain Management: General Approach

The WHO suggested five areas to target in approaching a patient with pain in 1990 and this remains applicable today (World Health Organisation 1996). These include:

- Modification of the disease process
  - Radiotherapy, hormone therapy, chemotherapy, surgery
- Psychological approaches
  - Understanding, education, companionship, cognitive behavioral therapy (CBT)
- Interruption of the pain pathways
  - Local anesthetics, neurolytic agents
- Medications
  - Analgesics, antidepressants, anticonvulsants, anxiolytics, neuroleptics
- Modification of activities of daily living or immobilization
  - Rest, cervical collar, splints or slings, orthopedic surgery

Cancer-related pain may respond well to treatment of the cancer itself including hormonal treatments, radiotherapy, and chemotherapy. For noncancer-related illnesses, other appropriate treatment options (e.g., antibiotics for pneumonia, internal fixation of a hip fracture) may help with analgesia.

6 Nonpharmacological Pain Management

All patients with pain should receive education on pain and its management as this has been shown to reduce cancer pain intensity (Scottish Intercollegiate Guidelines Network 2008; Rueda et al. 2011; Marie 2013; National Comprehensive Cancer Network 2016; Australian Adult Cancer Pain Management Guideline Working Party 2016). This process should involve the treating team being aware of the patient, family, and caregiver's existing knowledge of pain and treatment options and their level of understanding of the education provided. Patients should understand that describing their pain to health care workers is essential to allow the best plan of management to be made. It is important to convey that there is no medical benefit to suffering from pain and pain can usually be controlled, as can any side effects of treatment. Strategies to enable patients to be more involved in their own pain management appear to be most effective when employed as jointly created pain management plans, goal setting, and pain diaries.

Psychosocial and spiritual interventions have been shown to have a positive impact on pain (Sheinfeld Gorin et al. 2012) through their ability to provide active coping processes. CBT has been shown to be of benefit in patients with cancer pain (Tatrow and Montgomery 2006); however, a Cochrane review of psychological therapies for management of chronic neuropathic pain found insufficient evidence to support psychological interventions in this group (Eccleston et al. 2015).

When assessing the evidence for other nonpharmacological management of pain, there is low level evidence supporting orthoses for pain post stroke (Tyson and Kent 2011; Hebert et al. 2016) and Motor Neurone Disease (European Federation of Neurological Societies Task Force 2012). Transcutaneous Electrical Nerve Stimulation (TENS) is based on delivering low voltage electrical currents to the skin. Reviews have looked at the effectiveness of TENS in acute pain (tentative evidence for TENS) (Johnson et al. 2015b), phantom limb and stump pain (inadequate evidence to support TENS) (Johnson et al. 2015a), and cancer pain (inconclusive due to inadequate evidence) (Hurlow et al. 2012; Bao et al. 2014). It is unlikely that these interventions will cause harm so trialing on a case by case approach may be appropriate. There is currently insufficient evidence to support acupuncture for cancer pain in adults (Paley et al. 2015).

Music therapy may be of benefit for reducing pain in palliative care patients and palliative care patients suffering from cancer. Studies are generally weak (Archie et al. 2013; McConnell et al. 2016). There is weak evidence for massage therapy, either with or without aromatherapy oils for a pain population (Boyd et al. 2016). There is no

current evidence to support the use of massage for symptom relief in patients with cancer (Shin et al. 2016). There is low level evidence to support Reike, reflexology, homeopathy (Traumeel), and creative arts therapy (Bao et al. 2014).

7 Pharmacological Management of Pain

7.1 Paracetamol

Paracetamol (acetaminophen) is widely used as a treatment for pain. The mechanism of action of paracetamol remains uncertain (Schug et al. 2015; RACGP 2016) although it is thought that it inhibits central (but not peripheral) prostaglandin synthesis, modulates inhibitory descending serotinergic pathways, and possibly plays a role in activation of the endocannabinoid system (Schug et al. 2015). Paracetamol inhibits low level inflammation but does not suppress high level inflammation such as inflammatory arthropathies (Schug et al. 2015).

Recent studies have shown paracetamol is not as effective as nonsteroidal anti-inflammatory drugs (NSAIDs) in knee and hip pain osteoarthritis (da Costa et al. 2016).

Caution should be used in total paracetamol daily dosing given the risk of liver injury. Physicians should be aware of the possibility of excess paracetamol dosing due to combination medications. The total dose should not exceed 4 g of paracetamol per day (National Comprehensive Cancer Network 2016).

Paracetamol in Palliative Care

There is no high quality evidence to support or refute the use of paracetamol alone or in combination with opioids for cancer pain (Wiffen et al. 2017b). It is also noted that paracetamol dosing carries a significant tablet burden.

Paracetamol should be considered in the palliative care patient on a case by case basis (National Clinical Effectiveness Committee 2016); there is insufficient evidence to support the addition of paracetamol in palliative care patients taking high doses of strong opioids (National Clinical Effectiveness Committee 2016).

Research is ongoing comparing paracetamol in combination with opioids with opioids alone.

7.2 Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

NSAIDs are split into nonselective (nsNSAID, acting on both the COX-1 and COX-2 pathways) and selective (COX-2 inhibitors) (Schug et al. 2015). NsNSAIDS and COX-2 inhibitors have anti-inflammatory, analgesic, and antipyretic actions. Data have shown both groups of drugs to be more effective than paracetamol in treatment of osteoarthritis pain, with nsNSAIDs likely giving more effective analgesia than COX-2 inhibitors (da Costa et al. 2016). Both are effective in acute postoperative pain (Schug et al. 2015).

Significant side effects can be encountered with both nsNSAIDs and COX-2 inhibitors. Both nsNSAIDS and COX-2 inhibitors can provoke or worsen renal failure. They should be used in caution with patients at risk of developing renal failure or who are taking other potentially nephrotoxic drugs and patients' renal function should be monitored.

NsNSAIDS carry a higher risk of gastrointestinal complications than COX-2 inhibitors although both can cause ulceration which can extend throughout the gastrointestinal (GI) tract (Jarupongprapa et al. 2013). The risk is increased in patient age >65 years, those with previous peptic ulcer disease, significant alcohol use, major organ dysfunction, and with concomitant use of medications increasing the risk of ulceration (e.g., steroids) or bleeding (including low dose aspirin) (National Comprehensive Cancer Network 2016). Low dose ibuprofen (<1200 mg/day) has the lowest risk of gastrointestinal complications of nsNSAIDs. Ketoprofen and piroxicam have the highest risk of GI complications (RACGP 2016). Double dose H2 antagonists or single dose proton pump inhibitors (PPI) are effective prophylactic agents. It is possible that the combination of COX-2 inhibitors and a PPI are the safest for gastrointestinal protection.

NsNSAIDs inhibit platelet function through their action on COX-1; COX-2 inhibitors do not

inhibit platelet function. Both nsNSAIDs and COX-2 inhibitors are associated with an increased risk of cardiovascular effects and may increase blood pressure. It is likely that diclofenac has the highest risk of cardiovascular effects and naproxen the lowest of nsNSAIDs (RACGP 2016).

All NSAIDs are contraindicated in severe liver dysfunction.

NSAIDS in Palliative Care

There is no high-quality evidence to support or refute the use of NSAIDs alone or in combination with opioids for cancer pain. There is very low-quality evidence that some patients with moderate or severe cancer pain can obtain substantial levels of benefit within 1 or 2 weeks (Derry et al. 2017).

Given the lack of evidence for benefit and potential for side effects, NSAID use should be decided on a patient by patient basis, using the lowest effective dose and giving consideration to prophylactic GI protection (RACGP 2016). Patients not responding to one NSAID may gain effective analgesia from a different NSAID (RACGP 2016).

7.3 Step 2 WHO Ladder: Codeine, Tramadol

A traditional approach to pain management in palliative care has been following the WHO step-wise approach to pain (World Health Organisation 1996). Step two has traditionally involved the use of "weak" opioids including codeine, dihydrocodeine, hydrocodone, and tramadol. More recently, research has challenged this approach, suggesting that step 1 direct to step 3, bypassing weak opioids, may be a better approach (Caraceni et al. 2012). This is proposed to be of benefit by introducing potent analgesics early, preventing long periods of poor pain control, and giving good quality of life while using more potent Step 3 analgesics with similar side effect profiles to step 2 analgesics (Tassinari et al. 2011). A systematic review in 2011 concluded that the evidence available at that time to support either a two- or three-step approach was inconclusive (Tassinari et al. 2011). A multicenter RCT from 2015 compared low dose morphine with tramadol, tramadol plus paracetamol, and codeine plus paracetamol in patients with cancer with moderate pain. The results showed better analgesia from the low dose morphine with similar side effects to the weak opioids (Bandieri et al. 2015). Further research is currently being carried out in this area.

7.3.1 Codeine

Codeine itself is a very weak mu receptor agonist. Its main efficacy is based on its metabolism to morphine via the CYP2D6 cytochrome P450 isoenzyme (Crews et al. 2014). The amount of conversion is variable, usually around 10% (30 mg of oral codeine being the equivalent of 3 mg of oral morphine). In Caucasian populations, 8–10% of patients are poor metabolizers (receiving very limited analgesic action from oral codeine), while 3–5% are ultrarapid metabolizers, converting significantly more codeine to morphine, with consequently higher risk of opioid-related side effects. The proportion of ultrarapid metabolizers is significantly higher in Middle Eastern and North African populations (10–30%) and lower (0.5%) in Asians. Asians and African Americans are less likely to be poor metabolizers than Caucasians (Crews et al. 2014; Schug et al. 2015; RACGP 2016). Current research is evaluating CYP2D6 genotype targeted analgesia advice.

As codeine is metabolised to morphine, which has renally excreted metabolites, codeine should be avoided in patients with renal failure. Dose reduction may be required in hepatic failure (Schug et al. 2015; RACGP 2016). Its side effects are mainly related to its opioid action (constipation does not occur in poor metabolizers of codeine).

Codeine in Palliative Care Patients

While previous research in palliative care has used oral and intramuscular routes of administration, in Australia (and many other countries) codeine is currently only available in oral preparations (RACGP 2016). Current limited data suggest codeine is more effective than placebo for cancer pain in adults but with significant side effects (Straube et al. 2014).

There is no current evidence to support the use of paracetamol, with or without codeine or

dihydrocodeine, in adults with neuropathic pain (Wiffen et al. 2016a).

7.3.2 Tramadol

Tramadol is a dual action analgesic agent. It is structurally related to morphine and codeine and consists of two enantiomers. The (+)-Tramadol enantiomer and its more potent metabolite, (+)-*O*-desmethyl-tramadol, are mu opioid receptor agonists. (+)-Tramadol also inhibits serotonin reuptake. The (−)- Tramadol enantiomer inhibits norepinephrine reuptake (Schug et al. 2015; Grond and Sablotzki 2004). As with codeine, tramadol is metabolized via the CYP2D6 enzyme pathway, with significant interpatient variability and subsequently analgesic effect (Crews et al. 2014).

Ninety percentage of tramadol excretion is in urine; hence, dose reductions are necessary in renal failure (creatinine clearance <30 ml/min). Dose reduction may also be necessary in severe hepatic impairment (Schug et al. 2015; RACGP 2016).

Tramadol in Palliative Care Patients

There is limited, very low quality evidence from randomized controlled trials that tramadol reduces cancer-related pain in some adults. There is no evidence to support the use of tramadol in children. There is very low quality evidence that tramadol is not as effective as morphine. The role of tramadol for cancer pain as part of step 2 of the WHO analgesic ladder therefore is unclear (Wiffen et al. 2017a).

A systematic review investigating the role of tramadol to treat chronic neuropathic pain in adults (of any cause) showed low or very low quality evidence only (Duehmke et al. 2017).

Adverse Effects

The most common side effects are nausea, vomiting, fatigue, dizziness, weakness, and loss of appetite. Tramadol causes less constipation than codeine.

Much has been written on the risk of serotinergic syndrome with tramadol. This classically presents with the triad of altered mental status, autonomic hyperactivity, and neuromuscular abnormalities. It is important when prescribing tramadol that note is made of any concurrent serotinergic drugs, and side effects monitored for. Medications that may act on serotinergic pathways include SSRIs, SNRIs, other antidepressants including MAOIs, Trazodone, Mirtazepine, buproprion, St. Johns Wort, 5HT3 antagonists, opioids including fentanyl and methadone, triptans, antiepileptics including valproate and carbamazepine, dopamine agonists, and illicit drugs including cocaine, MDMA, LSD, and alcohol (RACGP 2016).

7.4 Strong Opioids

Opioids act by binding to receptors in three families: mu, kappa, and delta. The mu receptor has multiple subtypes partly explaining the differences in effects of opioids in patients. Most opioids are mu agonists. There are pure agonists (e.g., morphine, fentanyl, hydromorphone, oxycodone), partial agonists (e.g., buprenorphine), and drugs with mixed actions (e.g., tramadol and tapentadol) (Pasternak 2014; Portenoy and Ahmed 2014).

Morphine is suggested as the first line strong opioid for moderate to severe cancer pain by the WHO (1996). There is no current evidence suggesting one strong opioid has improved efficacy or toxicity in the cancer patient population (Caraceni et al. 2011).

When initiating opioid analgesia in the opioid naïve patient, several guidelines exist (Scottish Intercollegiate Guidelines Network 2008; Klepstad et al. 2011; Caraceni et al. 2012; Portenoy and Ahmed 2014; National Clinical Effectiveness Committee 2016; National Comprehensive Cancer Network 2016; Australian Adult Cancer Pain Management Guideline Working Party 2016). These suggest using the oral route if possible, starting at doses of 5 mg oral morphine equivalent regularly fourth hourly, with hourly review and titration of doses. However, in patients previously taking weak opioids starting a low dose fentanyl patch or oral long acting low dose opioid also may be reasonable (Klepstad et al. 2011; Wiffen et al. 2016b). All patients being treated with opioids should have psychosocial support provided, education about pain management,

prevention and management of dry mouth, nausea and constipation, and consideration of non-pharmacological interventions and adjuvant analgesics (National Clinical Effectiveness Committee 2016; National Comprehensive Cancer Network 2016). Opioids can be switched due to inadequate effect, side effects, or patient request for a change of route of drug delivery. There is varying conversion between different states in Australia (Syrmis et al. 2014) and in different countries. Conversion charts or smart phone apps are available to guide dosing (ANZCA and FPM 2017).

Example for initiating opioids:

Opioid naïve patient

(a) 5 mg oral morphine Q4H and review dosing each hour for sedation/ongoing pain.
(b) 10–15 mg extended release morphine twice daily with daily review for sedation/pain.

In the elderly or very frail patients initial dosing of 2.5mg oral morphine Q4H and review dosing each hour for sedation/ ongoing pain

In patients previously taking weak opioids

(a) calculate oral morphine equivalent dosing in 24 hours based on previous requirements.
(b) dose reduce by 33% when converting to oral morphine dosing.

Divide total oral morphine equivalent in 24 hours by 2 for extended release morphine dosing or divide total oral morphine equivalent in 24 hours by 6 for 4 hourly immediate release formulation dosing.

Side Effects

While all opioids may cause adverse events (e.g., nausea, constipation, dry mouth, drowsiness), there is a lack of systemized reporting in trials and therefore direct comparisons between the rate of adverse events in different opioids are difficult to ascertain (Oosten et al. 2015).

Opioid-induced constipation (OIC) remains a significant challenge. Although long-acting opioid preparations containing oral naloxone and new medications including peripherally restricted mu receptor antagonists such as tapentadol theoretically may be of benefit to patients, more evidence is needed of their clinical efficacy (Camilleri 2011). Current guidelines for opioid-induced constipation suggest preventative measures including ensuring adequate fluid/fiber intake, encouraging exercise and regular prophylactic aperients (National Comprehensive Cancer Network 2016).

Up to 40% of patients may experience opioid-induced nausea (OIN). Antiemetics should be prescribed to all patients commencing opioids to be taken in case of nausea. The management of OIN includes preventing constipation, excluding other causes of nausea, and use of regular antiemetics. Patients may become tolerant to OIN, however if not, trialing a change of route of delivery or opioid switch may be of benefit (Laugsand et al. 2011; National Comprehensive Cancer Network 2016).

Management of opioid-induced itch includes excluding other causes of itch, considering true opioid allergy and trialing opioid switching. If this is unsuccessful subcutaneous low dose naloxone infusion (Kjellberg and Tramèr 2001; Reich and Szepietowski 2010; Miller and Hagemann 2011), ondansetron and antihistamines may be of benefit (National Comprehensive Cancer Network 2016).

Breakthrough Analgesia

Once a patient's analgesic regimen is stabilized, most patients requiring strong opioids will require regular long acting opioids with as needed "breakthrough" or "intense episodic" pain relief (Løhre et al. 2016). It is important to enquire if patients perceive incident or idiopathic breakthrough pain (see Table 1 for definition), and also if the pain is end of dose pain rather than true breakthrough pain (Vellucci et al. 2016). Breakthrough assessment tools such as the Alberta Breakthrough Pain Assessment Tool (ABPAT) (Sperlinga et al. 2015) or the Breakthrough Pain Assessment Tool (BAT) (Webber et al. 2014) are available to help guide patient management.

Breakthrough analgesia is recommended in guidelines at 1/6–1/10 of the 24 hours oral morphine equivalent dose in an immediate release formulation. There are a number of transmucosal

Table 1 Definitions of terms relating to pain (International Association for the Study of Pain 2017; Schug et al. 2015). § This Taxonomy/statement has been reproduced with permission of the International Association for the Study of Pain® (IASP). The Taxonomy/statement may NOT be reproduced for any other purpose without permission.

Term	Definition
Acute pain	Pain of recent onset and probable limited duration. It usually has an identifiable temporal and causal relationship to injury or disease
Chronic pain	Commonly persists beyond the time of healing of an injury, often thought to be 12 weeks. Frequently there may not be any clearly identifiable cause
Nociceptive pain§	Pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors (a high-threshold sensory receptor of the peripheral somatosensory nervous system that is capable of transducing and encoding noxious stimuli)
Somatic pain	A type of nociceptive pain. Often sharp, well localized, throbbing or pressure like. From superficial or bony structures
Visceral pain	A type of nociceptive pain. Often diffuse, achy, or crampy. Due to compression, infiltration or distension of abdominal or thoracic viscera
Neuropathic pain§	Pain caused by a lesion or disease of the somatosensory nervous system
Hyperalgesia§	Increased pain from a stimulus that normally provokes pain
Dysesthesia§	An unpleasant abnormal sensation, whether spontaneous or evoked
Allodynia§	Pain due to a stimulus that does not normally provoke pain
Sensitization§	Increased responsiveness of nociceptive neurons to their normal input, and/or recruitment of a response to normally subthreshold inputs
Breakthrough pain	Pain of moderate or severe intensity arising on a background of controlled chronic pain. Breakthrough pain may be described as spontaneous (unexpected) or incident (expected or predictable)
Adjuvant analgesics	Drugs with other primary indications that can be effective analgesics in specific circumstances

fentanyl citrate preparations available for intranasal, buccal, or oral administration. However, a recent Cochrane review which suggested transmucosal fentanyl may provide superior analgesia for breakthrough pain has been withdrawn because of concerns that the findings were misleading (Zeppetella and Davies 2015).

7.4.1 Buprenorphine

Buprenorphine is a semi-synthetic, partial mu receptor agonist and kappa receptor antagonist with high receptor affinity. Buprenorphine dissociates slowly from the mu receptor. In transdermal (low) doses, buprenorphine effects are similar to a full mu receptor agonist, without antagonism of other administered mu agonist medications.

Buprenorphine has a lower risk of respiratory depression compared to other strong opioids. Two-thirds of the drug is excreted unchanged, and one-third is metabolized in the liver. Buprenorphine dosing is unaffected by renal impairment.

Buprenorphine is available in transdermal (TD) and sublingual preparations. The TD patch is applied weekly and takes approximately 3 days to reach steady state. Approximately one in eight patients may develop itch with the patch (Ale et al. 2009, Kress 2009). Applying topical steroid aerosol prior to the patch may help with TD system-induced itch (Hans and Robert 2009; Wen et al. 2013).

Sublingual buprenorphine has a bioavailability of 30–50%. It has a mean half-life of 28 hours and hence delayed respiratory depression with frequent use has been reported.

Buprenorphine in Palliative Care

Buprenorphine may be more effective in neuropathic pain than other strong opioids although a recent Cochrane review showed insufficient research to support this (Wiffen et al. 2015a). A Cochrane review assessing the effectiveness of buprenorphine for cancer pain suggested that it should probably be used as second line to pure agonist opioids in cancer pain; however, it may be useful in some patients, with the sublingual formulation having more rapid onset of action than transdermal (Schmidt-Hansen et al. 2015).

7.4.2 Fentanyl

Fentanyl is a highly potent synthetic opioid, metabolized mainly in the liver to minimally active metabolites. There is minimal renal excretion. Fentanyl is highly lipophilic. Transdermal and transmucosal delivery systems are available. Conversion charts are available to guide dosing in conversion from other opioids. It is likely that transdermal fentanyl causes less constipation than oral morphine (28% vs. 46%) in a Cochrane review, although data is limited (Hadley et al. 2013).

Transmucosal fentanyl should only be used in patients stabilized on a morphine equivalent dose of at least 60 mg per day (RACGP 2016).

Multiple transmucosal delivery systems are available for fentanyl. These are not interchangeable. Most studies have shown no specific dose conversion between background opioid dose and the effective dose of transmucosal opioid (Zeppetella 2011). If switching delivery system, the patient should use the lowest dose and titrate as appropriate (RACGP 2016).

Oral Transmucosal Fentanyl Citrate (OTFC) is a lozenge on a stick. This has a bioavailability of approximately 50% and a time of onset of analgesia of less than 5 minutes. Dosing should start at 200microg and be titrated up as needed to 1600microg. Doses should not be repeated within 4 hours. If the long acting opioid dose increases, OTFC should be re-titrated starting at the lowest dose (RACGP 2016).

Fentanyl buccal tablets (FBT) have a higher bioavailability (65%) and a time to onset of analgesia of 10 minutes.

Sublingual fentanyl citrate orally disintegrating tablets (ODT) dissolve under the tongue. They have a bioavailability of 70% and a time to onset of analgesia of 15 minutes.

Practice Points

Fentanyl patches should only be started in opioid tolerant patients with stable pain (Actavis 2012; RACGP 2016). Switching between brands is not advised due to possible changes in absorption.

If changing from a long acting oral opioid, apply the patch at the same time as giving the last dose of 12 hours acting opioid or 12 hours after the last dose of 24 hours acting oral opioid (RACGP 2016).

Fentanyl patches take 24–72 hours to reach maximum effect (RACGP 2016).

Used fentanyl patches must be disposed of safely as 30–50% of the fentanyl content remains after 72 hours of use (RACGP 2016).

For patch reactions, topical beclometasone inhaler may be used prepatch application (off label use).

Matrix patches may be cut diagonally to allow low dose titration (off label use) (Scottish Partnership for Palliative Care 2013).

Advise patients not to apply heat (e.g., hot water bottle) over the patch as this will increase local absorption of the fentanyl leading to possible opioid toxicity (RACGP 2016).

TD fentanyl absorption may be lower in cachectic patients compared to normal weight patients with cancer pain (Heiskanen et al. 2009).

7.4.3 Morphine, Hydromorphone, and Oxycodone

Morphine remains the gold standard opioid endorsed by the WHO although the evidence base is small (Wiffen et al. 2016b). Morphine is metabolized via glucuronidation in the liver to morphine-6-glucuronide and morphine-3-glucuronide. M6G is a highly active metabolite giving analgesia as well as respiratory depression. M3G does not give analgesia but may give neurotoxicity symptoms. M3G and M6G are both renally excreted; therefore, morphine is not recommended in patients with renal failure (Schug et al. 2015). If no alternatives exist, then the dose and the frequency of morphine administration should be reduced.

Hydromorphone

Hydromorphone is approximately five times more potent than morphine. The main metabolite is hydromorphone-3-glucuronide (H3G) which, like M3G, has no analgesic activity but may cause neurotoxic side effects. H3G requires renal function for clearance; hence, hydromorphone should be used with caution in renal failure. Low level evidence suggests the chance of opioid

toxicity in patients with renal failure is less than with morphine (King et al. 2011; National Clinical Effectiveness Committee 2016).

Oxycodone

Oxycodone has a higher oral bioavailability than morphine. Oxycodone's main metabolites are noroxycodone (via CYP3A) and oxymorphone (via CYP2D6). Oxycodone and oxymorphone are responsible for the majority of the analgesic effect. CYP2D6 polymorphism may explain the variation in analgesic effect between patients. CYP3A inhibitors (e.g., ketoconazole) may increase oxycodone effect and toxicity (Schug et al. 2015).

Morphine, Oxycodone and Hydromorphone in Palliative Care

Studies suggest that morphine, oxycodone, and hydromorphone have similar efficacy and toxicity in the cancer patient population (Caraceni et al. 2011, 2012; Wiffen et al. 2016b). In patients not responding to one opioid, it is reasonable to trial opioid switching (Dale et al. 2011; Mercadante and Caraceni 2011; Wiffen et al. 2016b; Schmidt-Hansen et al. 2017). Studies are currently underway comparing multiple opioids for efficacy in cancer pain.

Uncertainty continues for the possible role of opioids to treat neuropathic pain. There is currently a lack of high quality research data. Adverse effects from opioids being used to treat neuropathic pain are common (McNicol et al. 2013). A Cochrane review has found insufficient evidence to support or refute the use of hydromorphone (Stannard et al. 2016) or methadone for use in adults with chronic neuropathic pain (McNicol et al. 2017).

7.4.4 Tapentadol

Tapentadol is a combination mu agonist (20 times lower affinity than morphine) and noradrenaline-reuptake inhibitor. Due to its combination action, clinically tapentadol appears to be approximately three times less potent than morphine (Mercadante et al. 2013). Tapentadol has no significant effect on serotonin reuptake.

Tapentadol is metabolized by glucuronidation. Liver dysfunction may require a dose reduction. It has no active metabolites and at recommended doses (maximum 500 mg/24 hours) has no adverse effects on heart rate or blood pressure. It is recommended not to use tapentadol in severe renal failure (eGFR <30). Use of tapentadol is contraindicated within 14 days of treatment with an irreversible, nonselective monoamine oxidase inhibitor (MAOI) (Schug et al. 2015; RACGP 2016).

Tapentadol in Palliative Care

As a relatively recently introduced medication, there is limited research data available. A meta-analysis of oral tapentadol for cancer pain found limited evidence only. Analgesia and adverse effects were similar for tapentadol, morphine, and oxycodone (Wiffen et al. 2015b).

7.4.5 Methadone

Methadone is a synthetic opioid. It is available as a racemic mixture of R and L enantiomers; however, it is the R-enantiomer principally responsible for its mu receptor effect. Methadone also has weak NMDA antagonist and noradrenaline and serotonin reuptake inhibitor effects.

Methadone has good oral bioavailability (70–80%) and high potency and is metabolized via the cytochrome p450 pathway. Medications that induce or inhibit the cytochrome p450 pathway may lead to a relative decrease or increase in methadone levels. Methadone has a long, unpredictable half-life making titration complex and leading to the risk of accumulation. High doses of methadone have been associated with prolonged QTc in patients.

Dose adjustments may be required in severe renal failure. No dose adjustments are needed in stable liver disease. Use of methadone in severe hepatic failure is not advised unless for use in terminal care (Schug et al. 2015; RACGP 2016).

Methadone in Palliative Care

A recent meta-analysis investigating the role of methadone for cancer pain suggested based on low-quality evidence, methadone had similar efficacy to morphine (Nicholson et al. 2017). There is inadequate evidence available to form

conclusions on the use of methadone for chronic neuropathic pain (McNicol et al. 2017). The EAPC suggest that methadone can be used as a first line strong opioid for moderate-severe cancer pain (Caraceni et al. 2012).

Practice Points

Higher doses of methadone may increase the QT interval. Avoid co-administration of other medications, which may prolong the QT interval.

Consider ECG monitoring of QT interval if using high doses of methadone.

Methadone is metabolized by many Cytochrome P450 iso-enzymes – beware of interactions that may increase or decrease methadone plasma levels (Twycross 2016; RACGP 2016).

Subcutaneous methadone can cause local irritation. Intermittent boluses may cause less irritation than continuous subcutaneous infusion (Shaiova et al. 2008). If continuous infusion is required, the addition of low dose dexamethasone to the syringe driver may be if benefit; however, this may cause solution instability (Leppert 2009).

When switching from other strong opioids to methadone (as opposed to adding methadone as a co-analgesic), several conversion options are described (McLean and Twomey 2015):

Three-Day Switch (3DS)

Day 1: 30% of opioid given in equianalgesic TDS dose of methadone, 70% usual opioid.

Day 2: 60% usual dose of opioid given in equianalgesic TDS dose of methadone, 40% usual opioid.

Day 3: 100% of dose given as equianalgesic TDS dose of methadone.

Rapid Conversion (RC)

Original opioid is discontinued. Daily methadone dose is calculated according to evidence-based conversion ratios given in 3 equal divided doses. This dose is then titrated to give good analgesia.

Ad Libitum (AL)

Original opioid is discontinued. Equivalent daily total methadone dose is calculated. One-tenth (this may be too high, episodes of toxicity have been noted, some studies have had good effects as low as 1/40th) of calculated dose (max 30 mg) is given as needed (not more than three hourly. On day 6 the total requirement of the previous 2 days is calculated and split into 12 hourly dosing.

Outpatient Titration

Original opioid continued. Methadone is commenced at low dose (e.g., 5 mg Q4H) and then increased by 5 mg/dose every 3 days until good analgesia is achieved. The original opioid is weaned and methadone increased over a variable period.

Current evidence suggests the AL titration may be the safest (McLean and Twomey 2015). Methadone switch should only be done by a clinician experienced in its complex pharmacology and its uses. Preexisting opioid-induced hyperalgesia may lead to significantly higher calculated dosing of methadone than necessary causing subsequent toxicity.

Conversion tables are available. One of the commonly used conversion tables is from the Royal Perth Hospital (Ayonrinde and Bridge 2000).

7.4.6 Opioids in Renal Failure

There is low quality existing evidence for opioid treatment in cancer patients with renal failure (Twycross et al. 2016; Sande et al. 2017). Guidelines were published by EPCRC in 2011 (King et al. 2011).

These suggest for mild to moderate renal impairment (eGFR 30–89)

1. Assess for any reversible factors
2. Be aware estimations of GFR may be less accurate in cachexia, low protein states, edema, and acute renal failure.
3. Monitor for changes in renal function and consider pre-emptively changing opioids in rapidly deteriorating renal function
4. All opioids that are appropriate for cancer pain can be used with consideration of reduced dose or frequency.

Metabolite activity and risk stratification shows (King et al. 2011)

Group 1 (no clinically significant active metabolites)
Fentanyl, alfentanyl, methadone
Group 2 (active or probably active metabolites)
Tramadol, hydromorphone (possible reduced risk of toxicity)
Oxycodone, morphine, diamorphine, codeine
Group 3 (insufficient evidence)
Buprenorphine

Severe and end stage renal failure (eGFR <30) (King et al. 2011)
1st line: fentanyl
2nd line: alfentanyl
Use with care: tramadol, hydromorphone

It is suggested that automatic conversion to a possibly safer opioid, with which the prescriber has limited experience, may not be of benefit in the last hours to days of life if a current dose and time appropriate opioid providing symptom relief without significant side effects (Twycross 2016).

Opioid use in dialysis patients (King et al. 2011)
Fentanyl: not dialyzable, safe, use with caution
Methadone: not dialyzable, safe, use with caution
Tramadol: dialyzable, use with caution, max 200 mg/24 hours
Hydromorphone: metabolite dialyzable, safe, use with caution
Buprenorphine: not dialyzable, safe, use with caution
Avoid if possible: morphine, codeine.

Opioid Switch

Opioid switching or rotation to a different opioid may be of benefit either when pain control is inadequate, the patient prefers a different route of delivery, changing clinical status (e.g., unable to swallow tablets) or when side effects are intolerable (Dale et al. 2011; Mercadante and Caraceni 2011; Syrmis et al. 2014; National Clinical Effectiveness Committee 2016). It is postulated that improved analgesia is from incomplete cross-tolerance between strong opioids in individual patients. The current evidence base to support this is low (Dale et al. 2011).

Tables and electronic applications are available to guide dosing in opioid rotation although there remains variation between geographic sites and services (ANZCA; Mercadante and Caraceni 2011; Syrmis et al. 2014; Twycross 2016). See Fig. 8 for an example of an Opioid Conversion Chart. Conversion ratios are less predictable at higher doses (Schug et al. 2015). A dose reduction of 25% is often suggested on opioid switching given the possible incomplete-cross tolerance although this may not be necessary when severe pain is the reason for opioid rotation and rather should be assessed on a case by case basis (Mercadante and Caraceni 2011; Caraceni et al. 2012; National Comprehensive Cancer Network 2016). When switching opioids, frequent clinical review and reassessment of pain and adverse effects is recommended.

When converting from oral morphine or hydromorphone to subcutaneous, ratios of 2:1 to 3:1 (oral: subcut) are commonly used (i.e., 10 mg po morphine is equivalent to 3.3–5 mg subcutaneously (Scottish Intercollegiate Guidelines Network 2008; Caraceni et al. 2012). Because of oxycodone's high oral bioavailability a conversion ratio of 1.5:1 (oral to subcutaneous) may be appropriate (Twycross 2016).

Methadone has an oral bioavailability of approximately 80%. Guidelines when converting from oral to subcutaneous suggest a conversion of 2:1 or 1:1 at low dose (oral to subcut) and note that 2:1 may be underdosing requiring appropriate breakthrough analgesia doses to be available (Shaiova et al. 2008; Leppert 2009; Twycross 2016).

7.5 Adjuvant Analgesics: Antidepressants and Antiepileptics

Neuropathic pain descriptors are present in up to 40% of cancer pain patients (Caraceni and Portenoy 1999). Neuropathic cancer pain is associated with greater analgesic requirements and a larger impact on activities of daily living than nociceptive cancer pain (Rayment et al. 2013).

PALLIATIVE CARE OPIOID CONVERSION CARD
Conversion factors are a guide only; Patients should be titrated individually. Patients on opioids require regular laxatives (eg Coloxyl with Senna)

CONVERTING FROM MORPHINE TO OTHER OPIOIDS AND *VICE VERSA*

Drug	Oral	Subcut	Equi-analgesic conversion to oral Morphine
Morphine	10mg	5mg	
Hydromorphone	2mg	1mg	Multiply by 5
Codeine	100mg	Avoid	Divide by 10
Note : 1 tablet Panadeine Forte = 30mg Codeine.+ 500mg Paracetamol 1 tablet Panadeine = 8 mg Codeine.+ 500mg Paracetamol Doses of codeine over 60mg every 4-6 hours are not recommended			
Oxycodone	7mg	3.5mg	Multiply by 1.5
Tramadol	100mg	Avoid	Divide by 10
Methadone	Variable		Discuss with consultant

CONVERTING FROM MORPHINE TO TRANSDERMAL FENTANYL

Oral Morphine mg/4 hrs	Oral Morphine mg/24 hrs	Fentanyl Patch mcg/hr
5	20-59	12
10-20	60-134	25
35	135-224	50
50	225-314	75
65	315-404	100

PALLIATIVE CARE OPIOID CONVERSION CARD

CONVERTING FROM TRANSDERMAL BUPRENORPHINE AND TRANSDERMAL FENTANYL TO MORPHINE

	Patch size	Hourly rate	Conservative conversion to oral Morphine
BUPRENORPHINE (Norspan) (change weekly)	5mg	**5mcg/hr**	12mg/day
	10mg	**10 mcg/hr**	24mg/day
	20mg	**20 mcg/hr**	48mg/day
FENTANYL (Durogesic) (change every 72 hrs)	2.1mg	**12mcg/hr**	30mg/day
	4.2mg	**25 mcg/hr**	60mg/day
	8.4mg	**50mcg/hr**	120mg/day
	12.6mg	**75mcg/hr**	180mg/day
	16.8mg	**100mcg/hr**	240mg/day

Due to the possibility of poor transdermal absorption in palliative care patients,conversion from transdermal Buprenorphine (Norspan) or Fentanyl (Durogesic)
to Morphine should be **very conservative**

HammondCare Palliative & Supportive Care Service Opioid Conversion Card – revised September 2010

Fig. 8 Example of an Opioid Conversion Chart. (Reproduced courtesy of HammondCare Palliative and Supportive Care Service. These values are a guide only and doses should be reviewed for individual patients)

Adjuvant analgesics (e.g., antidepressants, antiepileptics, lignocaine) can be helpful in the management of neuropathic pain. There is limited evidence to support use of medications for neuropathic pain and often choice is guided by the side effects of the medication chosen (e.g., more or less sleep), the comorbidities of the patient, and potential drug interactions (Fallon 2013).

7.5.1 Adjuvant Analgesics in Neuropathic Pain in the General Population

As limited data is available regarding treatment options for neuropathic pain in palliative care patients, it is reasonable to assess the data for neuropathic pain in the general population in case there is some crossover (National Clinical Effectiveness Committee 2016).

Recent Cochrane reviews looking at antidepressants to treat neuropathic pain in the general population found evidence to support the use of duloxetine (Lunn et al. 2014), inadequate research but longstanding note of clinical effectiveness of amitriptyline (Moore et al. 2015a), and little or no evidence to support the use of milnacipran (Derry et al. 2015a), venlafaxine, nortriptyline, imipramine, and desipramine (Hearn et al. 2014a, b; Derry et al. 2015b; Gallagher et al. 2015).

Antiepileptic medication treatment for neuropathic pain has also been the subject of reviews by the Cochrane library. Pregabalin and gabapentin have been shown to be the most effective antiepileptics for neuropathic pain management (Moore et al. 2009; Wiffen et al. 2013b) with lesser evidence for levetiracetam (Wiffen et al. 2014b), lacosamide (Hearn et al. 2012), carbamazepine (Wiffen et al. 2014a), sodium valproate (Gill et al. 2011), and oxcarbazepine (Zhou et al. 2013). No evidence was found to support the effectiveness of topiramate (Wiffen et al. 2013a), zonisamide (Moore et al. 2015b), and there was inadequate research to support the role of clonazepam (Corrigan et al. 2012).

Opioids have equivocal evidence in the use of neuropathic pain. Intermediate term studies have been of poor quality, and the effects of opioids in long-term neuropathic pain management have not been studied (McNicol et al. 2013; Stannard et al. 2016).

A meta-analysis of pharmacotherapy for neuropathic pain in a general (nonpalliative) population was published by the Neuropathic Pain Special Interest Group (NeuPSIG) of the International Association for the Study of Pain (IASP) in 2015 (Finnerup et al. 2015). They note that patients with neuropathic pain often do not receive appropriate treatment.

Their research suggested first-line options (strong recommendations) for use of gabapentin, pregabalin, duloxetine, venlafaxine, and tricyclic antidepressants. There were weak recommendations (second line) for capsaicin 8% patches and lidocaine patches for peripheral neuropathic pain. Tramadol was also given a weak recommendation for use (second line). Strong opioids (with note of the risks of this) and botulinum toxin A (subcutaneously to the painful area, specialist use only) both received third-line, weak recommendations.

Similar findings have been published by NICE suggesting first-line treatments for all neuropathic pain (excluding trigeminal neuralgia) in the general population should be with amitriptyline, gabapentin, pregabalin, or duloxetine (NICE 2013).

7.5.2 Antiepileptics in Palliative Care Pain Management

The gabapentinoids gabapentin and pregabalin are structurally similar compounds thought to be presynaptic calcium channel blockers. Pregabalin has a higher oral bioavailability, hence requiring lower dosing. Pregabalin has a more rapid absorption and is more rapidly titratable (Pruskowski and Arnold 2015). Both undergo renal excretion and require dose reduction in renal failure. There are no known drug interactions with gabapentin or pregabalin. The main side effects are fatigue, sedation, tremor, and dizziness. Increases in peripheral edema can occur (RACGP 2016).

Recent reviews looking at gabapentinoids for cancer pain and opioids in conjunction with either antiepileptics or antidepressants for cancer pain comment on the limited evidence base, the challenge of purely assessing response to specific pain types (e.g., neuropathic pain), and the risk of

adverse effects. They suggest there may be benefits for some patients, and this should be balanced against the risks on a patient-by-patient approach (Kane et al. 2017; Jordan et al. 2018).

Sodium valproate has been studied in a phase 2 trial only (Hardy et al. 2001).

7.5.3 Antidepressants in Palliative Care Pain Management

There are very few studies assessing the benefits of amitriptyline (Kane et al. 2017). Given its widely accepted use in nonpalliative patients with neuropathic pain, it is reasonable to trial starting at low dose while observing for any intolerable side effects, particularly dry mouth, dizziness, urinary retention, and sedation (RACGP 2016).

It may be reasonable to trial duloxetine or venlafaxine given the evidence for their benefit in the nonpalliative patient population. There is inadequate evidence to support the use of SSRIs for neuropathic pain (National Clinical Effectiveness Committee 2016).

7.6 Other Analgesia Options

7.6.1 Ketamine

Ketamine is predominantly an antagonist of NMDA receptors, with some effects on muscarinic receptors, descending monoaminergic pathways, calcium channel and central opioid receptors (Prommer 2012; RACGP 2016). Ketamine is used as a general anesthetic, however at lower doses has a use as an adjunct in postoperative pain management, acute burns pain management, management of patients with opioid-induced hyperalgaesia, and specific neuropathic pain syndromes (Prommer 2012; Schug et al. 2015).

Side effects of ketamine include emergence reactions, which may include unpleasant dreams and hallucinations, local skin reactions, somnolence, and dizziness. In a randomized control trial in a palliative care patient population, low doses of ketamine (0.5–1 mg/kg/day) were not associated with significant side effects (Salas et al. 2012). High dose slow intravenous bolus injections of ketamine in palliative care patients were associated with patients developing hallucinations (Mercadante et al. 2000). The hallucinations were treated successfully with diazepam.

Evidence in Palliative Care

A recent meta-analysis looking at the role of ketamine as an adjuvant to opioids for cancer pain found a very limited evidence base and was unable to assess the benefits and harms of ketamine as an adjunct to opioids for the relief of cancer pain. There was no clinical benefit associated with a rapid dose escalation of ketamine (ketamine burst), and this may be associated with serious adverse events (Bell et al. 2017).

Ketamine should only be used on a patient by patient basis by experienced clinicians given the possible side effects.

Further trials looking specifically at groups with neuropathic pain and using a weight-based dosing approach may be of benefit.

7.6.2 Lidocaine

Lidocaine is a local anesthetic agent. It reversibly interrupts impulse conduction in peripheral nerves and inhibits depolarization of cell membranes by blocking sodium channels (RACGP 2016). It can be used topically, by local infiltration, regional nerve block, neuraxial routes, intravenously or subcutaneously (Schug et al. 2015; Twycross 2016; RACGP 2016). Side effects have been noted at higher dosing and include perioral numbness, metallic taste, nausea, tinnitus, sedation, and cardiac arrhythmias. ECG monitoring has been shown to not be necessary in the cancer pain population when appropriate doses are used-reported protocols include an infusion of 5 mg/kg over 1 hours, titrated up to a maximum of 10 mg/kg over 1 hours (Peixoto and Hawley 2014) or an initial bolus of 1–2 mg/kg over 15–20 minutes followed by a continuous infusion of 1 mg/kg/h (Thomas et al. 2004). Lidocaine should not be used in patients receiving class one antiarrhythmics (e.g., flecainide) (Scottish Partnership for Palliative Care 2013).

Topical lidocaine patches (5%) are licensed for treatment of post herpetic neuralgia (Meier et al. 2003); however, they can be expensive. The patches have a dual action, the mechanical action of the hydrogel patch, and the pharmacological

action of the local anesthetic. One to three patches can be applied (and can be cut to size) to dry, nonirritated skin. The patches are applied in a "12 hours on, 12 hours off" regime, ideally with showering happening in the patch free time. Skin reactions to the patch are common. There is some systemic absorption ($3 \pm 2\%$), but steady states were reached after 4 days with no evidence of accumulation (BioCSL 2015). Heat should not be directly applied to the patch as this may increase absorption.

A systematic review of pharmacotherapy for neuropathic pain in adults in all patient populations from 2015 found weak evidence to support the use of topical lidocaine patches (suggested second line treatment) (Finnerup et al. 2015).

Mexilitine and lidocaine administered systemically appear to be superior to placebo for neuropathic pain (Challapalli et al. 2005).

Systemic Lidocaine in Palliative Care

There is preliminary evidence for the benefit of systemic lidocaine in palliative care patients, and its use should be limited to specialist palliative care settings (Sharma et al. 2009; National Clinical Effectiveness Committee 2016; Seah et al. 2016).

Topical Lidocaine Patches in Palliative Care

High quality evidence is lacking. There appears to be benefit in neuropathic pain with associated allodynia. Patient satisfaction was high (65%) and adverse events rate low (Fleming 2009; Garzon-Rodriguez et al. 2013).

7.6.3 Steroids

Corticosteroids are potent inhibitors of inflammation and can exhibit predominately glucocorticoid effect (e.g., dexamethasone), mineralocorticoid effect (e.g., fludrocortisone) or both (e.g., hydrocortisone). Dexamethasone is often used in palliative care given its high potency anti-inflammatory effect. Dexamethasone is approximately 6–12 times more potent than prednisolone.

Side effects vary from early to late. Early side effects include hyperglycemia, hypocalaemia, psychiatric effects, and gastric irritation. Long-term side effects include proximal myopathy, fluid retention, bone density loss, and fat redistribution (Twycross 2016; RACGP 2016).

Steroids in Palliative Care

There is little high quality evidence to support the use of steroids for pain in palliative care patients (Paulsen et al. 2013, 2014; Haywood et al. 2015).

Dexamethasone may have a role in prophylaxis of radiation-induced pain flare after palliative radiotherapy for bone metastasis (Chow et al. 2015).

Guidelines suggest a limited trial of steroids may be undertaken, particularly for nerve compression or inflammation, if no benefit the treatment should be rapidly tapered (National Comprehensive Cancer Network 2016).

7.6.4 Bisphosphonates/Denosumab

Bisphosphonates are osteoclast inhibitors licensed for the treatment of osteoporosis, hypercalcaemia of malignancy, Paget's disease of bone, and prevention of skeletal-related events (SRE) in patients with malignancy involving bone (Twycross et al. 2016; RACGP 2016). Bisphosphonates are available in oral and intravenous forms. Side effects include hypocalcaemia, flu-like symptoms (particularly iv formulations), esophagitis (especially alendronate), reflux, and gastritis. The risk of osteonecrosis of the jaw (ONJ) is higher with increased potency, iv route, total dose of bisphosphonate, and a history of dental surgery. Zoledronic acid seems to have a higher risk of ONJ than pamidronate (RACGP 2016).

Calcium nadir is usually 4–7 days post-treatment. Adequate hydration must be ensured as bisphosphonates can affect renal function. No dose adjustment is necessary for mild-moderate renal failure (Twycross 2016).

Denosumab prevents activation of the receptor activated nuclear-kappa β ligand (RANKL), reducing formation and activation of osteoclasts. It is licensed for treatment of osteoporosis, hypercalcaemia of malignancy, and prevention of SRE due to bone metastases from solid tumors and has some indications in giant cell tumors of bone. Side effects include hypocalcaemia (calcium nadir is usually 8–11 days post-treatment, although may be later), musculoskeletal pain, and ONJ. Calcium and vitamin D supplements are recommended unless hypercalcaemia is present (RACGP 2016). Denosumab does not

require dose adjustment in renal failure (Twycross 2016).

Bisphosphonates and Denosumab for Pain in Palliative Care Patients

A Cochrane review has examined the role of bisphosphonates in multiple myeloma (2012) showing a reduction in pathological vertebral facture, SRE, and pain with a number needed to treat of 5–13 to reduce pain in one patient (Mhaskar et al. 2012). A Cochrane review looking at bisphosphonates and denosumab in patients with breast cancer bone metastases found bisphosphonates may reduce bone pain and improve quality of life (Wong et al. 2012).

A recent systematic review investigating the evidence for the analgesic role of bisphosphonates and denosumab in the treatment of pain due to bony metastases as a part of the European Association for Palliative Care guidelines project has shown weak evidence only for the role of bisphosphonates or denosumab for analgesia. Their main role may be in delaying the onset of bone pain (Porta-Sales et al. 2017). This review has replaced the Cochrane review of bisphosphonates for bone metastases pain from 2002 (Wong and Wiffen 2002).

A meta-analysis looking specifically at bisphosphonates or denosumab in patients with breast cancer showed high level evidence for reduction in skeletal related events and moderate level evidence for reduced bone pain (O'Carrigan et al. 2017).

8 Interventional Procedures

Procedures may be broadly categorized into local (e.g., nerve block), regional (e.g., sympathetic, plexus, roots, paravertebral blocks), or central (e.g., intrathecal, epidural blocks). Interventions may be temporary (e.g., local anesthetic/steroid injection), longer term (e.g., radiofrequency ablation, pump delivery device), or permanent (e.g., neurolysis, spinal cord stimulator). Evidence reports that 8–11% of palliative care patients could benefit from an interventional procedure (de Courcy 2011). Interdisciplinary collaboration with specialist pain services is supported by evidence-based guidelines (Scottish Intercollegiate Guidelines Network 2008; National Clinical Effectiveness Committee 2016; National Comprehensive Cancer Network 2016).

8.1 Coeliac Plexus Block

This is the commonest neurolytic sympathetic block and is used for relief of pain of pancreatic and other upper abdominal malignancies (de Courcy 2011). The block is performed either under radiological guidance or via endoscopic ultrasound guided approach. There is evidence to support improved analgesia, possible reduction in opioid use, and consequent reduction in side effects of medications (Arcidiacono et al. 2011; Mercadante et al. 2015).

8.2 Intrathecal Pumps

Intrathecal pumps deliver medication directly into the CSF. Intrathecal catheters have a lower risk of complications such as blockage and catheter tip fibrosis than epidural catheters (de Courcy 2011). Analgesics options for infusion include opioids, local anaesthetics, clonidine and baclofen. These can either be delivered via a subcutaneously tunneled line leading to an external pump or an implanted pump delivery system, which is refilled periodically (Lynn et al. 2011; Upadhyay and Mallick 2012). Implanted pumps are more expensive but have a lower infection risk and are likely to be more useful for people with longer life expectancies (Chambers 2008).

Complications include surgical, mechanical, or pharmacological complications (including the potential risk of decreased respiratory function with intrathecal opioids) and the risk of infection (Upadhyay and Mallick 2012).

8.3 Spinal Cord Stimulators

Wire stimulators are placed via the epidural space on the dorsal surface of the spinal cord. The

stimulation is thought to work via the gate theory principles, inhibiting peripheral noxious stimuli. They do not themselves use any medications and can be used in conjunction with multimodal analgesia. A meta-analysis from 2015 found case report evidence only. There were generally reduced analgesia requirements in patients, with the main adverse effects being implantation site infection, CSF leakage, dislodgement of electrodes, and system failure. It concluded current evidence was insufficient to establish the role of Spinal Cord Stimulators in refractory cancer-related pain (Peng et al. 2015).

8.4 Cordotomy

Percutaneous cordotomy can be of benefit to unilateral pain in a specific area, e.g., a limb or the chest wall. A relatively frequent indication is unilateral chest wall pain from mesothelioma. It is carried out under CT guidance targeting the C1/2 level spinothalamic tract contralateral to the side which is symptomatic for the patient (Shepherd et al. 2017). The patient must be able to lie flat for a period of approximately 30 minutes and answer questions appropriately when stimulation testing is carried out to allow adequate localization. It is a highly specialized procedure and not widely available (de Courcy 2011). Systematic reviews note poor quality evidence level but that cordotomy appears to be safe and effective (France et al. 2014).

Side effects are usually transient and include headache, weakness and mirror pain (France et al. 2014).

9 Conclusion

To best manage a patient's pain, the pain must be recognized, a full pain assessment undertaken and an appropriate management plan formed involving the patient and those around them. Evidence is continually evolving for many approaches to pain management. It is reassuring to note that most patients will manage good pain control, often using a multimodel strategy employing targeted treatments, nonpharmacological, and pharmacological options.

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Palliative Management of Breathlessness

11

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_11

Abstract

Breathlessness is pervasive in late stage disease both because of the disease itself, comorbidities, and cachexia. Given its high prevalence, it is sad that the options for symptomatic treatment (having optimized the management of underlying cause(s)) is so small. Careful assessment of potentially reversible causes contributing to breathlessness is paramount. Nonpharmacological interventions have a relatively strong evidence base as does regular, low dose, extended release oral morphine. There is a need for ongoing research into this pervasive and frightening symptom given the impact it has on patients, their caregivers, and health professionals.

1 Definitions

1.1 Chronic Breathlessness

Chronic breathlessness is a distinct clinical entity. In 2017, an international consensus document was published that identified chronic breathlessness as a distinct clinical syndrome defined as:

> Breathlessness that: persists despite optimal treatment of the underlying pathophysiology; and results in disability. (Johnson et al. 2017)

It is of note that a stated duration was not needed for "chronic." This means that the clinician determines that breathlessness is likely to persist from this point onward. The definition also does not seek to differentiate between underlying etiologies of breathlessness, especially given the fact that for many people a combination of a dominant cause and comorbidities contributes to the subjective sensation. The definition also does not seek to define the level of disability that a person needs to experience in order for it to be labeled *chronic breathlessness syndrome*.

Like other symptoms, breathlessness is a subjective sensation, and the person's own account of the experience forms the basis of the clinical evaluation. Studies have sought unsuccessfully to relate physiological changes to the degree of chronic breathlessness, but any relationships correlate poorly (Nishimura et al. 2002). Likewise, descriptors of the breathlessness most often do not help to distinguish underlying causes clinically. The one exception is in chronic obstructive pulmonary disease (COPD) where the description of breathlessness is more commonly associated with emotional descriptors like "frightening," "helpless," and "awful" (Williams et al. 2008).

In practical terms, this means that people with chronic breathlessness are likely to be experiencing problems with basic activities of daily living

(toileting, bathing, dressing, preparing meals) or in moving around their environment.

1.2 Acute Breathlessness

Recent work has defined episodes of acute breathlessness in the palliative care population that have been defined both in terms of duration and underlying etiology (Simon et al. 2016, 2013). The key characteristics that have clinical and management implications include:

- Significant burden as it is high frequency, high intensity and for a proportion of people has no identifiable precipitating cause; and (Simon et al. 2013)
- The duration of these episodes is often measured in minutes (median in people with chronic obstructive pulmonary disease (COPD) 7 min; lung cancer 5 min). (Weingartner et al. 2015)

The first of these factors is important because the unpredictability of these episodes is, in itself, a cause of anxiety and distress. For people with obvious precipitating causes, at least the precipitant can be avoided or, failing that, identified and managed proactively.

The latter is important because the available pharmacological symptom control measures are not going to be bioactive in the necessary timeframe even if they are immediately at hand to take. As such, other approaches are needed to lessen the impact of these distressing episodes.

1.3 Acute-on-Chronic Breathlessness

For many people, episodes of acute breathlessness are superimposed on chronic breathlessness in the palliative care setting. For practical purposes, this may need clinicians to consider management of the chronic breathlessness that occurs at rest or on minimal exertion *and* separately have a management plan for acute exacerbations, especially if there is no identified precipitant for the breathlessness in that setting.

2 Community Prevalence of Chronic Breathlessness/ Duration of Chronic Breathlessness/Patient Attributable Causes of Chronic Breathlessness/Preexisting Breathlessness as People Come to Palliative Care

Across the community, rates of chronic breathlessness have rarely been measured (in contrast to rates of breathlessness in specific care settings or with specific clinical conditions). Across the last 60 years, a handful of studies have been undertaken using a variety of measures. Ultimately, the rates vary slightly, but there are data that suggest more women than men experience breathlessness across the community and that the burden of breathlessness increases with age. Attributable causes include respiratory, cardiovascular, and neuromuscular disorders. By far the most prevalent causes relate to respiratory disease most frequently due to tobacco smoking. The duration of breathlessness in this population that impinges on day-to-day activity varies widely depending on the underlying cause(s), but for people with attributed respiratory causes, the duration of chronic breathlessness tends to be much longer than for other attributable causes. For many people significant symptom burden and limits to activities of daily living may last for decades in those with respiratory causes.

In the setting of palliative care, not all symptoms are attributable to the life-limiting illness. Indeed, many people have long-standing symptoms that predate their life-limiting illness. This is the case with breathlessness also. Given the community rates of chronic breathlessness, many people will experience this as an intercurrent symptom which may worsen during the course of their life-limiting illness due to the life-limiting illness, the comorbid condition, or a combination of both.

3 The Meaning of Breathlessness

As with many sensations, there is a stimulus, the transmission of the stimulus, and the response of the host. Models in pain and breathlessness have

an additional step between transmission and response. This involves the meaning of the symptom to the patient and involves cortical processing of the stimulus. It is one of the major reasons that there is a real gulf between studies of healthy volunteers where breathlessness is induced in a laboratory session (and therefore where there is control over the duration and intensity of the stimulus) and people who experience breathlessness as part of their existence with no likelihood of the underlying causes being further improved.

The lived experience of breathlessness must be considered when seeking to understand the magnitude of its impact on patients and their families. The meaning of breathlessness is important as clinicians seek to reduce the impact on people's lives. Different underlying etiologies give rise to potentially clinically important differences that may have relevance to how patients discuss their breathlessness and how clinicians respond. For example, in people with COPD, breathlessness is a constant reminder of mortality and help for it is only sought in crises (Gysels and Higginson 2010, 2011). Discussion about prognosis, even in the face of it shortening, is often limited or absent (Gysels and Higginson 2010). Worse still, for people with lung cancer, it is often perceived that the disease is self-inflicted, limiting patients' ability to elicit all of the help that they need from clinicians.

4 Mechanisms Leading to Breathlessness

Breathlessness is a complex sensation of breathing discomfort modulated by the interaction of physiological, psychosocial, and external factors (Nishino 2011). This is probably one reason why the experience of breathlessness varies so widely from person to person and might in fact correspond to different sensations depending on the relative weight of each contributor (Elliot et al. 1991).

Brain regions like the insular cortex, cingulate cortex, and amygdala (Herigstad et al. 2011) have been repeatedly implied in the perception of breathlessness in neuroimaging studies. For example, the perceptions of air hunger inflicted by ventilation restriction and the sensation of discomfort caused by resistive breathing are processed in the insular cortex (Banzett et al. 2000). In these cases, the intensity of breathlessness grows in direct proportion to the stimulus intensity which suggests a simple underlying physiologic mechanism. Conversely, the right posterior cingulate cortex seems to be involved in the modulation of the sensation of breathlessness which is unrelated with the stimulus intensity and may involve emotional processing (Peiffer et al. 2001). An additional study implied the anterior insula and amygdala process the unpleasantness of breathlessness (von Leupoldt et al. 2008). Notably, these were experimental studies with healthy volunteers in which breathlessness was artificially induced.

Neuroimaging studies in people with breathlessness, particularly chronic breathlessness, are rare. However, preliminary data shows that central processing of chronic breathlessness is different than experimentally induced breathlessness (Johnson et al. 2015) involving different brain regions and mechanisms. For example, chronic breathlessness in people with COPD is associated with activation of the prefrontal cortex that regulates fear-related memory and emotional learning. Similar to acute breathlessness, chronic breathlessness is also associated with activation of the anterior cingulate cortex. However, this activation directly correlates with emotional processes like depression, fatigue, and hypervigilance which may play a key role in modulating this symptom (Herigstad et al. 2015).

5 Measuring and Describing Breathlessness/MCID

5.1 Taking a History

Clinically, eliciting an accurate history of breathlessness is something that we do not do well. People who are obviously struggling to breathe will often deny that they are breathless. One crucial

reason for this is that people adjust their activities to minimize their risk of becoming more breathless.

When taking a clinical history, most of us ask "How are you doing?" rather than "What are you doing?" Arguably, the most important question is to ask *is* "What have you had to give up in order to avoid breathlessness?" People adjust their activities of daily living to minimize their experience of breathlessness, often leading to a shrinking footprint as the underlying cause(s) worsen. In turn, for many people with chronic breathlessness, this leads to increasing levels of social isolation that is distressing and a cause of suffering in itself.

5.2 Measuring Breathlessness

There are a large number of tools that help to measure breathlessness. Many of these are only suited to the research setting. In clinical practice, a simple 0–10 numerical rating scale (NRS) (Wilcock et al. 1999) asking about average and worst breathlessness intensity in the previous 24 h is going to most closely reflect the lived experience of that person. In acute breathlessness (such as an acute worsening of asthma), the minimum clinically important change in an NRS for a person to start to feel less breathless is 2 points on the NRS (Ries 2005). More recent work suggests that in chronic breathlessness, a reduction of one point will be discerned by patients as an improvement worth experiencing (Johnson et al. 2015). This is reflected strongly in qualitative work with people who are experiencing breathlessness and their caregivers (Rocker et al. 2013). In this study, respondents made it clear that even small reductions in the intensity of the symptom made a big difference to how they felt.

Although there are multidimensional tools that measure breathlessness and a number of established tools that take into account a range of domains that reflect the complexity of the symptom and people's response to it, their use is largely limited to the research setting. Tools such as the St George's Respiratory Questionnaire (SGRQ) (Jones et al. 1991), Baseline Dyspnea Index (BDI)/Transition Dyspnea Index (TDI) (Mahler et al. 1984), Multidimensional Dyspnea Profile (MDP) (Banzett et al. 2015), or the Chronic Respiratory Questionnaire (CRQ) (Guyatt et al. 1987) are important in helping to fully evaluate breathlessness; they are relatively long and take a great deal of time. Their utility in a busy clinical setting is therefore somewhat limited (Glaab et al. 2010).

6 Clinical Framework for Palliating Breathlessness

Good palliation of breathlessness reflects principles common to all symptom control (Wiseman et al. 2013). It is best outlined as a "breathlessness ladder" by the Canadian Thoracic Society (Marciniuk et al. 2011). As with any symptom, ensure that reversible causes are adequately addressed. Addressing these causes should only occur if they are going to be symptomatically relevant to the patient's symptom. The next step is to consider non-pharmacological approaches that can help to reduce the person's breathlessness or its impact on their lives and, finally, consider safe, evidence-based pharmacological therapies to improve the symptom.

7 Evaluating Reversible Causes of Chronic Breathlessness

Many clinicians assume that some other clinician has evaluated systematically each patient's potentially treatable causes of breathlessness. The one consecutive case series that has been published would suggest otherwise (Dudgeon and Lertzman 1998). In this consecutive cohort of 100 patients with cancer, there was a median of five causes likely to contribute to the person's breathlessness. These include people with hypoxemia (40%), anemia that was likely to be symptomatically significant (20%), and people with evidence of bronchospasm (52%). Optimizing the management of each of these contributing factors is pivotal to good symptom control, even very late in life.

8 Non-pharmacological Interventions for Breathlessness

There is a strong evidence base underpinning non-pharmacological interventions for chronic breathlessness. This includes a comprehensive systematic review of the available randomized studies (Bausewein et al. 2008). Key, evidence-based interventions with high levels of evidence include:

- Chest wall vibration which involves high-frequency chest wall oscillation administered by an inflatable vest worn by the patient for 10–15 min twice daily for 12 weeks.
- Neuroelectrical muscle stimulation of quadriceps, hamstrings, and calf muscles (thought to work by helping to reverse the breathlessness-deconditioning-worsening breathlessness cycle). Interestingly, although the benefit is there for the time it is being used (20 min/day, three times per week for six continuous weeks), by week 12 (6 weeks off therapy) any benefit had disappeared. This is an area where continued clinical trials are occurring.

Those with moderate levels of evidence include:

- Walking aids such as frames (likely by their impact on the mechanics of the chest wall and hence helping to make breathing more efficient).
- Breathing training, which requires to be cognitively intact and motivated to work with therapists. Elements of this include relaxation, activity pacing, and planning for activities.

9 Oxygen for Breathlessness

Oxygen is widely used in the setting of palliative care and people with breathlessness, often without adequate assessment of oxygenation (Currow et al. 2009). Oxygen is easily started in ambulances, in the emergency department, or on the wards. Having started oxygen, it is often difficult to cease oxygen even when there is little objective evidence of symptomatic improvement. Like any therapy, there are benefits and harms which need to weighed up when considering the use of oxygen.

For more than three decades, there has been evidence of survival advantage for people with severe hypoxemia ($PaO_2 \leq 55$ mmHg) or moderate hypoxemia (PaO_2 56–59 with cor pulmonale or polycythemia) (Tarpy and Celli 1995; McDonald et al. 2005). These data fail to speak to the symptomatic benefit of oxygen. Three recent studies help to inform this. One is a large, double-blind, randomized controlled trial (RCT) of oxygen compared to medical air, and the other two were meta-analyses of oxygen studies dating back 30 years (Abernethy et al. 2010; Uronis et al. 2008, 2015).

The RCT enrolled 239 participants, none of whom qualified for long-term oxygen therapy (LTOT) (Abernethy et al. 2010). Participants were asked to use oxygen or air for greater than 2 L per min for more than 15 h per day for 7 days. No primary measure was significantly different across the study although those with worse hypoxemia tended to benefit more, and morning scores were better in the oxygen study, with the likelihood that people tended to use oxygen overnight as one way to achieve their required use although this was not measured in the study.

The first meta-analysis was of oxygen in people with cancer as their life-limiting illness who did not qualify for LTOT. There was no symptomatic benefit from oxygen over medical air (Uronis et al. 2008). By contrast, the other study focused on RCTs in people with COPD who did not qualify for LTOT but where breathlessness was measured as a secondary outcome (Uronis et al. 2015). Every 1 of the 18 studies favored oxygen over medical air, and the point estimate with very tight confidence intervals was strongly in favor of oxygen. Fundamentally, this is a change in the way oxygen is currently prescribed and funded. Uptake of this finding into practice has been variable.

Clinically, given the evidence base from rigorous clinical trials, people with chronic breathlessness should be considered for a time-limited trial

of LTOT. Clearly defined end points are needed for such n-of-one trials.

9.1 Patients', Prescribers', and Caregivers' View of Oxygen in the Palliative Setting

Caregivers tend to support the use of oxygen for people with chronic breathlessness in the palliative setting. Oxygen is considered to have a vital role in relieving breathlessness, decreasing breathlessness-associated anxiety, and essentially in sustaining life (Collier et al. 2017). Caregivers also think that oxygen has a major role in improving patient's quality of life (Goldbart et al. 2013). Disadvantages reported include mobility conditioning, the equipment required, and associated costs (Collier et al. 2017).

10 Pharmacological Interventions for Reducing the Sensation of Chronic Breathlessness

10.1 Opioids

10.1.1 Basic Science Including Mechanisms of Action for Opioids for Chronic Breathlessness

Meta-Analyses

All adequately conducted meta-analyses for the use of opioids for the reduction of chronic breathlessness indicate clinical benefit without the harms that many clinicians associate in their minds for people with respiratory disease and opioids – respiratory depression. The largest studies have used extended-release preparations of morphine orally as the basis for the pharmacological intervention.

Jennings et al. (2002), Ekström et al. (2015; for COPD only, with an emphasis on steady state), and a more recent Ekström et al. review (2018) all show that symptomatic benefit consistently favors morphine. These are now sizable meta-analyses with results reflected across a range of study designs and outcome measures.

Initiation and Titration of Morphine for Chronic Breathlessness

The largest randomized studies to date have initiated therapy in opioid-naïve patients with once-daily extended-release morphine 20 mg (Currow et al. 2017). Titration has not been widely studied. One large longitudinal dose ranging study suggested that when responding symptomatically to successful titration (with a maximum dose of 30 mg per 24 h), there was a marked benefit in the first 24 h, but the maximal benefit was not seen for up to 5 days (Currow et al. 2013b). This suggests that upward titration should occur cautiously. There is no evidence to support the use of supplemental or "as-needed" immediate-release morphine solution in people with chronic breathlessness nor in the setting of acute-on-chronic breathlessness. In people already on opioids for other indications, the only guidance from randomized controlled trials is that an upward titration of 25% of the baseline dose is likely to be of benefit (Allard et al. 1999; Currow et al. 2011).

Predictors of Response

Pooled data from prospective studies of morphine for chronic breathlessness identify two major predictors of response for the symptomatic reduction of chronic breathlessness: younger age and more severe breathlessness (Johnson et al. 2013). Further work needs to be done to understand fully the factors that underlie response and, importantly, lack of response. The latter may include factors relating to variations in opioid metabolism or receptors (Currow et al. 2015).

11 Other Pharmacological Approaches

11.1 Buspirone

The largest study done to date was a randomized, double-blind, placebo-controlled trial of buspirone 20 mg/day orally for 4 weeks, an

anxiolytic in 432 participants (Peoples et al. 2016). Despite being adequately powered and with a cogent underlying theoretical base that reducing anxiety would help people to cope with breathlessness, this was a strongly negative study. The intervention was well tolerated but delivered no symptomatic benefit for breathlessness nor anxiety. Physiologically, there was no difference in oxygen expenditure.

11.2 Anti-depressants

There are tantalizing pilot data that suggest there may be benefit from the use of antidepressants in reducing chronic breathlessness. The mechanism of action has yet to be defined, but it appears to be independent of underlying anxiety or depression. A large placebo-controlled, randomized trial has been completed and the results are awaited with interest (Watts et al. 2016).

11.3 Benzodiazepines

Benzodiazepines are widely used in people with breathlessness. In a meta-analysis, the evidence base for their use has not demonstrated benefit over placebo (Simon et al. 2016), and although one may be able to make a case for benefit in someone who is acutely distressed by new breathlessness, the case for their use in the chronic setting (and the tolerance that rapidly develops to them) mitigates against their use for chronic breathlessness.

12 Clinician Education

The existing workforce of both family physicians/general practitioners and specialists are likely to have been trained before currently available evidence for the existence of a distinct syndrome nor that it is safe and effective to use low-dose, regular extended-release morphine to reduce the intensity of chronic breathlessness. This means that clinician education should target both existing practitioners and tomorrow's practitioners also.

In qualitative work, prescribers identify very similar themes. Family physicians and specialists both identify the concerns about insufficient knowledge as this was not part of their training and fear of legal censure for prescribing opioids for an indication other than pain (Young et al. 2012; Rocker et al. 2012; Collier et al. 2015). These identified barriers require specific interventions that target clinicians' concerns (Currow et al. 2013a; Hutchinson et al. 2017). Simply publishing guidelines or presenting data at conferences or in peer-reviewed journals, for example, is not sufficient.

13 Implications for Caregivers

Providing care for someone with chronic breathlessness is a challenge for caregivers. The role most often falls to family and friends. It is daunting to watch someone that you love struggle to breathe. It goes to the very heart of being alive and having that life threatened. One challenge is that the care that needs to be offered can be for very long periods of time (often measured in years) with stable but debilitating disease (Johnson et al. 2012). As noted, many people experience worsening of their chronic breathlessness, sometimes without an obvious precipitant (Simon et al. 2013). Not only is this challenging for patients, but it is difficult for caregivers. Structuring an agreed approach for the things that will help the patient in this setting is one of the most important conversations to have with patients and their caregivers. Like many such plans, the agreed approach will need to be revisited as social and clinical issues change. A clear level at which to escalate care to the emergency department is part of this work (Luckett et al. 2017).

14 Health Service Implications of Breathlessness

Breathlessness is a frequent cause of contact with health services – in primary care 0.9% of all adult consultations relate to breathlessness

(Currow et al. 2013b). Acute-on-chronic breathlessness is a major reason for the use of prehospital services such as ambulance and in attendances at the emergency department (Hutchinson et al. 2017). In one large consecutive case series in a high-income country, acute-on-chronic breathlessness accounted for 20.2% of all major emergency presentations to the emergency department and 5.2% of all presentations (Hutchinson et al. 2017). In primary care, breathlessness increases the likelihood of the consultation being a home visit or a visit to a residential aged care/skilled nursing facility threefold and increases the likelihood of an urgent transfer to hospital by 2.5-fold (Currow et al. 2013a). A large proportion of the presentations to the emergency department appear to be related to acute-on-chronic exacerbations of breathlessness and have often settled from the crisis point that precipitated the decision to seek professional help by the time that they are assessed clinically (Hutchinson et al. 2017).

14.1 Self-Management Strategies

Such patterns of presentation raise the important question of whether there are opportunities to improve systematically self-management skills for patients and their families to reduce reliance on emergency services. Tentative steps are being taken in formative studies to improve the way people are educated and supported when they have a chronic condition and breathlessness that may lead to acute exacerbations (Disler et al. 2014; Luckett et al. 2016, 2017).

Ensuring that people are able to identify the precipitants of their breathlessness and have specific management plans for the likely triggers is an important first step. Having good caregiver understanding of the condition and ways that its impact can be minimized is also likely to be helpful. Caregivers consistently identify that they do not fully understand the lived experience of chronic breathlessness and are not sure how best to help but clearly want to be able to do something during acute exacerbations (Gysels and Higginson 2011).

15 Driving and Breathlessness: Opioids

Being able to drive is crucial for most adults enhancing their participation in different daily activities and providing a sense of personal freedom and independence (King et al. 2011). Conversely, driving cessation is associated with social isolation, worse health-related outcomes, higher mortality, and decreases in quality of life (Marottoli et al. 2000; Mezuk and Rebok 2008; Chihuri et al. 2016). Importantly, 23% of people receiving palliative care are still driving and an additional 16% still considering it in the future (Widman and Bergstrom 2014). Many of these patients are prescribed opioids for symptom control and are advised not to drive while taking them (Weir et al. 2017). However, a systematic review on the quality and generalizability of the studies evaluating therapeutic opioids and driving reported a large heterogeneity in study designs which may contribute to conflicting results and limited generalizability (Mailis-Gagnon et al. 2012). The most recent systematic review on opioids and driving reported no significant impact of oral or transdermal opioid agonist formulations on patient's driving-related skills (Ferreira et al. 2018). However, only three empirical studies were included in this review in which the need for further research is this area is highlighted.

At this stage, some guidelines recommend that clinicians advise patients not to drive while initiating and up-titrating therapeutic opioids (Drug & Alcohol 2008; Austroads 2014). This precautious approach is mainly based on research with healthy volunteers using single-dose, immediate-release opioid formulations. Also, psychometric tests are frequently the outcome measures although their translation for on-the-road driving outcomes is questionable. Interestingly, it is not known if initiating therapy with extended-release formulations would have detrimental effects on driving-related skills.

There is also some data showing the impact of uncontrolled symptoms on people's driving-related skills. In one study, nonmalignant pain was shown to be more detrimental than opioid intake for driving-related outcomes assessed

by a driving simulator (Nilsen et al. 2011). In another study, participants with chronic malignant pain performed worse in psychometric tests than controls taking opioids (Sjøgren et al. 2000). Although no similar studies are available for other symptoms, there is evidence suggesting that chronic breathlessness significantly also affects outcomes on the road (Karakontaki et al. 2013).

Given the scarcity of robust evidence in this field, clinicians face some challenges when providing advice in regard to opioids and driving. At this point, it is important to recognize that (i) advising a patient not to drive may have severe psychosocial implications, (ii) there is limited evidence associating oral and transdermal opioids with negative driving-related outcomes, and (iii) symptoms may play an important role in the ability to drive safely. As such, it is recommended that advice should be tailored individually based on the anamnesis (including symptom severity), physical exam, and, for some doubtful cases, a driving assessment. It is important to note that all patients should be advised not to drive if they experience side effects like sedation, dizziness, or confusion.

Disclosures DCC – Consultancy to, and intellectual property payments from Mayne Pharma Pty Ltd; advisory board roles with Helsinn Pharmaceuticals and Specialist Therapeutics.

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Fatigue

12

Martin Mücke and Dmitrij Kravchenko

Contents

Abstract

Fatigue is a subjective multidimensional illness that plays an immense role, sometimes having an even greater impact than symptoms such as pain, nausea, and vomiting, in a patient's quality of life. Once treatable causes

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_12

for fatigue are excluded, a multimodal therapy plan should be developed with considerations toward the wishes and preferences of the patient. Research suggests that feelings of physical well-being and emotional stability are the most important aspects with respect to the quality of life, regardless of cultural and individual differences. Similarly, the social integration of the patient and their ability to self-reliantly live out their day-to-day life is also of great importance.

1 Introduction

Fatigue is part of a regulatory system that serves to keep the balance between activities and rest. Unfortunately, patients who are suffering from life-limiting disorders tend to experience fatigue with an overwhelming intensity, leading to a state of imbalance where sleep and rest do not lead to recuperation. This combination of physical, emotional, and cognitive weariness or exhaustion is termed fatigue. The exact causes and mechanisms are not yet well understood, with no definitive diagnostic criteria or lab markers available, making fatigue difficult to recognize and properly diagnose. A thorough description of the symptoms ailing the patient is of utmost importance in the clinical setting. What is known to date is that in most cases, fatigue is not attributable to one single cause; it has a multifactorial genesis and is more than just the sum of its causes. It is an ailment with multiple layers which severely limits the patient's quality of life during their disease trajectory. The vast majority of palliative care patients are subjectively affected by this complex symptom. Fatigue in patients with life-limiting diseases reduces, alone or in combination with other symptoms such as pain, dyspnea, or nausea, the overall quality of life considerably and plays a significant role as one of the most important prognostic factors. Fatigue can manifest itself at any time in the course of a life-limiting disease and can even be observed many years after cancer therapy. Data regarding the prevalence of fatigue varies tremendously depending on the clinical definition of fatigue, diagnostic tools, the form of therapy, and the point in time during which examinations are carried out. The clinical appearance of fatigue has many faces and includes physical, cognitive, and affective aspects. Problems such as the multidimensional clinical appearance of fatigue and the lack of a unifying model explaining its etiology and pathogenesis make it most difficult to formulate a universal definition of this syndrome.

The identification and treatment of fatigue is an interdisciplinary task which involves all parts of the health care team. In the last few years, there has been enormous growth in literature regarding clinical experience with fatigue, as well as fundamental research into the mechanisms of this syndrome. This chapter is geared toward all professional health care groups which provide care to palliative care patients. By discussing topics such as the clinical manifestation of fatigue, etiology, leading theories and promising research, diagnostics, management, non-pharmaceutical therapies, pharmaceutical therapies, and rehabilitation, this chapter aims to provide an overview but also highlights how much is left to research and how little we understand this prevalent syndrome. We hope that this chapter will aid our colleagues in the health care field to better recognize, understand, and effectively treat this very complex ailment.

2 Overview

Fatigue is defined by the EAPC (European Association of Palliative Care) as a subjective feeling of tiredness, weakness, or lack of energy (Radbruch et al. 2008). It can be thought of as a cluster of symptoms affecting the physical and cognitive capabilities of a person. These two aspects can then be further generalized as weakness representing the physical part and fatigue/weariness representing the cognitive aspect. Approximately up to 80% of advanced stage cancer patients suffer from fatigue, making it next to pain and cachexia one of the most common symptoms of late-stage cancer. Fatigue can affect people of all ages, although there is currently insufficient research regarding children

and adolescents. Unlike healthy individuals, who recover their energy during rest and sleep, cancer patients suffering from fatigue do not, leading to a feeling of a heavy continuous strain and disability, as well as a lower perceived quality of life. Glaus, a leading expert on fatigue, stresses the importance of the qualitative differences between general fatigue that healthy people may experience and cancer-related fatigue (CFR), the latter which affects the long-term physical, affective, and cognitive aspects of the patient's well-being. However, other authors have stressed that differences between general fatigue seen in healthy people and fatigue in palliative care patients may be due to the more overwhelming intensity of fatigue in palliative care patients rather than the qualitative difference between cancer patients.

The pathophysiology is not yet fully understood; this makes it difficult to suggest a broad general therapeutic approach. Fatigue is a multidimensional condition which requires a multimodal therapy. This includes physical, psychiatric, social, and spiritual interventions, which together can lead to an improved disease management and to a better quality of life.

3 Definition and Prevalence

Multiple definitions have been suggested for the tumor-associated fatigue, also referred to as "cancer-related fatigue." David Cella, who was the first to define fatigue in 1995, defined it as "a subjective state of overwhelming, sustained exhaustion and decreased capacity for physical and mental work that is not relieved by rest" (Cella et al. 1998). Over time, criticism emerged regarding the seemingly arbitrarily chosen duration and intensity of the symptoms. A consensus was reached when the Fatigue Coalition USA suggested to use the ICD-10 criteria, shown in Table 1 (Cella et al. 2001).

The National Comprehensive Cancer Network (NCCN) defined fatigue as follows: "Cancer-related fatigue is a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning" (Berger et al. 2015).

Table 1 Proposed ICD criteria for CFR

	Six (or more) of the following symptoms have been present every day or nearly every day during the same 2-week period in the past month, and at least one of the symptoms is significant fatigue (A1)
A1	Significant fatigue, diminished energy, or increased need to rest, disproportionate to any recent change in activity level
A2	Complaints of generalized weakness or limb heaviness
A3	Diminished concentration or attention
A4	Decreased motivation or interest to engage in usual activities
A5	Insomnia or hypersomnia
A6	Experience of sleep as unrefreshing or nonrestorative
A7	Perceived need to struggle to overcome inactivity
A8	Marked emotional reactivity (e.g., sadness, frustration, or irritability) to feeling fatigued
A9	Difficulty completing daily tasks attributed to feeling fatigued
A10	Perceived problems with short-term memory
A11	Post-exertional malaise lasting several hours
B	The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning
C	There is evidence from the history, physical examination, or laboratory findings that the symptoms are a consequence of cancer or cancer therapy
D	The symptoms are not primarily a consequence of comorbid psychiatric disorders such as major depression, somatization disorder, somatoform disorder, or delirium

The EAPC definition considers the physical and cognitive dimensions of fatigue as the least common denominator in their discussion, regarding the affective attributes as part of a natural consequence of the reduced quality of life. On the other hand, other definitions have highlighted additional dimensions of fatigue. Glaus, for example, described fatigue as a multidimensional symptom complex, which consisted of 59% physical, 29% affective, and 12% cognitive sensations (Glaus 1998). The physical symptoms are made

up of decreased performance, weakness and lack of strength, extreme physical exhaustion, as well as an unusually increased need for sleep and rest. The affective and emotional level is comprised of a sense of helplessness, irritability, limited participation in usual activities, sadness, fear, and lethargy. The cognitive symptoms consist of difficulty concentrating, thought disorders, as well as sleep problems (falling asleep, staying asleep).

Research has shown that fatigue is the most common and most debilitating of the problems faced by tumor patients after the conclusion of cancer therapy (Lawrence et al. 2004; Stark et al. 2012). Symptoms such as lack of energy and drowsiness have been observed in 74% and 60% of tumor patients, respectively. Around 30–50% of these patients reported undiminished fatigue even years after successful cancer treatment. The chances of suffering from fatigue rise to nearly 99% after chemo- or radiotherapy, making fatigue one of the most debilitating side effects of these therapies. Not only cancer patients are plagued by this syndrome, patients suffering from other chronic life-threatening illnesses such as congestive heart failure, respiratory failure from COPD or lung fibrosis, or HIV/AIDS have a high chance of being afflicted by a significant fatigue symptom burden. For multiple sclerosis, fatigue is reported as the most common symptom with 83% of the patients being affected. In contrast to disease-related fatigue, the long-lasting chronic fatigue syndrome (CFS) can be observed in 0.3% of the population. Seventy percent of the CFS cases develop after an infection, so that an immune disorder or viral component is being hypothesized. The proposed diagnostic criteria are made up of three main criteria: a substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social, or personal activities that persist for more than 6 months and are accompanied by fatigue, which is often profound, is of new or definite onset (not lifelong), is not the result of ongoing excessive exertion, and is not substantially alleviated by rest; post-exertional malaise; and unrefreshing sleep (Committee on the Diagnostic Criteria for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome, Board on the Health of Select Populations, and Institute of Medicine 2015). A psychological component is found in 40% of CFS patients.

Fatigue in palliative care patients must be differentiated from cachexia, or the anorexia-cachexia syndrome (ACS).

Fearon et al. defined cachexia as:

> . . . a multifactorial syndrome characterised by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment. The pathophysiology is characterised by a negative protein and energy balance driven by a variable combination of reduced food intake and abnormal metabolism. (Fearon et al. 2011)

Further diagnostic criteria for cachexia include weight loss of over 2% over 2 months, more than 5% over 6 months, or a body mass index (BMI) less than 20 kg/m^2. Muscle mass and stomach fat are not the only tissues affected by cachexia: atrophies and loss of functionality are seen in other systems, and until ultimately, heart failure leads to death.

3.1 Potential Causes of Fatigue

Patients presenting with fatigue should be checked for treatable causes of the symptoms. For example, depression or side effects from medications can mimic fatigue and should be excluded before the diagnosis of fatigue is made. Depression can be difficult to distinguish from fatigue due to overlapping symptoms such as weakness and lack of energy. Symptoms such as recurrent feelings of worthlessness or recurrent thoughts about death can be an indication for depression rather than fatigue. A list of potential causes of fatigue can be found in Fig. 1.

3.2 Etiology and Pathophysiology

To date, there exists no unifying theory which explains the etiology and pathogenesis of fatigue. Although, multiple different pathophysiological pathways have been described, it is widely

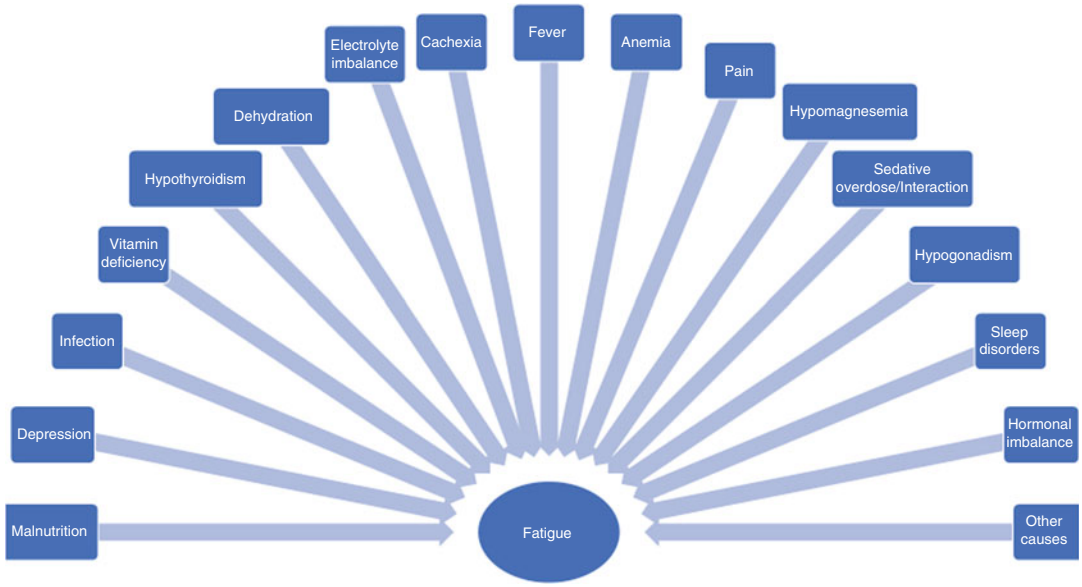

Fig. 1 Possible disorders leading to fatigue

believed that the origin of fatigue can be categorized as either peripheral or central. Peripheral fatigue has been associated with changes in muscle metabolism, while central fatigue has been related to a disorder in the hypothalamic-pituitary-adrenal (HPA) axis as well as the circadian rhythm, resulting in cognitive disabilities (Stone and Minton 2008; Wang 2008). It is possible that the various causes of fatigue require specific therapies and management. The etiology of cancer-related fatigue (CRF) has not been yet fully explained. Cancer-associated symptoms, including CRF, are influenced by polymorphisms. For example, polymorphisms of genes regulating inflammatory cytokines were shown to be risk factors for cancer-related fatigue (Bower and Lamkin 2013; Collado-Hidalgo et al. 2008). Because of this, a multifactorial pathophysiology is presumed. The development of CRF can either be due to direct influences of the cancer or can result as a side effect of antineoplastic radio- or chemotherapy. Radio- or chemotherapy may also cause other side effects such as paraneoplasias, anemia, metabolic disorders, or cachexia, all of which may aggravate CRF.

Cancer-related fatigue may also be classified into primary and secondary. Primary CRF is thought to be directly related to the tumor itself, while secondary CRF is the result of physical distress related to pain, sleeping disorders, infections, malnourishment, hypothyroidism, and anemia, but also emotional stress and depression. Many factors are likely to contribute to CRF in late-stage cancer, so that a clear distinction between primary and secondary is not always possible (Radbruch et al. 2008). The use of pharmaceuticals can also contribute to the development of fatigue. For example, the use of opioids can lead to an opioid-induced fatigue due to their sedative attributes.

Due to our poor understanding of the pathophysiology of fatigue in palliative care patients, there is a pronounced need for more research. A few talking points which are currently being discussed as contributing or causal factors are:

- An increased production of pro-inflammatory cytokines, such as TNF-α, IL-1β, and IL-6 either by the tumor, as a reaction of the immune system, or by the paraneoplastic entity.
- A high serotonin level due to a dysregulation favors a reduction in the somatomotor drive.
- Activation of afferent vagal nerves by released neuroactive substances leads to suppression of

somatic muscle activity and induction of weakness and weariness.
- Disruptions in the hypothalamic-pituitary-adrenal (HPA) axis pathway through cytokines, IFN-α, or IL-2 lead to ACTH (adrenocorticotropin) suppression and consequently a reduction in cortisol secretion.
- ATP (adenosine triphosphate) dysregulation in muscle cells due to a defect in ATP regeneration, muscle mass loss caused by cortisone intake, or certain chemotherapeutic substances.
- Disruption of the circadian rhythm and melatonin secretion. These hypotheses are partly based on studies that focused on illnesses characterized by the occurrence of fatigue, such as work-induced tiredness, CFS, and rheumatoid arthritis.

4 The Patient's Perception

Most patients view CRF as part of an inevitable progression of their disease, which results in them rarely addressing it in conversation with their physicians. This may be reinforced by the patient's assumption that there is nothing that can be done to alleviate CRF or that CRF treatment could have unwanted side effects. If the maintenance of physical performance is an important part of the patient's self-perception, it may be difficult for them to admit a weakened resilience. In oncology, medical staff tend to put the emphasis of care on the main illness, leading to fatigue being perceived as a symptom of secondary importance which may distract from the primary goal of treating the cancer. A structured assessment with the help of questionnaires like the Edmonton Symptom Assessment System (ESAS) or the "minimal documentation system" (MIDOS) is helpful for the screening of relevant symptoms in clinical practice. The MIDOS2 is a German adaptation of the ESAS and functions as a tool for repeated symptom self-assessments by the patients. It tests ten items (with two additional items being labeled as "other" which the patient can specify) on a four-step visual rating scale ranging from "not present," "light," "middle," and "strong." The ten items include pain, nausea, vomiting, dyspnea, constipation, weakness, lack of appetite, tiredness, depressive mood, and fear. In addition, the current state of well-being is also assessed (very bad, bad, moderate, good, and very good). Screening instruments such as the ESAS or MIDOS are easy to use and require little time to fill out, resulting in a lower burden for the patient but allowing a good overview of the patient's situation for the medical staff (Stiel et al. 2010).

4.1 Fatigue and Depression

It is not uncommon to see depression being associated with CFS. Differentiation between depression and fatigue is difficult, as there is considerable overlap in the diagnostic criteria. This becomes apparent when comparing the ICD criteria for depression with those for fatigue. For example, weariness is a pronounced symptom of depression, while sadness, fear, and lethargy have been described as part of an affective dimension of fatigue. Depression may aggravate the perceived burden of fatigue and the subjective suffering of the patient. Vice versa, it has been shown that fatigue is able to induce and intensify depression. However, differentiating between which parts of the symptom burden are attributable to fatigue and which to depression, and if predominantly one or both are contributing, may be important for the therapeutic regimen. In some cases, depression may be easier to treat than fatigue, and the successful treatment of depression may partly or even completely alleviate the fatigue symptomatic. When considering differential diagnoses, keep in mind that feelings of guilt, self-deprecation, and a sense of imminent death are more typical of depression rather than fatigue. The differentiation between depression and fatigue is not always possible, even a skilled psychiatric specialist utilizing a structured clinical interview will sometimes not be able to distinguish the two. The patient history can be a helpful tool for separating the two syndromes if it includes questions regarding previous depressive episodes, if the symptoms of fatigue preceded the depressive symptoms, and whether the fatigue

symptomatic is a new experience which occurred parallel to the underlying disease.

5 Fatigue and the Social Sphere

Fatigue is not just distressing for the affected patient, but is also a challenge for the whole surrounding social system, including the partner, family, and friends. The chronic form of fatigue, especially after long periods of therapy, often makes it difficult for patients to return to a daily routine. Friends and family have to realize that joint activities are no longer a trivial thing due to the lack of energy of the patient. Interpersonal roles, relationships, and social relations can change as a consequence of the illness. Friends might be reluctant to spend time together, as they feel overwhelmed by the condition of their friend and might not know how to react. This often leads to a feeling of disappointment and isolation by the patient and may in turn produce negative developments and setbacks in the course of the illness. Afflicted patients should be informed that their limitations due to exhaustion, their needs, and their expectations should be openly communicated within their social sphere. Only the greatest possible candor can minimize misunderstandings and help improve relationships. Professional help in the form of psychotherapists should also be offered early on to not only the patient but also to family and friends.

6 Fatigue When Returning to Work

For most patients, the ability to work is an integral part of their quality of life and strengthens their sense of self-reliance and purpose. Patients may be limited in their ability to work due to a lack of concentration, memory problems, and the reduced ability to think clearly, depending on the level of exhaustion. This can often lead to a delayed reintegration into their work life. Thus, patient information and education on topics such as acceptance of their illness, neuropsychological deficits, and the complex somatic limitations that go hand in hand with fatigue is of utmost importance. Rehabilitation assessments can offer a possibility to gauge the patient's personal performance deficits, making it possible to arrange a personalized rehabilitation plan for the reintegration of the patient back into the workforce. An important aid for the return to work are stepwise reintegration programs where employee, employer, and physician agree on a step-by-step workload increase over a period of time until either a 100% workload or the highest possible workload that does not affect the patient's recovery is reached. Unfortunately, this is not always feasible so that individual solutions must be found. An excessively demanding workload must be avoided as it can create recurring frustration and commonly ends in resignation which further amplifies the fatigue symptomatic. A similar strategy of openness and candidness as with family and friends is recommended in the work environment and with the employer. Problems should be addressed early on and openly to find solutions that include, for example, reduction of work hours per week or transfer to a different workstation within the company if possible. Patients should take their time with tasks and be aware of their physical needs, taking special consideration as to possible signals of over-working. A detailed consultation with the health care provider team (physician, social worker, psychologist/psychiatrist) should take place to allow the planning of a personalized reintegration plan and offer a chance for the patient to ask questions, as well as considerations to be made for disease-related retirement.

7 Diagnostics

The goals of fatigue diagnostics in seriously ill patients are:

- To better understand the symptoms and problems ailing the patient
- To capture the "as is" status of the patient at that moment
- To aid in the structuring of their day-to-day life
- To be able to effectively prioritize energy reserves to complete vital tasks

– To document the successes, but also failures, of therapeutic options

Screening should include explicit questions regarding unusual tiredness or exhaustion as part of the patient's history, as there are no reliable lab parameters or physical tests for fatigue. Answers to these screening questions will always be subjective, but self-assessment is the cornerstone of the fatigue diagnosis. Rating fatigue intensity on categorical, numerical, or visual analog scales, akin to the ones used to assess pain, can be useful to gauge the progression of the syndrome and the impact of therapeutic interventions. A differentiated and detailed fatigue and performance assessment also includes social anamnesis, physical activities and limits, and sleeping habits (Fig. 2).

In addition to the patient history, physical examination, and routine lab parameters, specific fatigue questionnaires are an effective way to round up the assessment. Some of the most commonly used quality-of-life questionnaires include the Short Form-36 Health Survey (SF-36) and the Quality of Life Questionnaire-C30 (QLQ) from the European Organisation for Research and Treatment of Cancer (EORTC), the latter being the official standard to assess quality of life in oncology which includes items regarding fatigue. The "Brief Fatigue Inventory" (BFI) and the fatigue extension of the FACT-F (Functional Assessment of Cancer Therapy: Fatigue) are used in scientific research.

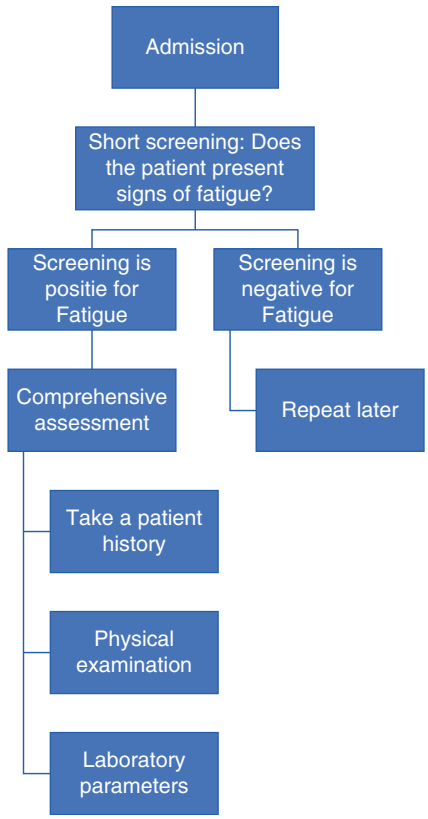

Fig. 2 Fatigue and weakness assessment on admission

8 Short Form-36 Health Survey (SF-36)

The SF-36-Item Health Survey looks at eight concepts: physical functioning, role limitations due to physical health, role limitations due to personal or emotional problems, energy/fatigue, emotional well-being, social functioning, pain, and overall health perceptions. A single item is included to gauge the perceived change in health. The answers to the questions have a weight tied to them with one getting a score of 0 and 5 a score of 100 or vice versa so that an answer with the score of 1 yields a weight of 100. Similar items get grouped together in the aforementioned categories and are averaged to form a scale. This is a good system for research but is not a quick way to assess the patient's condition in the clinical setting (Ware 2000).

8.1 European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30)

The QLQ-C30 is a 30-item self-assessment questionnaire about the quality of life. Items include questions like "During the past week: Were you short of breath? Have you had pain? Did you need to rest?" with 28 of these questions scored from 1 (not at all) to 4 (very much). The last two items are scored from 1 to 7. Similar to the SF-36, some items have to be reversed to get all scales in the

same direction and then computed in groups and single items: physical functioning, role functioning, social functioning, emotional functioning, cognitive functioning, fatigue, nausea and vomiting, dyspnea, sleeping disturbances, appetite loss, constipation, and diarrhea. This scoring system, again like with the SF-36, makes it difficult for physicians to draw conclusions at a glance (Jocham et al. 2009; "Questionnaires | EORTC" 2017; Aaronson et al. 1993).

8.2 Functional Assessment of Cancer Therapy: Fatigue (FACT-F)

The FACT-F is a 41-item questionnaire used to assess fatigue and anemia-related problems in patients suffering from cancer. It consists of the four groups of items from the general FACT: physical well-being (7 items), social/family well-being (7 items), emotional well-being (6 items), functional well-being (7 items), and the additional module on fatigue (13 items). Items, for example, "I feel weak all over. . .," are scored on a 5-point Likert rating scale ranging from 0 (not at all) to 4 (very much). As with the questionnaires above, some items must be reversed for the scoring. As an example, the fatigue subscale is scored by summing the scores of the relevant items, multiplying by 13, and dividing by the number of items answered for the subscale score, with a higher score indicating a better quality of life. The questionnaire only requires a sixth-grade level of reading comprehension to complete and usually takes no longer than 10 min to finish (Yellen et al. 1997).

8.3 Brief Fatigue Inventory (BFI)

An explicit look will be taken at the BFI Score. The BFI was specifically developed for the evaluation of fatigue in patients with oncological illnesses and can be completed (by a patient with no cognitive disorders) in about 5 min. The questionnaire entails ten items and allows to capture six different dimensions that are affected by fatigue with the question "during the past 24 h, fatigue has interfered with your: general activity, mood, walking mobility, normal work (includes both work outside the home and daily chores), relations with other people, and enjoyment of life." Each category is scored from 0 (does not interfere) to 10 (completely interferes), plus the three other questions relating to fatigue levels now, at worst time, and usually are also scored from 0 to 10 which leads to a maximum score of 90. Values between 30 and 40 indicate a moderate fatigue, while scores over 70 are typical for a severe fatigue. The advantage of the one-page BFI is that it is shorter than other questionnaires, lowering the burden for patients to complete it (Mendoza et al. 1999).

A quick screening can be performed on admission to judge a patient's level of fatigue if they are presenting symptoms. For the screening, a short survey composed of two questions inquiring about the patient's weakness (physical dimension) and tiredness (cognitive dimension) can be very effective and useful. If the screening is positive, a comprehensive assessment should be performed. Symptom severity should be evaluated, for example, with the BFI, to define the starting point before initiating treatment. The next step would be to identify treatable causes for fatigue and weakness. Figure 2 shows a suggested procedure for a fatigue screening, while Fig. 3 presents important aspects which require special attention during the taking of a history. Some laboratory parameters which could help to shed light onto treatable causes for fatigue are listed in Fig. 4.

The assessment should be repeated during causal and symptomatic treatment, with assessment intervals individually adjusted for the patient. The fatigue intensity will most likely change over the course of the disease trajectory, and periods of increased burden on the patient should be identified and the symptom management intensified accordingly. Reassessment also helps medical staff to evaluate the effectiveness of the treatment and make decisions regarding whether to initiate additional or alternative interventions if the current regimen shows inadequate effectiveness. As an objective assessment of fatigue is not possible, the patient is the only person who can assess their well-being. Subjective self-

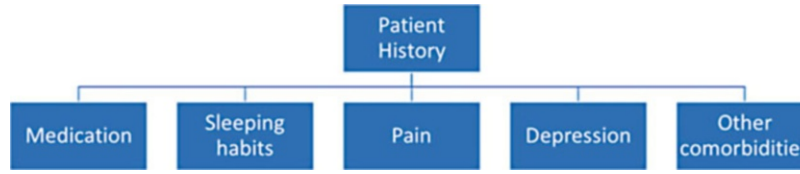

Fig. 3 Items which require special attention during a patient's history

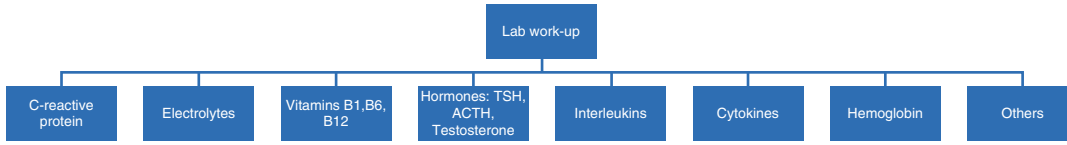

Fig. 4 Laboratory parameters suggested for routine assessment of fatigue

assessments of fatigue are an important part of the patient-reported outcome measures (PROMs) process, which is the gold standard of outcome measurement in palliative care (Bausewein et al. 2016). Unfortunately, in advanced stages of the disease, the patient's cognitive abilities may be severely impaired, preventing the use of self-assessment questionnaires. In this setting, assessment may be done by family caregivers or medical staff.

9 Therapy and Management

Fatigue management is based on comprehensive internal medicine and oncological care, which includes the treatment of comorbidities, infections, hormonal and endocrine irregularities, and a review of the medication regimen. The underlying philosophy of palliative care should be considered in all aspects of assessment and treatment of fatigue. The patient's individual needs and preferences should also be considered, and shared decision making should prevail in all situations. Discussions with the patient should take place along every step of the way, with them participating in all health care decisions. The physician should be able to clearly communicate the pros and cons of all available treatment options to the patient using language that the patient can understand so that informed consent and shared decision making can take place for all pharmaceutical as well as non-pharmaceutical interventions. The management of fatigue requires a high level of cooperation and communication between the health care provider, the patient's family and friends, and the patient themselves. Therapeutic goals, for either pharmacological or non-pharmacological interventions, can only be achieved when all persons around the patient actively work together.

Fatigue in end-stage terminally ill patients should be viewed as a natural part of the dying phase and not be considered a symptom that requires treatment. In this setting, fatigue may ease the transition to death, shielding the patient from distress, anxiety, and burdening symptoms. Symptomatic treatment of fatigue in dying patients could worsen the patient's well-being by forcing them to experience the last excruciating hours of their lives in full detail. Medical staff should recognize the appropriate time to stop treatment for fatigue to allow patients to die without distress (Mücke et al. 2016).

10 General Supportive Measures When Treating Fatigue

A fatigue diary is a useful tool in the management of fatigue. This diary should include a timeline for each day, the activity that was being performed and at what time it was performed, a comments section, and separate columns for intensity of weakness and tiredness. These last two columns should use simple scales such as a four-step categorical scale (no = 0, slight = 1, moderate = 2, severe = 3, intensity of weakness/tiredness). The diary serves as a visualization of the symptom

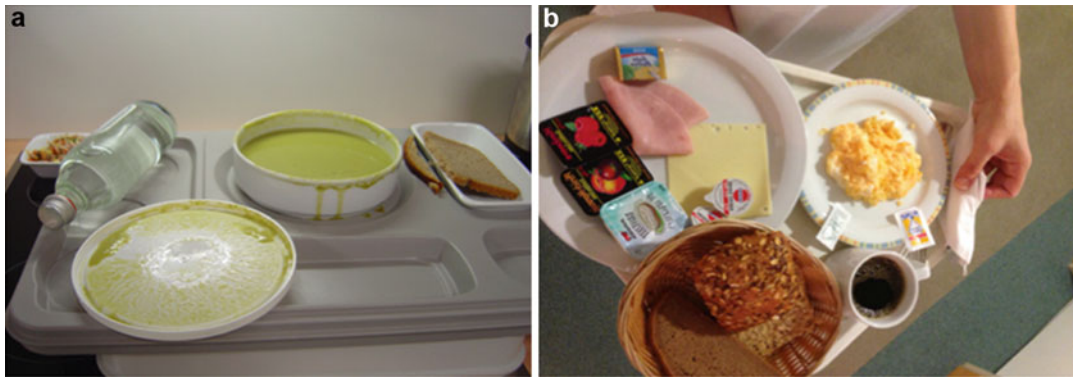

Fig. 5 (**a**) Shows unappealing, sloppily prepared food that would most likely dampen the appetite of a healthy individual. (**b**) Presents an esthetically pleasing meal which does not take much more effort to prepare than A but is more likely to be appetizing

burden and allows patients to better plan their energy reserves when they become familiar where the main limitations are. For the health care team, it allows the monitoring of the effectiveness of interventions.

A sufficient intake of water and vitamin supplements has been discussed as having a positive effect on fatigue, although there are currently no scientific studies to support this (Mochamat et al. n.d.). Drinking more fluids has been hypothesized to increase the elimination of fatigue inducing metabolites which form during chemo- and radiotherapy or other processes. Most palliative care patients suffer from a vitamin deficiency, so that a substitution with multivitamins and minerals can be justified in most cases. Nutrition plays another key role in the energy imbalance of fatigue. Diverse and varied meals should be prepared and administered in small portions. Sometimes the support of nutritional specialists and ecotrophologists (specialists in nutrition, household management, and home economics) may be needed. Clinical experience has shown that the way food is presented plays an important role on appetite in severely ill patients with appetite disorders. This is demonstrated in Fig. 5, which meal would you rather eat? Patients with severe fatigue prefer meals that do not require much effort to chew and are easy to swallow. Studies have shown that appetite and cachexia may influence each other and that treatment of appetite loss with megestrol acetate can decrease fatigue intensity. Beverages such as coffee, tea, or soft drinks can have a stimulating and pleasing effect on the patient. Alcohol, especially in the form of a predinner apéritif, has the potential to kick-start the appetite so that a glass of wine or beer is potentially recommended for those patients who report this as favorable from their history. Air quality, temperature, smells, sounds, light, and colors can also have profound effects on the well-being and should be utilized in the management of fatigue.

11 Recommendations for Pharmacological Therapies

Treatable causes of fatigue should be excluded before symptomatic pharmacological treatment of fatigue is initiated (Fig. 1). Anemia should be treated with iron supplements, vitamin B12 substitution, or folic acid depending on the cause. Even blood transfusions or erythropoietin substitution (EPO) can be considered albeit with rigid indications. Electrolyte imbalances should be corrected, and infections should be adequately treated. Endocrine disorders such as adrenocortical insufficiency or a hypothyroidism should be substituted with the respective treatment. Side effects of medications such as analgesics (especially opioids), sedatives, anticonvulsants, antiemetics, or antihypertensive drugs should be kept in mind as causes or enhancers of fatigue,

and switching to similar medications with fewer or less severe side effects should be considered.

Symptomatic pharmacological treatment of fatigue is restricted to very few options. Two Cochrane reviews have summed up the evidence on this topic (Mücke et al. 2016; Minton et al. 2010), but were not able to present clear recommendations. There are a sufficient number of studies included in these reviews, but patient numbers were small or patients from heterogenous groups were included. The comparability of the included studies was difficult due to a wide range of assessment instruments used.

Methylphenidate was evaluated in five studies including cancer patients (Bruera et al. 2006; Butler et al. 2007). One study showed no significant effect with a daily dose of 18–54 mg/day, while the other four displayed a slight improvement under a continuous intake of dosages between 5 and 30 mg/day. The mechanism of action of methylphenidate includes the inhibition of noradrenaline and dopamine reuptake in the synaptic cleft, thus resulting in increased sympathetic nervous system activity. But noradrenaline and dopamine seem not to be the only systems affected by methylphenidate; research suggests it plays another role as a serotonin receptor agonist.

Modafinil seemed to be able to effectively treat severe fatigue with dosages of 100 and 200 mg/day according to two studies (Lange et al. 2009; Spathis et al. 2014), but had no effect on mild to moderate fatigue. Similarly, modafinil was not effective in treating CFS patients with lung cancer. The therapeutic effect of modafinil is attributed to its ability to affect the sleep-wake rhythm, but due to its numerous side effects, which include severe psychiatric symptoms and cutaneous reactions, its indication is limited to the treatment of profound drowsiness in adults.

Taking a look at corticosteroids for the treatment of fatigue, dexamethasone and methylprednisolone were only included in two studies although these two drugs are recommended in official guidelines and extensively used in clinical practice. It is assumed that glucocorticoids play a positive role in managing tumor-associated fatigue due to their ability to influence the central nervous system and their anti-inflammatory attributes (Shih and Jackson 2007). A recent study demonstrated that 4 mg/day of dexamethasone was significantly superior to placebo (Yennurajalingam et al. 2013). However, there was no significant difference in the improvement of individual symptoms, psychological distress, anxiety, and depression in the dexamethasone group compared with placebo. Further studies examining the effects of dexamethasone on fatigue are needed.

Mistletoe extract PS76A2 improved fatigue symptoms in a study including breast cancer patients (Marvibaigi et al. 2014), while thyreoliberin (thyrotropin-releasing hormone, TRH) was also successfully tested but has yet to receive licensing. TRH exhibited an important influence on the central regulation of energy homeostasis, inflammatory processes of the organism, and fatigue. This is most likely due to its extra-hypothalamic and central nervous system activity (Kamath et al. 2009). Ginseng showed positive results in a few studies. Its possible pharmacological effects in the treatment of CFS are theorized to lie in its affinity to glucocorticoid receptors, its membrane stabilizing effect, and its anti-inflammatory feature (Radad et al. 2011; Rasheed et al. 2008). Erythropoietin was, until 2004, globally one of the most successful drugs for cancer-related fatigue. Unfortunately, in 2009 a meta-analysis consisting of 53 clinical trials with almost 14,000 patients concluded that the mortality rate of cancer patients after receiving EPO treatment increased by a factor of 1.17. This may be related to EPO receptors that were found on various tumor cell surfaces, leading to the hypothesis that EPO could stimulate malignant neoplasm growth. Not only did EPO increase the likelihood of tumor progression, but it also contributed to a higher risk of venous thromboembolisms in patients with solid mass tumors. This restricted the use of EPO to symptomatic adult patients with therapy-induced anemia, but only for hemoglobin levels below 12 g/dl.

Acetylsalicylic acid (aspirin, ASA) showed impressive results in the treatment of fatigue in patients with multiple sclerosis (Wingerchuk et al. 2005; Shaygannejad et al. 2012), but, according to the latest publications, has not yet been tested for CRF. Paroxetine was investigated in one study with cancer patients (Morrow et al. 2003) and

another with patients suffering from chronic obstructive pulmonary disease (COPD), but neither study was able to confirm a significant improvement. In consequence, selective serotonin reuptake inhibitor (SSRI) antidepressants only seem to present a therapeutic option when a depressive disorder is diagnosed. The systematic review also found no significant improvements for drugs like testosterone, amantadine, carnitine, megestrol, or medroxyprogesterone.

Thalidomide has become a talking point as a treatment for cachexia in tumor patients but has so far failed to show tangible results (Davis et al. 2012; Reid et al. 2012; Yennurajalingam et al. 2012).

Based on limited evidence, we cannot recommend a specific pharmaceutical for the treatment of fatigue in palliative care patients. Fatigue research in palliative care seems to focus on modafinil and methylphenidate, which may be beneficial, although further research regarding their efficacy is needed. Dexamethasone, methylprednisolone, acetylsalicylic acid, armodafinil, amantadine, and L-carnitine should also be further examined.

12 Non-pharmacological Management

The preservation and protection of available energy reserves as well as the patient's self-reliance in day-to-day activities plays an especially important role for tumor patients with fatigue. The proper management includes a conscious intake of calories and a protein-rich diet, as well as maintenance of a proper sleep routine which avoids caffeinated drinks before bedtime, too much daytime sleep, or arousing activities in the late afternoon or evening. The patient will need time to get used to this new activity and energy management. Priorities must be set to differentiate between useful/important and less important activities. Energy and stamina should be rationed accordingly and necessary breaks between activities planned for. Moderate physical exercise is useful, even for cancer patients suffering from exhaustion and reduced physical ability, in order to retain existing physical abilities and to counteract progressive muscle loss, reduced efficiency of the cardiovascular system, and general condition. Multiple studies have shown the benefits of light endurance training during anticancer therapy (Hilfiker et al. 2017; Safari et al. 2017) regardless of the type of exercise. Physiotherapy can contribute significantly to the patient's well-being with mobilization, breathing exercises, and teaching techniques for self-training. On the other hand, the use of medical aids such as a wheelchair or walker has to be learned and accepted. Psychosocial measures such as stress management and relaxation therapy (autogenic training, progressive muscle relaxation, or yoga) contribute to the management of CRF. Cognitive behavioral therapies are also of great value. Psychosocial support from caregivers is, likewise, beneficial to relieve the patient from fears and concerns. However, a recent review from 2017 was unable to recommend any specific non-pharmacological intervention, although physical exercise and psychoeducational therapies seem to be promising options and should be researched further.

13 Conclusion

Fatigue is a subjective feeling of extraordinary weakness, tiredness, and energy loss which affects the body (physical aspect), feelings (affective aspect), and mental function (cognitive aspect) and can occur at any age. Fatigue is not, or only incompletely, alleviated by sleep and rest. CRF is a subjective, multidimensional illness, with significant impact on the quality of life of patients. Once treatable causes for CRF are excluded, a multimodal treatment regimen should be developed. Symptomatic management of fatigue requires a high level of cooperation and communication between all health care professionals attending to the patient, the patient's social sphere, and the patient themselves. Treatment strategies must be multimodal and multi-professional. Past systematic reviews have provided no clear recommendations for pharmacological or non-pharmacological interventions for the relief of cancer-related fatigue. Treatment of underlying causes, such as infections, may be an effective measure to reduce fatigue

symptoms. Current ongoing studies are exploring therapeutic options such as energy homeostasis, glucocorticoid receptor stimulation, as well as influencing neurotransmitter receptors and anti-inflammatory processes. Physical training can be effective and should be used in combination with pharmaceutical interventions.

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Edema and Lymphedema

13

Elizabeth S. Dylke and Sharon L. Kilbreath

Contents

Abstract

Edema or swelling is a common occurrence during the palliative care phase for many conditions. Various causes and forms of edema are possible, with most palliative care patients suffering from a mixed form with lymphatic and venous contributions. Edema is most frequently present in the limbs but may be found in any region of the body, including the head and neck, trunk, and genitals. Edema can cause significant distress, reducing mobility and independence. Screening and assessment for edema therefore should be comprehensive and systematic to ensure the underlying causes of the swelling are discovered. Furthermore, the treatment goals of the patient should be accounted for in determining the treatments offered. Various treatments, with particular focus on compression and exercises, may be used but often require modification from traditional usage in the palliative care setting. In this setting, treatment focus is often on symptom management rather than volume reduction.

1 Introduction

Edema and lymphedema are common in the palliative care setting, with many possible contributing factors. The aims of this chapter are to:

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_13

1. Explore the pathophysiology, incidence, and presentation of edema in a palliative care setting.
2. Describe screening and assessment requirements for determining the presence, severity, and distress caused by edema.
3. Explain the conservative treatment options commonly used for edema in a palliative care setting.

2 Pathophysiology of Edema in Palliative Care Setting

Swelling is a frequently reported symptom during the palliative care phase of many conditions. While the lymphatic form of swelling, lymphedema, is commonly associated with cancer treatments, particularly breast cancer (Fig. 1), edemas and lymphedema can occur during the palliative care phase of many diseases including chronic renal and heart failure, end-stage liver disease, and neurological conditions such as Parkinson's and chronic obstructive pulmonary disease, among others (Real et al. 2016). Patients with swelling may suffer from edema, lymphedema, or a mixed presentation (Real et al. 2016).

In non-palliative care patients, non-lymphatic edema occurs as a result of change in the permeability of the capillary walls. As a consequence, a gradient change occurs between the hydrostatic pressures of the blood vessels and tissues. This results in extraneous fluid in the tissues (Real et al. 2016). In contrast, lymphedema results due to disruption to lymphatic pathways caused by surgery or other treatments or traumas affecting the lymphatic pathways, the congenital absence or limited presentation of lymphatic pathways, or an overload of lymphatic fluid beyond the capacity of the lymphatic system (Real et al. 2016; Padera et al. 2016; Lawenda et al. 2009). Additional causes or contributing factors to the development of edema and/or lymphedema in a palliative care setting have been summarized by Real et al. (2016) and may include:

- Lymph node blockage and/or lymphadenopathy
- Abdominal involvement/blockage caused by tumors or ascites
- Medical causes such as hypoalbuminaemia (Bar-Sela et al. 2010), anemia, venous hypertension, cor pulmonale, and general deterioration
- Symptomatic or asymptomatic deep vein thrombosis (DVT)
- Dependency and/or immobility
- Organ failure
- Overhydration (Nwosu et al. 2016)
- Previous or ongoing treatments such as taxane-based chemotherapies or long-term steroid use

In palliative care, both forms of edema are seen, often with the two forms combining (mixed edema), resulting in possible significant swelling. A recent retrospective study found that 46% of edemas were of the mixed variety, 29% were lymphedema, and 10% were non-lymphatic-related edema (Real et al. 2016). While clearly there are many forms of swelling, the more general term edema will be used from here on in this chapter to avoid confusion.

The incidence of edema varies among studies and disease states. For example, various studies found that swelling occurs in 39% (Lau et al. 2010) to 73% (O'Connor and Kumar 2012) of chronic renal failure patients. This lack of agreement may be due, in part, to differences in diagnostic criteria for determining the presence of the edema (Dylke et al. 2016). A conservative estimate would suggest that at least one-third of patients with cancer or noncancer end-stage conditions suffer from some form of edema (Lau et al. 2010).

Edema may present in any region of the body during palliative care, although peripheral edema is the most common presentation

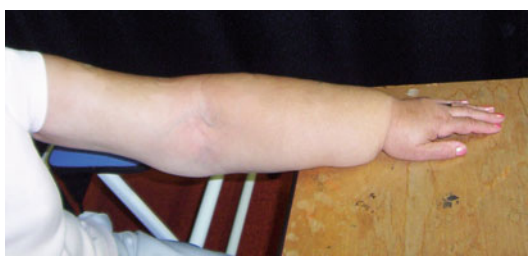

Fig. 1 Breast cancer patient with significant lymphedema of the forearm

(Steindal et al. 2013). It is most commonly found in the lower limbs irrespective of the underlying disease state (Real et al. 2016), particularly in older patients (Steindal et al. 2013), possibly due to immobility and deconditioning. The location of edema may also depend on the underlying condition that has led to the swelling. For example, secondary to breast cancer treatment, the edema may present in the affected side's upper limb, while secondary to oral cancers, the swelling may present in the head and neck region.

Edema presentation can change or progress (Lawenda et al. 2009). This progression may either be an increase in volume or change in tissue composition or a combination of both (Lawenda et al. 2009). When edema first develops, the increase in volume of the swollen region is fluid-based, due to increase in either intracellular fluid, extracellular fluid, or a combination (International Lymphedema Framework and Canadian Lymphedema Framework 2010). For some, despite treatment, the volume of the limb may continue to increase, while for others the limb volume may stabilize (Dylke et al. 2013) and reduce in response to treatment (Ezzo et al. 2015). Beyond the increases in volume, particularly with edema with a lymphatic contribution, the edema may lead to changes in the tissue composition of the limb (Dylke et al. 2013). This change in tissue composition is not well understood but likely has multiple underlying causes including the high protein levels and inflammatory factors found in extracellular fluid (Padera et al. 2016). In the early stages, the high protein fluid in the limb leads to a presentation of pitting, where localized pressure leaves an indent in the tissues (Lawenda et al. 2009; International Lymphedema Framework and Canadian Lymphedema Framework 2010). With progression, pitting may cease and localized increases in fatty and fibrotic tissue occur (Dylke et al. 2013). These changes in limb composition are not simply a result of time with edema and have been found in patients with both large and small limb volume increases (Dylke et al. 2013). As with increases in limb volume, it is currently unclear which patients are most at risk for changes in tissue composition.

Another possible consequence of edema progression is skin changes. For some this will result in fibrotic, woody, or thickened skin (Padera et al. 2016; Lawenda et al. 2009), while others may experience fragile skin (International Lymphedema Framework and Canadian Lymphedema Framework 2010). Which presentation occurs may be due to the underlying condition causing the edema, with heart and liver failure-related edema as well as dependency edema all being more likely to lead to fragile skin (International Lymphedema Framework and Canadian Lymphedema Framework 2010). Both thickened and fragile skin cause susceptibility to lesions or ulcers as well as skin infections (cellulitis) (Moffatt et al. 2003). Lymphorrhea, a leakage of lymphatic fluid through the edematous skin, may also occur with progressing edema. Lymphorrhea also causes susceptibility to cellulitis and has been shown to be a poor prognostic indicator in a palliative care setting (Real et al. 2016).

3 Screening

Screening for edema should be done systematically, through the use of targeted questioning or a questionnaire. Reliance on patients to volunteer that edema is present likely leads to vast underdiagnosis of its presence as well as its impact. Homsi et al. (2006) found that without systematic questioning, only 4% of palliative care patients volunteered that they were experiencing swelling. However, the incidence rose to 30% of patients when they were systematically questioned about the presence of edema, a finding also identified by others (White et al. 2009).

In addition to identifying more cases of edema through systematic questioning or the use of a questionnaire, on average, eight more symptoms were identified than when a patient was left to self-report what they were experiencing (White et al. 2009). Importantly, the symptoms discovered on systematic questioning were often as severe in presentation and as distressing to the patient as those that were self-reported without prompting (Homsi et al. 2006). Notably, for edema, the relationship between physical

changes of edema and level of distress was asynchronous, with small increases in limb volume associated with high levels of distress in some patients but not all (Homsi et al. 2006). Severity and distress caused by the edema, therefore, should be assessed separately in determining the priorities for treatment.

Due to the commonality of edema, a standardized approach to screening and onward referral for assessment of edema is required. Without such processes in place, many of those with edema are likely not detected and therefore not offered treatment (Thomson and Walker 2011). There is currently no agreed upon questionnaire nor screening method for detection of edema in either the non-palliative or palliative care setting. Commonly used, validated multi-symptom cancer assessment instruments such as the MD Anderson Symptom Inventory (Portenoy et al. 1994) and the Edmonton Symptom Assessment System (Bruera et al. 1991) do not include a question related to edema. Of the small number of questionnaires validated in the palliative care setting that focus on symptom presence (Stromgren et al. 2002), only the Memorial Symptom Assessment Scale Short Form (Chang et al. 2000) specifically asks about swelling or edema. This scale includes a single item, in which patients are asked whether or not edema is present in either the arms or legs. If the patient indicates that swelling is present, further questioning of the patient occurs in regard to the severity and distress. However, a limitation of this scale is that it does not ask about swelling elsewhere, e.g., the head and neck or trunk. As the currently available validated questionnaires are not comprehensive in assessing all of the symptoms reported by patients and symptoms are not comprehensively recorded in patient records (Homsi et al. 2006), screening for edema and likely other symptoms cannot rely on a single questionnaire; screening should be supplemented by questioning of the patient.

In the non-palliative care setting, the limb is also physically measured to detect the presence of swelling. Tools used to assess whether swelling is present in the "at-risk" limb include a tape measure to quantify limb circumference and/or used to derive limb volume, water displacement and Perometry to assess limb volume, and bioimpedance spectroscopy to assess extracellular fluid volume (of which lymph is a major contributor). The measurement methods for using these tools will be discussed further below.

Ideally, edema is detected and treated when it is mild. However, one of the challenges for all edemas has been the determination of criteria for its detection in a clinical environment. The lack of clear diagnostic criteria has resulted in the formation of a range of arbitrary thresholds (Dylke et al. 2016). This issue has been addressed for detection of mild upper limb lymphedema arising from treatment for early breast cancer. Comparison of a range of commonly used and normatively based thresholds against a reference standard led to the identification of evidence-based diagnostic thresholds for detection of upper limb lymphedema (Dylke et al. 2016). However, similar evidence-based diagnostic thresholds for other regions, such as the lower limbs, have not been developed for either a non-palliative or a palliative care setting.

4 Comprehensive Assessment

If swelling is likely present, it is important to determine the underlying cause(s) as this will inform treatment. While imaging methods such as lymphoscintigraphy, magnetic resonance lymphography, or indocyanine green lymphography can provide additional information about the underlying morphology of the lymphatic system (Munn and Padera 2014), they are rarely undertaken in a palliative care setting unless they will alter management strategies (Real et al. 2016). The focus, instead, is on a thorough clinical assessment of the areas with or at risk for swelling. As there are many factors that may contribute to both the edema and the treatment decisions associated with assessment findings, only those with advanced training in edema should undertake both the assessment and treatment of edema.

The clinical assessment for edema is multifaceted. As part of any standard assessment, the history related to the edema, treatments received,

and any benefit they received from the treatment in controlling the swelling and symptoms is obtained. A review of the medications prescribed may be useful, as a number of common medications, such as nonsteroidal anti-inflammatories (NSAIDs), may contribute to the development or severity of the edema (International Lymphedema Framework and Canadian Lymphedema Framework 2010). Importantly, the patient is asked whether they are experiencing any symptoms in relation to the edema and, if present, the level of distress associated with the symptoms and swelling. Typical symptoms of edema may include sensations of heaviness, achiness, discomfort, or fullness (Lawenda et al. 2009). In addition, patients are asked about the extent to which the edema impacts on their physical abilities.

Visual inspection and palpation of the region with edema will identify issues that could impact on treatment (Lawenda et al. 2009). The region should be inspected for the presence of wounds, skin breakdowns, signs of venous insufficiency, skin infection, and lymphorrhea, all of which may contraindicate certain treatments for the edema and/or require modification of other treatments. Signs indicative of venous insufficiency include the presence of varicose veins, difficultly locating ankle pulse, and pain or discomfort in the legs that is relieved when legs are elevated. Hands-on assessment will provide an indication as to the state of the tissues. The presence of pitting edema, tested by the application of pressure for a specified amount of time (often 10–30 s) and then observing for the presence of a dent in the tissues once pressure is removed, provides an indication of edema progression. In contrast, palpation of fibrosis or skin and tissue hardening indicates a later progression of edema, which may respond better to different treatments than does pitting edema.

Measurement of the limb size can be done to indicate the severity of the edema and provide a benchmark against which response to treatment can be determined. However, for some patients, this may be too burdensome for the patient to undertake (International Lymphedema Framework and Canadian Lymphedema Framework 2010). Multiple assessment tools may be used, which one (or ones) selected depends on the availability of the tools and the location of the swelling. For upper and lower limb edema, the most commonly used tool is a simple tape measure with which circumferential measurements are taken at regular intervals along a limb. When completed in a standardized manner, they have excellent reliability (Czerniec et al. 2010). If one limb is swollen, its circumference measurements are often compared to the unaffected limb to give an indication of extent and severity of edema. For bilateral swelling where this is not possible, circumference measurements may be most useful to monitor the changes in the size as a response to treatment. Protocols have also been developed for the measurement with a tape measure of head and neck (Deng et al. 2016) and breast edema (Kovacs et al. 2007). Circumference measurements may also be converted to a volume; however, this is mostly done in a research setting and unlikely to provide additional assessment or treatment guidance in a clinical environment. Other ways of measuring limb volume may include water displacement or Perometry, both of which are less commonly used in clinical settings.

If the edema likely has a lymphatic component, bioimpedance spectroscopy (BIS) may provide an alternative for assessment of limb swelling, measuring the volume of extracellular fluid specifically. Surface electrodes are attached to extremities, and a harmless low-level current is passed though the region to determine the resistance. Each limb is assessed separately and an interlimb ratio determined. BIS has several advantages to other measures of limb volume, including less intrusive and being specific to extracellular fluid. Other measures used to assess limb volume, such as tape measurements, include fat, bone, muscle, and all fluids and therefore may miss small increases in extracellular fluid. Indeed, BIS is particularly well-suited to detection of mild edema (Ward et al. 2008) but is also suited to monitoring change in edema over time (Czerniec et al. 2016). When standardized protocols are used, BIS has excellent reliability (Czerniec et al. 2010). Currently standardized protocols are available for the measurement of unilateral and

bilateral upper and lower limb lymphedema (Ward et al. 2011a, b).

Further objective assessments may be required to ensure appropriate treatments are offered dependent on the region affected and additional symptoms being reported. These may include a measurement of range of motion or strength of both the area with swelling and the whole body, an assessment of speaking or swallowing, gait assessment, or a pain and/or neuropathic pain assessment. After completing the subjective and objective assessments, if questions remain about the contributing factors to the swelling, additional investigations may need to be undertaken to ensure the cause of the edema is determined and appropriate treatment is given (Box 1).

Although the physical assessments used for edema are well-described and reliable to perform, there are gaps. For example, it is unclear what are the expected responses to treatments for most forms of edema. The measurements ascertained, therefore, need to be used in conjunction with the results from the additional investigation, as well as the patient's self-report of the issues and clinical reasoning to guide the intensity, level, and types of treatments offered.

Box 1 Additional assessments may need to be undertaken if the cause of the swelling is unclear and/or to guide treatment decisions

Assessment	Reason	Possible alternations to treatment decisions
Electrocardiogram (ECG)	Cardiac failure	Medical management including medications may be indicated Lower compression pressure may be indicated
Ankle-brachial pressure index (ABPI)	Venous insufficiency	An ABPI of less than 0.8, particularly in the presence of ulceration or wounds, suggests that high pressure bandaging is contraindicated
Blood tests	Albumin levels	Albumin is a protein that assists in preventing fluid leakage into the tissues Low levels of albumin (hypoalbuminemia) may be indicative of kidney or liver disease or the body not absorbing enough nutrients Further investigations and/or medical management of underlying condition required
Ultrasound	Deep vein thrombosis (DVT)	Medical management may be indicated Use of compression may need modification

5 Treatment of Lymphedema

To date, management of most edemas is conservative or surgical and not with pharmaceutical approaches. Surgical approaches are rarely warranted in a palliative care setting. However, with better understanding of the underlying contributions to edema, pharmaceutical approaches may become available. For other edemas encountered in the palliative care setting, medical management (including pharmaceutical) in combination with conservative treatment such as the use of compression may be warranted.

Ideally, edemas are detected when the condition is mild. At this phase, the impact on function is minimal; the aim of treatment, therefore, is to manage symptoms through reduction in swelling volume. Exercises and compression may be all that is required in the mild stage (International Lymphedema Framework 2006). Frequently, however, more comprehensive treatments are required.

Traditionally, conservative treatment for edema is divided into two phases: (i) intensive phase in which the aim of treatment is to reduce the volume of the limb and improve its shape and (ii) maintenance phase in which the aim is to

maintain the reduction (International Lymphedema Framework 2006). However, in the palliative care, it is recognized that these distinct phases are blurred (International Lymphedema Framework and Canadian Lymphedema Framework 2010), with treatment focused on reducing the burden to the patient in terms of both the impact of the disease and the treatment.

5.1 Complex Decongestive Therapy

The most common treatment advocated for edema is complex physiotherapy treatment (a.k.a. complex decongestive therapy) (International Lymphedema Framework 2006). Complex decongestive therapy is multifocal and comprises the following components: (i) manual lymphatic drainage, (ii) compression therapy, (iii) skin care, (iv) education, and (iv) exercise. This approach is time-consuming and, in its fullness, may not be tolerated by patients in the palliative care setting (Cheville et al. 2014).

(i) Manual Lymphatic Drainage

Manual lymphatic drainage (MLD) is a specialized form of light massage designed to encourage the drainage of lymphatic fluid from the limb (International Lymphedema Framework 2006). It is performed by MLD therapists trained in the anatomy and physiology of the lymphatic system to facilitate lymph drainage of the vessels (Ezzo et al. 2015). It is proposed that MLD can "assist nature" by stimulating the natural peristaltic contractions of the lymphangions, reducing hydrostatic resistance to lymph flow, and rerouting lymph away from areas of stasis and into viable lymphatic vessels (Ezzo et al. 2015). The evidence supporting its use, however, is weak, particularly for upper limb lymphedema secondary to breast cancer (Ezzo et al. 2015). However, synthesis of the data in a Cochrane review provided preliminary data in a secondary analysis that MLD may be particularly effective early in the development of edema, where the lymphatic system is still functioning relatively well (McNeely et al. 2004). Consequently, massage would be capable of both stimulating lymphatic flow and rerouting lymphatic flow via collaterals. When edema has progressed, MLD may not have a major impact on reduction in limb volume. The addition of MLD to compression in studies which included moderate to severe upper limb lymphedema only reduced limb volume by 7% (Ezzo et al. 2015).

While MLD may not contribute to significant volume reduction, it does have additional benefits, particularly in the palliative setting. In a study investigating the effect of MLD on palliative patients, it was noted that MLD was tolerated by most patients, and it was associated with significant reduction in both pain and dyspnea above that received from administration of opioids in combination with analgesics and co-analgesics (Clemens et al. 2010). MLD is typically given in a quiet, calm environment; this form of massage is very gentle and soothing which may contribute to the improved dyspnea and reduced pain. In contrast to simple massage, manual lymphatic drainage is also associated with improved emotional function in terms of reducing worry, irritability, tension and feelings of depression, dyspnea, and reduced sleep disturbance (Williams et al. 2002). Thus, while MLD may not be effective in addressing the increase in limb volume, it does offer benefit to the patient in other domains.

Although MLD can be beneficial, there are instances when it is contraindicated. Particularly when swelling is present in the lower leg, it is important to first rule out the presence of deep vein thrombosis. If present, MLD to that region may be contraindicated.

(ii) Compression

Compression is considered a keystone for treatment of edema. The mechanisms underpinning the impact of compression on the lymphatic and vascular system are currently unclear, particularly as tissue composition within the edematous limb changes over time. Studies, particularly in relation to compression on venous blood flow, suggest that the increase in local pressure obtained from compression limits capillary fluid filtration while improving lymphatic drainage. The

increased tension on the anchoring filaments of the initial lymphatics contributes to the opening of these initial lymphatics. As the valves in these lymphatics are unidirectional, fluid is pulled in and toward the lymph collectors which will be pulled open. Although the mechanism underlying how it works is unclear, it does contribute to decrease in limb volume (Ezzo et al. 2015; Badger et al. 2004). Compression may be delivered through a range of products. Types of devices used to apply compression include short-stretch bandages, off-the-shelf or customized compression garments, Velcro wraps which are easy to don and doff, or the use of compression pumps.

Short-stretch bandaging is typically advocated as part of Phase 1 of complex decongestive therapy to reduce volume and improve the shape of the limb (International Lymphedema Framework 2012). For upper limb lymphedema, compression levels are suggested in the range of 20–30 mmHg, whereas with lower limb lymphedema, compression levels of 60 mmHg are recommended (Partsch et al. 2011). These bandages, in contrast to others such as traditional tensor or "ace" bandages, stretch less than 50% when extended longitudinally. The pressure mediated by the bandages can be controlled by the width and number of layers used in combination with the tension of the fabric (Partsch et al. 2008). Another advantage in the use of bandaging is that it can be used in combination with padding and "chip bags" to ensure pressure is not applied to bony areas and to help soften hard fibrotic regions. The traditionally used multilayer compression system for reduction of limb volume has some limitations: this form of bandaging is associated with inconsistency in application techniques resulting in inconsistent pressures, variable results, and bulkiness, which can impede patients from wearing normal footwear and clothing, leading to a low level of adherence and the potential risk of falling (Lamprou et al. 2011). Another problem can be slippage and bunching, leading to uneven distribution of compression, which can result in discomfort at night and the potential for skin breakdown.

New approaches to bandaging are being explored. For example, the two-component compression 3M Coban system is less bulky, with preliminary data suggesting that the findings are equally effective in both treatment of chronic venous insufficiency (Moffatt et al. 2008) and moderate to severe lower limb lymphedema (Lamprou et al. 2011). Importantly, although not formally assessed, participants treated with the two-component compression system reported enhanced mobility and comfort during walking than with previously worn compression systems (Lamprou et al. 2011). The two-component Coban system comprises latex-free roll bandages in which the inner layer is polyurethane foam and the outer layer is a cohesive bandage. The foam replaces the padding used in traditional multilayer bandaging, protecting bony prominences and providing the necessary grip to prevent slippage. The cohesive outer surface enables the layers to bond to each other, providing a stiff stable layer with no internal movement (Lamprou et al. 2011; Moffatt et al. 2012). Rosidal Soft (Activa Healthcare Ltd) foam rolls have also been used to replace bulky wadding typically used with patients with lymphedema. Following application of the foam, cohesive short-stretch bandages were applied in figure of eight techniques, leading to significant reduction in the volume of the affected leg after a course of 12 days of bandaging (Whitaker et al. 2015).

The evidence clearly supports bandaging to reduce limb volume in lymphedema (Badger et al. 2004). However, the patient in palliative care may not tolerate this form of intervention, nor has its effectiveness been explored for other causes of edema. Alternative methods of compression may need to be explored.

Compression garments are readily available. Depending on the severity and location of the swelling, garments may be off-the-shelf or custom-made. However, patients may not tolerate the sustained pressure or be able to complete the application and removal of the compression garment. Other factors may also interfere with the use of compression garments, such as fragile skin, which can be stressed with the use of compression garments, lymphorrhea, and open wounds. An alternative to compression garments are compression "wraps," in which low-elastic material

section wrap across the limb and are secured with Velcro (Williams 2016). The advantage with a wrap is that they are easy to put on and adjust the pressure. However, it was noted that there is difficulty in using wraps if the person is overweight or inflexible or if there were severe shape distortion of the limb (Mosti et al. 2015).

(iii) Exercise

Typically, as part of standard treatment for edema, patients are encouraged to exercise (International Lymphedema Framework 2006). Depending on the individual's ability in relation to disease status, exercises such as resistance training, stretching, and aerobic exercise may be beneficial. Exercises are typically performed while using a form of compression, e.g., compression garment. In non-palliative care patients, resistance training has been shown to be protective against exacerbations of lymphedema, and associated with reduced symptoms, and increased strength (Schmitz et al. 2009). However, at the palliative stage, vigorous exercises may not be feasible. Rather, the focus may be on functional activities, such as rising from a chair and walking or repetitive contractions and relaxation of muscle groups in the lymphedematous region (Cheville et al. 2014).

5.2 Alternative Treatments for Patients in Palliative Care

Subcutaneous drainage of lower limb edema has been piloted in patients in palliative care due to advanced cancer (Bar-Sela et al. 2010; Jacobsen and Blinderman 2011). Patients with severe lymphedema of the lower body and leg, in whom diuretics and other conservative approaches were not providing any benefit, were offered this novel treatment. As part of the informed consent, patients were explicitly informed of the lack of supporting evidence for this treatment as well as the potential side effects of treatment (Bar-Sela et al. 2010). This approach evolved, from inserting subcutaneous catheters into the medial and lateral sides of the ankle and then connecting the catheter via tubing to an enclosed drainage baggage to creating subcutaneous tracts with needles in both ankles and following removal of the needles, wrapping the region with absorbent pads (Bar-Sela et al. 2010). The most recent modification was to remove both the needles and padding and let the region drain into a bucket. Five of eight patients who underwent this procedure identified improvement in mobilization that impacted their quality of life (Bar-Sela et al. 2010).

There are currently no medications available for the prevention or treatment of most forms of edema (International Lymphedema Framework 2006). In a non-palliative care setting, diuretics have been shown to be ineffective in the management of lymphedema (Kligman et al. 2004). However, in other forms of edema, particularly if the peripheral edema is a result of congestive heart failure, diuretic therapy can help reduce the severity of the swelling (Brake and Jones 2017). The dosage of diuretics given may need up or down titration depending on various factors and needs to be done in the context of the wider symptoms and medical presentation (Brake and Jones 2017). Alternatively, as some medications, such as methadone for pain, may cause or worsen edema, a review of the medications being taken by the patient may lead to improvements in symptoms (International Lymphedema Framework and Canadian Lymphedema Framework 2010; Dawson et al. 2014).

Hydration levels may also impact on edema severity, with patients with higher hydration levels, suffering from worse edema (Nwosu et al. 2016). However, following guideline-based artificial hydration therapy protocols has been shown to lead to a significant improvement in edema (Nakajima et al. 2014).

6 Conclusion and Summary

Edema in a palliative care setting is a common, complicated, multifaceted, and often distressing side effect of the end stage of many diseases. It can have numerous contributing factors, thereby requiring thorough screening and assessment to

ensure the underlying causes are known and appropriate treatments are offered. Treatment of edema in a palliative care setting has been shown to improve quality of life and mobility and reduce other symptoms such as pain and dyspnea. While there are a range of treatments available, in a palliative care setting, the focus is often on managing the symptoms and distress caused by the edema rather than reducing the volume of the limb. This often results in necessary modifications to the approach and intensity of the treatment. A growing understanding of the lymphatic system and its role in fluid management may lead to new treatments in the future.

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14 Gastrointestinal Symptoms: Constipation, Diarrhea, and Intestinal Obstruction

Katherine Clark

Contents

Abstract

Disturbed bowel function, including constipation, diarrhea, and bowel obstructions, commonly affects palliative care patients. This chapter aims to summarize these problems, focusing on the current understanding of the prevalence, etiology, and palliative management. The first issue that will be discussed is the most prevalent distal gut problem of constipation. Despite the fact that the majority of

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_14

palliative care patients require laxatives, the etiology of constipation in palliative care is not well described. The next topic is diarrhea, which, although less, common is still equally distressing. A systematic approach to assessment and management is recommended. Lastly, the evidence that describes the palliative management of inoperable bowel obstructions will be explored.

1 Constipation

1.1 Definition

Although a common symptom in palliative care, there remains sparsity of information to best define, diagnose, and effectively manage this problem.

Gastroenterology guidelines highlight that the Rome III criteria are a useful and standardized tool on which to base an objective diagnosis of constipation (Vazquez and Bouras 2015). In order to fulfill these criteria, people must have experienced at least two clusters of symptoms for 12 weeks of the last 6 months including straining at defecation on at least one quarter of occasions, stools that are lumpy/hard on at least one quarter of occasions, sensation of incomplete evacuation on at least one quarter of occasions, and three or fewer bowel movements a week.

However, the Rome criteria are not considered useful in palliative care (Erichsen et al. 2015). This is despite the fact that many people are likely to have experienced problems for many years before their diagnosis of a life-limiting illness (Currow et al. 2015). Recently, observational data highlight that many of the same problems of infrequent bowel actions, straining, and dissatisfaction are equally bothersome to constipated palliative care patients as other groups (Clark et al. 2016a). There is a real need for agreed diagnostic criteria to objectively diagnose and assess the severity of constipation in palliative care using a tool that is sensitive to change over time (Clark and Currow 2013).

In the meantime, it is inadequate to base a diagnosis of constipation solely on the frequency of bowel actions per week as the normal frequency of bowel actions varies so widely between individuals. Perhaps a much more meaningful measure is what is perception of each person as to what is a normal bowel habit for them, how their experiences have changed over time, and what problems are they experiencing that they attribute to disturbed bowel function.

1.2 Prevalence

The prevalence of constipation is variously quoted as likely to affect between 10% and 100% of palliative care patients (Erichsen et al. 2015; Clemens et al. 2013). While there is little doubt that this problem commonly affects patients being cared for with palliative care intent, there are reasons that quoted prevalence ranges are so broad. This includes the lack of agreed definition of constipation as highlighted above, and, as a result, reported figures are based on different observations including clinician's observations, prescription of opioids, patient's reports, and the types and numbers of laxatives prescribed. While some of these appraoches are objective, assessments of altered bowel function, the personal experinces of constiaption are highly subjective. Given this, it seems most appropriate to focus on patient's self-reports at a population level to understand the extent of the problem. To this end, there are a number of reasonably large population-based studies conducted in Europe, Australia, and the United States (Laugsand et al. 2009; Kamal et al. 2015; Clark et al. 2012). Combined, the results of these studies support that constipation symptoms affect at least 30% of palliative care patients with the incidence of the problem affected by diagnosis (cancer vs. non-cancer) and possibly performance status.

1.3 Impact of the Problem on Palliative Care Patients

There are a number of aspects of the impact of the problem that need to be considered. This includes the physical, psychological, and cost aspects of this problem.

The term "constipation" is used interchangeably in palliative care as both a diagnostic label and to indicate a bothersome physical symptom. However, it may be more correct to consider constipation as a cluster of symptoms that occur as the result of disordered function of the normal structures of defecation. Frequently occurring symptoms that affect people who identify themselves as constipated include straining, dissatisfaction, difficult or painful passage of stool, bloating, abdominal pain and discomfort, and nausea. Similar to chronically constipated patients, recent observations support palliative care patients also have a similar intensity most akin to those chronically constipated gastroenterology patients who are dissatisfied with their treatment (Clark and Currow 2014). This becomes even more problematic when the detrimental impacts of constipation symptoms on people's quality of life are considered (Clark et al. 2016a).

Even aside from the impacts of constipation symptoms on people's physical and psychological well-being, there are other impacts that affect the care of palliative care patients experiencing constipation symptom. These include the fact that constipated patients are more likely to receive more visits from community palliative care teams and more likely to be hospitalized (Addington-Hall et al. 1998; Addington-Hall and Altmann 2000). When hospitalized, these patients tend to occupy more of the ward staff's time (Wee et al. 2010).

1.4 Etiology

Constipation may be a primary disorder of the enteric nervous system of the colon or a functional disorder of defecation also known as dyssynergic defecation (Sbahi and Cash 2015; Wald 2016) with these disorders classified in the table below. It is estimated that up to 14% of the total population are likely to be affected by these primary causes of constipation to varying degrees (Table 1).

In some groups such as older patients or palliative care patients, the problems of disturbed bowel function are much higher. This is because not only are these groups equally likely to be affected by primary disorders of constipation but in addition are exposed to other factors that might contribute to disordered bowel habits such as increasing weakness, increased dependency, and polypharmacy. As a result, the incidence and prevalence of the problem in these specific cohorts is much higher compared to the general population (Vazquez and Bouras 2015; Clark et al. 2012). Despite this, the objective data that describes the physical impact on gut structures is weak in all area but especially so in palliative care as highlighted in Table 2.

Table 1 A summary of functional bowel problems (Sbahi and Cash 2015)

Slow transit constipation: This occurs as the result of impaired colonic propulsive motor activity, inadequate gastrocolic reflex, and delayed emptying of the proximal colon. Typically, people experience infrequent defecation sometimes less than one bowel action per week. The cause of this problem is still poorly defined
Functional defecation disorders: These disorders occur as a result of impaired rectal propulsive forces, paradoxical anal contraction, and/or inadequate relaxation of the anal sphincter. Typically, people experience prolonged and excessive straining (even with soft stool), the need for digital manipulation including exerting vaginal or perineal pressure to pass a bowel movement, and a failure to respond to standard laxatives

1.5 Assessment

1.5.1 History and Physical Examination

The history and clinical presentation of disordered bowel habits is highly variable. This is not surprising given this is so personal and subjective. Although it is common in palliative care to pay attention to the frequency with which people are able to pass a bowel action, palliative care data highlights that it is not uncommon for this cohort to be symptomatic with other problems including excessive straining, discomfort, or a sense of incomplete evacuation. The assessment must include a comprehensive history of people's subjective experiences which includes an appreciation of the duration that people have

Table 2 Factors commonly suggested as contributory to constipation

Factors suggested as contributory to secondary constipation in palliative care	Studies conducted in a palliative care cohort		Studies conducted in other patient groups	
	Constipation diagnosis	Contributes to constipation based on most objective research available	Constipation diagnosis	Contributes to constipation based on most objective research available
Opioids (Wald 2015)	Objective diagnosis of slow transit	Yes	Objective diagnosis of slow transit	Yes
Anticholinergic load (Leroi et al. 2000; Clark et al. 2014):				
Extrinsic	Use of laxatives	Yes	Objective diagnosis of slow transit	Yes
Intrinsic (i.e., secondary to age, inflammatory states)	Use of laxatives	Yes	–	Not examined
Blockade of gut histamine receptors (Fosnes et al. 2011)	–	Not examined	Patient report	So far, impact based on theory and patient reports
Blockade of gut serotonin receptors (Bjornsson et al. 2002)	–	Not examined	Objective diagnosis of slow transit	Yes
Physical activity (Kamal et al. 2015; Bjornsson et al. 2002; Muller-Lissner et al. 2005; Kim et al. 2014)	Use of laxatives	Yes	Objective diagnosis of slow transit	Mixed results
Age (Clark et al. 2016a; Bai et al. 2016)	Patient report	No	Objective diagnosis of slow transit	No
Gender (Clark et al. 2016a; Fischer and Fadda 2016)	Patient report	No	Objective diagnosis of slow transit	No
Duration of constipation symptoms (Clark et al. 2016a; Brandt et al. 2005)	Patient report	Yes	Patient report	Yes
Hypercalcemia (Lamy et al. 2001; Ragno et al. 2012)	Frequency with which bowels open	Yes	Rome criteria	No
Metabolic causes:				
Diabetes (Faria et al. 2013)	–	Not examined	Objective diagnosis of slow transit	Yes
Chronic renal failure (Wu et al. 2004)	–	Not examined	Objective diagnosis of slow transit	Yes
Hypothyroid (Rahman et al. 1991)	–	Not examined	Objective diagnosis of slow transit	Yes

experienced problems. This should include not only rectal problems and difficulty passing bowel actions but, in addition, abdominal problems such as bloating, pain, and nausea. Other history should include an appreciation of oral intake, performance status, comorbid illness aside from the problem that has underpinned referral to palliative care, and medication history.

Table 3 Components of a rectal examination that correlate with objective investigations of constipation (Talley 2008)

Inspection Inspect the appearance of the perineum looking specifically for external hemorrhoids, rectal prolapse, and evidence of fecal soiling or scarring	The presence of a scar at the anus correlates with lower incremental anorectal squeeze (Dobben et al. 2007)
Ask the patient to strain and observe the perineum in particular for a gaping anus	The presence of a gaping anus indicates lower resting pressures on anorectal manometry (Dobben et al. 2007)
Assess the anal sphincter tone at rest (internal anal sphincter) and on squeezing (external anal sphincter)	There appears to be a good correlation between absent, decreased, and normal resting and squeeze pressures with anorectal manometry (Dobben et al. 2007)
Ask the patient to strain and push the finger of the examiner away. This should result in the perineum descending 1–3.5 cm. A failure to descend is representative of pelvic dyssynergia	Perineal descent assessed by examination correlates with descent assessed by dynamic MRI (Bharucha et al. 2005)

A comprehensive and systematic physical examination is also necessary which includes assessment of hydration, abdominal examination, and neurological and rectal examination. The abdominal examination includes an assessment of bloating, tenderness, masses, and bowel sounds.

The rectal examination is perhaps the section of the examination that will provide the most objective evidence to help guide management of the problem as many of the steps involved in such an examination are well correlated with objective assessments of constipation (Table 3). A well-conducted rectal examination should involve up to eight steps including consent, observation, palpation, and dynamic maneuvers such as straining down to observe the degree to which the anus gaps or the pelvic floor descends (Talley 2008). Despite the fact that aspects of this physical examination are well correlated with objective investigations, it is increasingly neglected (Clark et al. 2010).

Other investigations are aimed at understanding whether there are factors that might be easily reversible. However, it is important to remain cognizant that in palliative care situations, investigations must be considered in the context of the disease trajectory and patient's ability to tolerate them. Beyond a full blood count, renal and liver function tests, thyroid function tests, and electrolytes such as calcium and magnesium, few other tests are warranted. Although palliative care guidelines not uncommonly recommend plain radiographs to assess the severity of the problem, there is little data to support this practice (Clark et al. 2016b). Furthermore, recent data highlights the lack of interrater agreement suggesting that this tool in its current context is insufficiently accurate and should not be used to base treatment decisions (unpublished data).

1.5.2 Constipation Assessment Scales

There are numerous constipation assessment tools in common use with palliative care guidelines suggesting that the use of such tools is appropriate. While many such tools are available, the optimal tool for use in palliative care is not yet clear. It is generally recommended that should such a tool be required to assist patients with recall or descriptions that the tool selected should be easy to use and quick to complete (Izumi 2014). Some of the constipation assessment tools previously recommended in palliative care guidelines or adopted in palliative care studies (references) are summarized in Table 4 with respect to their content and the population the tool was validated in.

1.6 Management

1.6.1 Pharmacological

While there are many recommendations made regarding the choice of laxatives in palliative care, the fact remains that the evidence is still limited, and this is particularly true when objectively considering whether one medication is more effective than another (Clemens et al.

Table 4 Constipation assessment tools (Izumi 2014; Coffin and Causse 2011)

Tool	Description	Validation population	Comments
The Bristol Stool Form Scale (BSFS) (Saad et al. 2010)	This commonly used tool is used to assess stool characteristics based on the observation that stool form accurately reflects colon transit times	Healthy and constipated volunteers	The tool has been validated in healthy populations where colon transit was artificially altered and chronically constipated patients not taking laxatives. The accuracy of the tool for chronically constipated requiring regular laxatives is not known
Constipation Assessment Scale (CAS) (McMillan and Williams 1989)	This eight-item scale was designed to assess the presence and severity of constipation in less than 2 min. The criteria for constipation include straining, a sensation of incomplete defecation, bloating, gas, oozing, rectal pressure, rectal pain, and small stool volume	Cancer patients treated with morphine or vinca alkaloids	While some of the elements of the Rome criteria are incorporated into this tool, whether or not stools are hard is missing
Victoria Bowel Performance Scale (Hawley et al. 2011)	This quick to complete scale was designed to assess three parameters including stool shape, bowel patterns, and ability to control defecation	Palliative care	While this tool has been tested in a palliative care population, it does incorporate the appearance of stool as a marker of successful treatment. This remains a problem given stool form has only been validated in patients with normal bowel function when taking laxatives and constipated patient not taking laxatives
The Bowel Function Index (Rentz et al. 2009)	This three-item scale is simple to use and is based on the patient's experience over the last 7 days. People are asked to numerically score ease of defecation, feeling of incomplete defecation, and their impression of the severity of the problem	Cancer and non-cancer patients treated with opioids	To date, this has been best validated in opioid-induced constipation
Patient Assessment of Constipation Symptoms (Slappendel et al. 2006)	Twelve-item scale that is based on the Rome criteria divided into three domains. These include abdominal symptoms, rectal symptoms, and the experiences of passing a bowel action based on the patient's experiences over the last 14 days	Chronically constipated patients and patients with lower back pain taking opioids	While this tool has been shown to be reliable and responsive to change, the studies that report its use have been mostly performed in the context of opioids being the main constituting factor to constipation

2013; Pitlick and Fritz 2013). This current lack of robust evidence to inform evidence-based prescribing guidelines reinforces the need for clinicians to understand as best as possible (1) the possible causes of constipation; (2) the currently available medications, their actions, and adverse profiles; and (3) the patient's experiences. This information may then be used to implement a trial of therapy. For standard laxatives, the correct choice of laxative is most likely to be an agent that is well tolerated by the individual and acceptable to them in terms of restoration of more usual bowel function. This may require a period of trial and error. The different classes of laxatives that are available are summarized in Table 5.

Table 5 Laxatives by class

Laxative class	Mode of action	Expected time to effect	Adverse effects	Evidence for use in palliative care
Osmotic: saline and sugar laxatives (Wald 2016; Pitlick and Fritz 2013)	Saline laxatives promote an influx of fluid into the gut lumen Sugar-based laxatives such as lactulose pass unchanged into the colon. In the colon, the sugar is broken down into fatty acids and lactic acid which in turn changes the intraluminal pH and increases intraluminal pressures. These changes increase peristalsis and promote water retention in the lumen	1–2 days	Bloating, abdominal pain, cramping, electrolyte disturbances	Moderate when co-prescribed with senna
Polyethylene glycols (Pitlick and Fritz 2013)	Polyethylene glycol possesses a water binding capacity. The orally administered fluids soften the stools in the large bowel without causing an influx of fluid into the bowel lumen	1–3 days	Abdominal pain, bloating, nausea	Poor but in routine use
Stimulant (Wald 2016; Hawley and Byeon 2008)	Stimulants include medications such as senna and bisacodyl which induce propagated colonic activity leading to increased colon transit times. Bisacodyl may also be given as a suppository with the main action being in the rectum	8–12 h	Watery diarrhea, cramping abdominal pain, nausea, dehydration, and electrolyte disorders	Moderate
Softeners (Pitlick and Fritz 2013)	This includes both emollients and lubricants. Emollients include docusate and lubricants include mineral agents. The aim of these agents is to make the actual passage of the stool easier	These agents do not induce laxation but cause softening in 2–3 days	Fecal soiling	Low but in routine use
Prokinetics: prucalopride (Quigley and Neshatian 2016)	The neurotransmitter serotonin has well-documented effects on gut motility. Based on this, a number of agents that are the highly selective 5-HT4 agonists have been developed including prucalopride	Hours	Headache, nausea, abdominal pain, diarrhea	Low
Intestinal secretagogues (Quigley and Neshatian 2016)	Alternative ways to increase gut transit include activation of the epithelial ion channels to promote secretion. Lubiprostone is a secretagogue that activates gut-based chloride channels resulting in water secretion to the gut lumen	Within 24 h	Diarrhea, nausea	Low

1.6.2 Management of Opioid-Induced Constipation

While there are numerous causes of constipation symptoms in palliative care patients, this is also a group who are highly likely to be receiving opioid analgesia. It is estimated that up to 40% of patients receiving opioids (Prichard et al. 2016) will develop constipation with this symptom unlike other adverse effects of opioids unlikely to moderate over time (Bell et al. 2009). While the initial treatments should be as usual, there are a number of agents including naloxone and methylnaltrexone which are the two most commonly used agents in palliative care. Either of these could be considered if the patient has not responded to simple treatments; opioids are considered the agents predominantly contributing to the problem and the person as no factors would contradict the use of these agents.

Methylnaltrexone is a peripheral opioid antagonist that has been studied in a palliative care population (Prichard et al. 2016; Nelson and Camilleri 2015). It is recommended for patients with presumed opioid-induced constipation who have not responded to standard treatments. It is administered as a once-daily subcutaneous injection and is expected to induce laxation within hours of administration. The main adverse effects include abdominal pain, diarrhea, nausea, and sweating. It should not be administered until a bowel obstruction has been excluded.

Naloxone combined with oxycodone was developed with the intent of naloxone displacing oxycodone from the opioid receptors in the gut. While it has been identified as effective when compared with oxycodone alone, it is notable that this combination reduces but does not eliminate opioid-induced constipation, and standard laxatives are often still required (Anon 2011). The maximum strength available is oxycodone 40 milligram (mg) with naloxone 20 mg with suggestions that at doses higher than this the medication is less effective (Mercadante et al. 2011) presumably because first-pass metabolism of the naloxone is decreased. The main adverse effects are nausea, vomiting, headache, and diarrhea. The medication should be used with great caution in those patients with liver dysfunction.

1.6.3 Nonpharmacological

Although the evidence in both chronic constipation and palliative care is weak, nonpharmacological approaches to improve constipation symptoms are routinely recommended as summarized here:

- Ensuring that people have privacy, avoid difficult situations such as the use of bedpans (Folden 2002) and try to maintain a regular routine. This latter point is often made in conjunction with the recommendation that people aim to pass a bowel action in the morning as this is when the colon is most active (Rao et al. 2001).
- Keep a bowel diary with this recommendation based on the fact that people's recall of their bowel actions is not always accurate (Hsieh 2005).
- Maintain adequate fluid intake (Spinzi et al. 2009).
- Remain as mobile as possible (Spinzi et al. 2009).

As noted above, while such recommendations are included in palliative care guidelines, they must be considered in the context that this population is heterogeneous, and while they might be applicable earlier in disease trajectories, as people become frailer, capacity to tolerate interventions becomes more difficult.

2 Diarrhea

2.1 Definition

Diarrhea is defined as the passage of loose or watery stools occurring at least three times per day (reference). It may occur as an acute short-lived problem (<14 days), a persistent problem (>14 days but <30 days), or chronic (>30 days) (Gale and Wilson 2016).

2.2 Prevalence

While diseases associated with diarrhea account for significant numbers of deaths worldwide, the problem of diarrhea in wealthy countries is far less significant. As a result of this, while still considered a distressing problem for individuals treated with palliative intent, estimates suggest that less than 10% of palliative care patients are likely to be bothered by this (Fallon and O'Neill 1997).

2.3 Impact: Physical, Psychological, and Cost

The fact that this problem, when more than a shorted-lived episode, is not commonly examined in the palliative care literature does not mean that it is a problem that should be ignored. This is because, regardless of the cause, severe and persistent diarrhea may have significant physical and psychological detrimental effects (Cherny 2008).

Physically people with persistent diarrhea may be very symptomatic. This is because of both the constancy and frequency of bowel actions and their complications. The physical symptoms may depend upon the site of the problem and the subcategory of the problem. The complications of diarrhea of small bowel include large volume and watery stools often associated with urgency and cramping. These patients are at risk of excessive fluid losses leading to dehydration which in turn may cause postural symptoms and other complications. In contrast, diarrhea that originates from problems in the large bowel is likely to cause frequent but painful, small bowel movements. Other problems likely to be experienced by patients include increasing fatigue due to both the constant activity of passing bowel actions and the resultant loss not only of fluid but electrolytes.

Aside from physical impacts, diarrhea may have detrimental psychological impacts again as the result of a number of issues. Many people express embarrassment at this problem not only due to the constant bowel movements but, in addition, embarrassment due to noise, malodorousness, and soiling as the result of urgency.

2.4 Etiology

Diarrhea may be classified as watery, fatty, or inflammatory with the definition of these disorders and examples that may affect palliative care patients summarized in Table 6.

2.5 Assessment

2.5.1 History and Examination

The most critical first step is to understand what the patient is experiencing exactly when he/she complains of diarrhea. This includes the frequency with which they are passing bowel actions, the appearance of the stool (including consistency and color), associated symptoms such as pain or bloating, and the duration of the problem. Other features that are important to glean include a description of the person's normal bowel habits and how has this changed. For example, if the patient is experiencing intermittent constipation and diarrhea, it is important to consider whether in fact this is a presentation of fecal impaction. Lastly, the history must include current medications and changes to medications; recent use of antibiotics; food history; recent surgery, radiotherapy, or other tumor treatments; and family history (Table 7).

Physical examination is also important. This includes abdominal and rectal examination. In particular it is important to consider whether the patient has evidence of bloating and pain or signs of peritoneal irritation including rigidity or rebound.

2.5.2 Investigations

The extent of investigations depends not only on the capacity of a person to tolerate investigations but equally on the duration which the person has been experiencing problems and the features of physical examination.

Table 6 Subtypes of diarrhea with some clinical examples that may affect palliative care patients (Gale and Wilson 2016; DuPont 2016)

Watery	Fatty	Inflammatory
Secretory Alcohol withdrawal Bacterial enterotoxins (e.g., cholera) Bile acid malabsorption Hyperthyroidism Medications (e.g., antineoplastics colchicine, NSAIDs, antibiotics) Neuroendocrine tumors Non-osmotic laxatives (e.g., senna, docusate) Postsurgical (e.g., cholecystectomy, gastrectomy, bowel resection)	*Malabsorption* Amyloidosis Carbohydrate malabsorption (e.g., lactose intolerance) Lymphatic engorgement (e.g., congestive heart failure, some lymphomas) Mesenteric ischemia Noninvasive small bowel parasite (e.g., *Giardia*) Postresection diarrhea Short bowel syndrome Small bowel bacterial overgrowth	Inflammatory bowel disease Diverticulitis Ulcerative colitis *Clostridium difficile* Invasive bacterial infections (e.g., tuberculosis) Invasive parasitic infections (e.g., *Entamoeba*) Viral infections (e.g., cytomegalovirus, herpes simplex virus) Tumors (e.g., colon carcinoma, lymphoma) Radiation colitis
Osmotic Celiac disease Osmotic laxatives (e.g., magnesium, phosphate, sulfate)	*Maldigestion* Hepatobiliary disorders Pancreatic exocrine insufficiency	

Table 7 Clinical features of subcategories of diarrhea

Watery	Fatty	Inflammatory
Secretory: Watery stools that do not change with fasting Nocturnal bowel actions	Greasy or bulky stools that are difficult to flush Oil in the toilet bowl that requires a brush to remove	Frequent, small-volume, bloody stools May be accompanied by tenesmus, fever, or severe abdominal pain
Osmotic: Watery stools that decrease with fasting		

Acute-onset diarrhea probably does not warrant testing unless the person is exhibiting signs of dehydration or features of peritoneal irritation. In the former, depending upon the person's capacity to tolerate investigations, it may be appropriate to check the person's renal function. The latter may require abdominal radiography to exclude either an ileus or bowel obstruction.

When the problem is more chronic or the etiology is not clear from the history, further investigations may be necessary. However, even in this context, it is important to consider whether it is the best interests of a patient to investigate further and whether the burden of investigations and treatments outweighs the benefits. If investigations are considered necessary, recommendations suggest that it is preferable to try and categorize by type of diarrhea based on history and, by doing so, narrow the diagnostic possibilities. This has the benefit of both reducing unnecessary testing and enhancing the diagnostic yield (Sweetser 2012; Juckett and Trivedi 2011) (Table 8).

2.6 Management

It has been suggested that the most common cause of loose bowel actions experienced by palliative care and other patients remains to be medications in particular, laxatives (Fosnes et al. 2011; Fallon and O'Neill 1997; Chassany et al. 2000). The initial step after assessing the patient's hydration and comfort is to cease medications that are likely contributing factors.

Table 8 Diagnostic approach (Sweetser 2012; Juckett and Trivedi 2011; Barr and Smith 2014)

1. Determine whether or not the person really has diarrhea
2. Eliminate drug causes
3. Define whether this is an acute or chronic problem
4. Stool cultures are indicated for patients with bloody stool, severe dehydration, signs of inflammatory disease, or persistent symptoms lasting more than 3–7 days, immunocompromised patients, or those with suspected hospital-acquired infections
5. Routine testing for ova and parasites in acute diarrhea is not necessary in developed countries unless the person has been recently overseas or at high risk (e.g., HIV +ve)

The most important next step to manage acute onset of diarrhea is oral rehydration therapy with fluids that contain glucose and electrolytes for those who can tolerate. Less effective but sometimes more easily tolerated are parenteral fluids. Usually, acute onset of diarrhea does not require medications. However, when more rapid symptom control is required, anti-diarrheal medications are indicated with the combinations of loperamide together with simethicone more likely to provide more rapid relief and more complete relief of symptoms (Barr and Smith 2014). The main caveat to this recommendation is if the stool is bloody. In this situation, loperamide should be avoided as it may lead to a more prolonged course of illness (Barr and Smith 2014).

More persistent problems require both the provision of symptom control and prescription of medications likely to correct the underlying problem. With regard to symptom control, this may include either oral codeine or parenteral morphine. Treating the underlying causes may include:

- Antibiotics according to the identification of the underlying infection
- Pancreatic enzymes for pancreatic insufficiency
- Aspirin and cholestyramine for radiation-induced colitis
- Octreotide for profuse secretory diarrhea (Kim-Sing et al. 1994)

3 Intestinal Obstruction

3.1 Definition

Bowel obstruction is defined as any mechanical or functional obstruction of the intestine that limits or prevents the physiological transit of gut contents and the normal processes of digestion. However, this definition is very broad and likely to apply to many different situations: benign or malignant, curable or incurable (Tuca et al. 2012). In any situation, patients presenting with a bowel obstruction are critically unwell with this problem even more challenging when a patient has an underlying malignancy. Internationally agreed criteria to definitively diagnose a malignant bowel obstruction (MBO) include (1) clinical evidence of bowel obstruction, (2) obstruction occurring distal to the ligament of Treitz, (3) the presence of primary intra-abdominal or extra-abdominal cancer with peritoneal involvement, and (4) the absence of reasonable possibilities for a cure (Anthony et al. 2007). It is this cohort of people who almost universally have a very poor prognosis that this next section will specifically focus on.

3.2 Prevalence

Overall, it is estimated to be between 3% and 15% of all cancer patients who are likely to be affected by a MBO with women at greater risk than men (Tuca et al. 2012). The incidence is much higher in specific malignancies including ovarian cancer where 20–50% of patients with stage III–IV disease are likely to be affected. Further, up to 30% of patients with advanced colorectal cancers will experience this problem (Ripamonti et al. 2008; Ferguson et al. 2015). Other cancers have also been identified as more likely to result in MBO including cancers that arise from the abdomen and cancers that arise elsewhere as summarized in Table 9.

Table 9 Tumors most likely to result in MBO

Intra-abdominal cancers most likely to result in MBO: Colon, ovary, stomach, pancreas, bladder, endometrium
Extra-abdominal cancers most likely to result in MBO: Breast, melanoma

3.3 Impact: Physical, Psychological, and Cost

The most common physical symptoms that accompany a MBO include nausea, vomiting, colicky abdominal pain, constant pain secondary to gut distension, and changes in bowel habits. It is estimated that nearly 100% of people will have nausea with the other symptoms likely to occur in up to 80% of people (Arvieux et al. 2006). Clinically, the presenting symptoms may occur intermittently or progressively depending upon whether the obstruction is complete, partial, or resolving.

While the majority of people will experience nausea and vomiting, it is generally accepted that the pattern of vomiting may help define whether the obstruction is more proximal or distal. More proximal obstructions tend to present with constant and frequent vomiting with this occurring as a later presentation in more distal obstructions. Eventually the vast majority of patients experience vomiting which is often dark and malodorous. This is often described perhaps erroneously as feculent vomiting. However, this is not as sometimes believed a presentation of retrograde transit but rather the result of bacterial liquefaction of intraluminal contents proximal to the obstruction.

Many people will experience both colicky pain and constant pain with the colicky pain likely to be due to both exaggerated peristaltic movements and gut spasms. A more constant pain is likely to be multifactorial and occurring as the result of gut distension, tumor deposits, and irritation of the peritoneum.

Along with the unpleasant physical symptoms, MBO are likely to expose people to significant emotional and psychological stressors (Dolan 2011). These problems are likely to be complex and, like other symptoms, may impact quality of life. Previous qualitative work has identified the fact that people are unable to eat is not only physical debilitating but, for some people, a significant emotional and social issue. The loss of capacity to eat for some has been identified as confronting to people's sense of social relevance and perhaps a sign of transition from a life worth living to impending death. Other patients described the experience as bewildering with a sense that there was no direction in their treatment and they were left wondering and waiting as to what might occur in the future (Gwilliam and Bailey 2007).

Table 10 Factors that underlie MBO (Frago et al. 2015; Lynch et al. 2012)

Tumor-related factors:
Extrinsic compression of the gut
Intraluminal occlusion
Intraluminal tumor causing intussusception
Mesenteric or omental caking
Malignant infiltration of the myenteric plexus
Paraneoplastic neuropathies
Non-tumor-related factors:
Chronic constipation
Medications
Mesenteric thrombosis
Biochemical (chronic renal failure, hypercalcemia)
Adhesions
Dehydration

3.4 Etiology

The majority of malignant bowel obstructions occur in the more advanced stages of illness (Tuca et al. 2012). Obstructions may present as partial or complete affecting one or multiple levels simultaneously. The reasons that obstructions occur are complex and varied as summarized in Table 10 (Frago et al. 2015; Lynch et al. 2012).

A mechanical obstruction results in a sequence of self-perpetuating events of distension and secretion. Gastric, pancreatic, and biliary secretions accumulate which in turn stimulate further intestinal secretions proximal to the obstruction. At the same time, the gut's capacity to absorb salt and water is decreased, and instead, there is increased secretion of fluid into the lumen as the result of both increased distention of the gut and

Table 11 Radiological investigations

Test	Changes in BO	Sensitivity and specificity
Plain erect and supine radiographs	Distended gut with the presence of air-fluid levels	The diagnostic sensitivity and specificity of plain radiographs in diagnosing obstruction is 82% and 83%, respectively (Thompson et al. 2007)
Abdominal CT	Compared with plain radiographs, CT provides more detailed information including the extent of disease and the level of obstruction	The diagnostic sensitivity of CT in determining the obstruction level is 93%, with a specificity of 100% (Peck et al. 1999)
MRI	Compared with CT, MRI increases the ability to diagnose peritoneal disease	The sensitivity of MRI in diagnosing the level of the obstruction is 93–95%, with a specificity of 63–100% (Beall et al. 2002)

as an inflammatory response around the site of obstruction (Roeland and von Gunten 2007). This inflammatory response includes secretion of serotonin which in turn leads to the release of substance P, nitric oxide, acetylcholine, somatostatin, and vasoactive intestinal peptide. This combination exacerbates local gut wall edema increasing secretion of secretions, exacerbating dissention, and increasing intraluminal pressures (Ferguson et al. 2015).

3.5 Assessment

3.5.1 History and Physical Examination

Patients with advanced cancers who present with the combination of nausea, vomiting, and abdominal pain (colicky and constant) along with disturbed bowel function should prompt consideration of whether this could indicate this patient has developed a bowel obstruction. Such changes should prompt a physical examination. In particular, patients need to be examined for abdominal distention, tenderness including signs of peritoneal irritation, and changes to auscultated bowel sounds. With regard to the latter signs, changes consistent with MBO include either absent bowel sounds or isolated metallic sounds with the latter presumed to result from the accumulations of air and fluid in the distended gut proximal to the obstruction.

3.5.2 Investigations

The extent of investigations depends upon the person's estimated prognosis. For some patients this is purely a clinical diagnosis based on history and physical examination. For others, more invasive investigations are required to inform discussions with interventional radiologists, gastroenterologists, or surgeons. This includes investigations to both (1) confirm the diagnosis and (2) assess the physiological status of the patient (Table 11).

3.6 Management

There are a range of strategies to manage MBO. While all are conservative in that this is universally a condition with a poor prognosis, this may at times include surgery while at other times a more conservative approach is necessary. Above all, it is important that treatments are based on the following:

1. An understanding of the underlying pathophysiology of the obstruction
2. Detailed clinical assessment including the extent of disease and whether there are life-prolonging treatments available to this person, overall prognosis, health and performance status, the presence of ascites, and whether this is the first or a recurrent presentation of a bowel obstruction
3. The patient's and family's expectations of care

3.6.1 Interventional

There are three main options if interventional treatment is being considered: namely, stenting, venting, and surgery (Table 12). While there is an

Table 12 Therapeutic interventions for MBO

Intervention	Patients for whom this is applicable	Complications
Self-expanding metallic stents (Kim and Kim 2016; Kaplan et al. 2014; Hong and Kim 2014)	Single site of obstruction that is accessible by upper GI or colonic scope Limited expectancy, unable to tolerate surgery but otherwise well-controlled pain	Stent occlusion Perforation Stent migration Bleeding Pain Infection
Percutaneous gastrostomy (DeEulis and Yennurajalingam 2015)	Intractable vomiting due to inoperable MBO	Stent occlusion Perforation Infection Bleeding
Surgery (Folkert and Roses 2016; Paul Olson et al. 2014)	Patient not actively dying and if the obstruction was reversed, would have life-prolonging therapies available. While not absolute, the following have been suggested as poor prognostic indicators and should be taken into account if surgery is considered: complete small bowel obstruction (SBO), non-gynecological cancer, ascites, decreased albumin, elevated total white cell count age >65 years, poor nutritional status, poor performance status, liver metastases, previous abdominal radiotherapy, pulmonary metastases	It is estimated that there is a 40% mortality associated with surgery in this group Other complications of surgery include enterocutaneous fistula, wound infection, wound dehiscence, early obstruction, high output ostomy, myocardial infarction and cardiac failure, deep vein thrombosis and pulmonary embolus, pneumonia, and other infections
Oral gastrografin (Mercadante et al. 2004)	Recent data suggests that administration of gastrografin, a hyperosmolar water-soluble contrast agent, results in an increased pressure gradient at the level of obstruction in the bowel resulting in resolution of the bowel obstruction	

increasingly robust body of literature that describes such interventions, much of the evidence that supports them is observational and, in some instances, very limited in number (Bischoff et al. 2015). As such, this is a very poor situation that at present leaves people with limited surgical options (Kucukmetin et al. 2010).

3.6.2 Pharmacological

Regardless of whether a patient is referred for an intervention, knowledge and implementation of strategies to improve symptom control are required. The most commonly recommended types of medications and the reasons for their use are listed in Table 13. As ever, it is important to critically appraise clinical guidelines as the levels of evidence that support most of recommendations are limited.

3.6.3 Nonpharmacological

One of the main concerns experienced by both patients and families is the fear that the person will not be able to eat, feel hungry, and even worse starve to death (Whitworth et al. 2004). This concern must be discussed as the implications of this fear are significant for all involved. It is imperative that families are reassured that MBO is typically a problem associated with very advanced disease with such patients very typically experiencing anorexia and early satiety. Oral intake may in fact make the person feel worse. More important is the need to ensure that all are reassured that this is a presentation of very advanced disease from which the person is now dying (Soriano and Davis 2011).

It is important to work with patients and families to ensure that their concerns are appropriately

Table 13 Symptom control in MBO

Problem	Typically recommended	Reason for prescription	Comment
Bowel obstruction	IV or SC dexamethasone (Bischoff et al. 2015; O'Connor and Creedon 2011; Lee et al. 2012)	Anti-inflammatory Antiemetic	A previous review suggested a trend toward successful resolution of BMO. However, this was not statistically significant and further work is required to objectively document net harms and benefits
Pain	Parenteral (IV, SC, transdermal) opioid (Tuca et al. 2012; O'Connor and Creedon 2011)	Constant severe pain presumed due to gut distension, peritoneal inflammation, or infiltration of the myenteric plexus	According to the WHO ladder, severe pain requires opioid analgesia
	SC or IV hyoscine butylbromide or hyoscine hydrobromide (Tuca et al. 2012; O'Connor and Creedon 2011; Currow et al. 2005; Prommer 2013)	Cramping abdominal pain	Clinical guidelines recommend antispasmodic agents should be added if cramping pain persists despite opioids. Clinical guidelines recommend caution given that such agents may transition an incomplete obstruction to a complete obstruction
	Somatostatin analogues such as octreotide or lanreotide (Ferguson et al. 2015; O'Connor and Creedon 2011; Kubota et al. 2013)	Reduced secretions and intestinal blood flow presumed to reduce abdominal distension	Somatostatin analogues have been recommended in MBO based on the fact that they reduce secretions. However, as an analgesic intervention, their use is questionable given a recent trial demonstrated statistically higher use of hyoscine in MBO compared with placebo
Nausea	IV or SC metoclopramide (O'Connor and Creedon 2011; Dolan 2011)	Facilitate gastric emptying and concurrent central activity	There is no data to support the benefit of one antiemetic over the other
	SC haloperidol (Dolan 2011)	Predominately central effect on nausea	Metoclopramide has both peripheral and central action. Ongoing cramping is commonly listed as an adverse effect in MBO
	SC, IV, or sublingual serotonin antagonists (Tuca et al. 2012)	Reduce serotonin release from enterochromaffin cells of the stomach and with central effects on the chemo trigger zone	Haloperidol has a predominantly central effect with little impact on the gut
	Sublingual Olanzapine (Dolan 2011; Kaneishi et al. 2012)		Lastly serotonin antagonists may be useful in bowel obstruction when other agents are proving less effective with this statement based on observational data

(*continued*)

Table 13 (continued)

Problem	Typically recommended	Reason for prescription	Comment
Vomiting	SC or IV hyoscine butylbromide or glycopyrrolate (Tuca et al. 2012; Prommer 2013)	Anti-secretory to reduce the incidence of vomiting	Although there are three different approaches to reducing the amount of vomiting people experience, the data to date that recommends one agent as superior over the over is limited. Further, it is not clear if agents are best used on combination or as single agents
	Somatostatin analogues such as octreotide or lanreotide (Tuca et al. 2012; Ripamonti 2000)	More specific anti-secretory	
	H2 receptor antagonists or proton pump inhibitor (Tuca et al. 2012; Clark et al. 2009)	Specifically target gastric secretions	

addressed. This includes preempting advice as how to best manage a dry mouth. Many people will require reassurance that this does not routinely require total parenteral nutrient or artificial hydration. Rather, reassurance must be provided that rather than improve outcomes, in some situations, such interventions may even worsen symptoms (Ripamonti et al. 2008; Dy 2006). It is important however that this advice is not treated as a blanket rule and each case considered on an individual basis (Soriano and Davis 2011).

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Gastrointestinal Symptoms: Nausea and Vomiting

15

Bertrand Behm, Carlos Fernandez, and Mellar P. Davis

Contents

Abstract

This chapter examines nausea and vomiting affecting patients who suffer from serious illness. A deeper understanding of these physiologic processes allows for better assessment and management. There are several different pharmacological and nonpharmacological options to improve palliation, including complementary and alternative medicines. Ultimately, there should be an individualized approach that considers the trajectory of illness and comorbidities, and most importantly it should be patient centered.

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_15

1 Demographics

Nausea is a symptom proven difficult to define and not as clearly as the objective sign of vomiting. Its first use in medicine can be traced back to the Greek terms ναυτια and ναυσα, both referring to the physical effects of seasickness. It was then translated into the Latin, and came to mean "a sense of queasiness" or "qualm" (Andrews and Sanger 2014). The concept of nausea, as it was understood in ancient times, related more to a constellation of symptoms that included asthenia, inability to carry out focused activities, and tendency to avoid work of mental or physical kind. Today nausea has a narrower definition that refers primarily to the subjective feeling of a need to vomit.

Vomiting is the forceful expulsion of gastrointestinal contents by mouth through retropulsion that is accomplished by involuntary contractions of thoracoabdominal and gut muscles. Typically vomiting is preceded by nausea, but this is not always the case. Teleologically, vomiting constitutes a reflex that allows the body to eliminate toxins.

Both sign and symptom have a significant negative impact on patients suffering from serious illness (Bruera et al. 2000; Bliss et al. 1992). There are a limited number of studies that have looked at the prevalence of nausea and vomiting in palliative care. Solano et al. carried out a systematic review looking at 11 symptoms, including nausea and vomiting, in adult patients. The prevalence of nausea in advanced cancer ranged from 6% to 68%, in AIDS it ranged from 43% to 49%, in advanced heart disease 17% to 48%, and in renal failure 30% to 43% (Solano et al. 2006). Thirty six percent of referrals to outpatient palliative care were nauseated, and 22% had vomiting (Kirkova et al. 2012). In the same study, nausea and vomiting were more prevalent among women, and the prevalence increased with age. Others have suggested that there is a relationship between worsening performance status and both nausea and vomiting (Glare et al. 2011; Kirkova et al. 2012).

Despite advances in our understanding of the pathophysiology of nausea and vomiting, both remain a major challenge in caring for palliative care patients. Nausea becomes a common symptom with declining performance status and near the end of life (Glare et al. 2011; Chang et al. 2004). Both nausea and vomiting are undertreated, and those suffering from more severe symptoms are less likely to receive antiemetic drugs (Greaves et al. 2009). Nausea and vomiting rarely occur in isolation. Nausea clusters with anorexia, fatigue, lack of energy, shortness of breath in patients with advanced malignancies (Cheung et al. 2009). Clarifying the potential demographic influences on symptom prevalence will hopefully lead to better tailor our treatment approach.

2 Nausea and Vomiting Pathophysiology

Nausea is a multidimensional symptom which includes interoceptive, emotional, and cognitive domains (Napadow et al. 2013). Teleologically, nausea is a control mechanism that signals one not to eat when the food is poisonous, when the stomach is malfunctioning, or when a threat is perceived for which a full stomach would have a survival disadvantage (Stern 2002). Similarly, Vomiting is not a reflex that can be predicted based on the intensity of neurophysiologic stimulation. The threshold for emesis is variable and response is modified by experience and can be conditioned based on experience (Horn 2008).

There have been advances in our understanding of the pathophysiology of nausea and vomiting; however, the final common pathway for emesis has yet to be defined. Although nausea and vomiting are usually seen together, it is believed that nausea and vomiting have at least partially separate physiologic processes; some patients experience them independently. Treatment of emesis is not necessarily effective in controlling nausea (Chiu et al. 2016). Furthermore, there is more information about the physiologic basis for vomiting than nausea which is subjective and more difficult to study in animal models (Horn 2008).

The causes of nausea and vomiting are numerous and in patients with serious illnesses is often multifactorial (Collis and Mather 2015). Nausea and vomiting can be seen in diseases arising from almost any organ. Treatments may be perceived as "toxic," including medications commonly used in

palliative medicine such as opioids, chemotherapy agents, and radiation therapy.

The development of nausea and vomiting is the end result of a complex interplay between the GI tract (interstitial cells of Cajal, ICC), autonomic nervous system, brainstem, vestibular system, higher CNS centers, and endocrine system (Singh et al. 2016).

2.1 Gastrointestinal Tract

There is a growing interest in gastric electrophysiology, especially in the setting of gastroparesis, nausea and vomiting. The ICC are gastric slow wave pacemakers governing smooth muscle resting membrane potential gradients. Abnormalities of the ICC are a common histological finding in both idiopathic and diabetic gastroparesis, and the severity of ICC loss has been correlated with the severity of gastric retention, and electrogastrography (EGG) abnormalities. Motion sickness causes gastric dysrhythmias resulting in nausea/vomiting in humans. The shift from the normal gastric 3 contractions per minute slow wave rhythm to a faster 4–9 contractions per minute rhythm precedes the development of nausea and the intensity of this tachygastric response/motility pattern correlates with the severity of nausea. The resolution of nausea and vomiting in gastroparesis has been associated with improvements in EGG abnormalities (O'Grady et al. 2014).

2.2 Autonomic Nervous System

Activation of mechano-, osmo-, and chemoreceptors in the gut stimulate vagal afferent fibers which carry information about the state of the GI tract to the dorsal vagal complex (DVC: nucleus of tractus solitarius (NTS), dorsal motor vagus (DMV), and area postrema(AP) in the caudal brain stem). The role of vagal afferents has been most extensively studied in the context of chemotherapy-induced nausea and vomiting. Chemotherapy cause the release of serotonin, (5 HT), and tachykinins (substance P) from intestinal enterochromaffin cells which activates 5 HT3 and tachykinin receptors on vagal afferents. The action does not seem restricted to the peripheral sites since there are also 5-HT3 and tachykinin receptors in the CNS (Babic and Browning 2014; Hasler 2013; Tageja and Groninger 2016). Neurokinin 1 receptors antagonist, like the 5-HT3 receptor antagonists, are effective in treating CINV as well as postoperative nausea. The combination of NK1 receptor and 5-HT3 receptors antagonists is synergistic in reducing nausea and vomiting (Rojas and Slusher 2012; Steinhoff et al. 2014).

2.3 Brainstem

Vagal afferents activate neurons in the NTS which then project to groups of loosely organized neurons throughout the medulla, called "central pattern generator" (CPG) rather than a "vomiting center." The CPG coordinates the vomiting reflex through diverse population of neurons in the ventral medulla and hypothalamus (Hornby 2001). Under normal conditions, the NTS exerts a tonic gamma aminobutyric acid (GABAergic) influence over the adjacent DMV. The DMV contains preganglionic parasympathetic neurons that transmit to the GI tract via the efferent vagus nerve. In this way, the sensory inputs from the vagal afferents and AP result in activation of abdominal muscles, diaphragm, and esophagus culminating in the emetic response (Rojas and Slusher 2012). This DMV output can be modulated by numerous neurotransmitters and neuromodulators, including opioid peptides, serotonin, endocannabinoids, tachykinins, and dopamine.

The area AP is a chemosensitive organ adjacent to the NTS that was first identified as the chemoreceptor trigger zone. It is extensively vascularized with highly fenestrated capillaries and, therefore, it is not isolated from peripheral circulation by the blood brain barrier. This allows AP neurons to receive both neuronal and humoral signals for emesis and relay this information to the NTS. The AP contains receptors for multiple neurotransmitters: dopamine, neurokinins, serotonin, opioids, as well as, neuropeptides and hormones

involved in the regulation of gastrointestinal, cardiovascular, and immune function (Babic and Browning 2014; Richards and Andrews 2007).

2.4 Vestibular System

The vestibular system is critical to generating nausea and vomiting with motion. Nausea and vomiting are frequent symptoms of vestibular pathology such as: vertigo, vestibular neuritis, labyrinthitis, and benign paroxysmal positional vertigo. Motion sickness is a mismatch of converging visual input, vestibular, and visceral signals. Vestibular neurons have receptors for several neurotransmitters, including acetylcholine, muscarinic, dopamine D2, serotonin 5-HT2, and histamine H1 and H2. In practice, only antagonists to muscarinic cholinergic receptors and antihistamines are effective in relieving motion sickness (Babic and Browning 2014).

2.5 Higher CNS Centers

Higher CNS centers are important in the integration of various sensory, affective, and emotional responses which govern nausea and vomiting, but how these are related to nausea is not well understood (Farmer et al. 2015). The sensation of nausea is assumed to involve the cerebral cortex; in contrast, the emetic reflex is elicited in decerebrate animals demonstrating that vomiting can occur independent of forebrain involvement. Recent studies using fMRI in patient with motion sickness revealed activation of cerebral areas prior to the sensation of nausea: amygdala, putamen, and dorsal pons/locus cerueleus. Furthermore, severe nausea was associated with sustained activation of the insula and middle cingulate cortex. Linked connectivity between these two areas is postulated to integrate the cognitive, affective, and interoceptive domains leading to the experience of nausea (Napadow et al. 2013). Another study revealed that nausea in the healthy was associated with an increase in sympathetic activity with a concomitant reduction in parasympathetic activity. Nausea caused the release of vasopressin and impaired release of ghrelin, an orexigenic gastric hormone that is associated with appetite. This might explain anorexia experienced with nausea sensation. The significance of vasopressin with the nausea stimulus is not known. Water retention occurs ahead of anticipated vomiting, followed by reduction of mesenteric blood flow, gastric dysrhythmias, then activation of central emetic pathways via the area postrema. Functional MRI demonstrates activation of the inferior frontal gyrus and decrease activity in other areas such as: cerebellar tonsil, declive, lingual gyrus, culmen, cuneus, and posterior cingulate cortex. The decreased activity in the posterior cingulate cortex explains in part the decreased parasympathetic activity with nausea. Taken together, these studies suggest that nausea is associated with changes in brain activity (region specific increases and decreases) in a diverse regions involved with sensory discrimination, cognitive evaluation, and affective motivation consistent with the nature of nausea (Farmer et al. 2015; Sclocco et al. 2015).

A better understanding of the neurobiology of nausea and vomiting provides targets for potential therapies and is a step toward developing drugs which retain efficacy, but lack nausea and vomiting as side effects (Horn 2008).

3 Assessment and Management of Nausea and Vomiting

It is helpful to clarify first if the patient is truly presenting with nausea, or if the complaint is better described as dyspepsia. The same applies to vomiting versus rumination. This step is critical, as it will direct the diagnostic approaches and treatment considerations. Dyspepsia as defined by the Rome IV criteria is the presence of at least one of three symptoms: early satiety, postprandial fullness, or epigastric abdominal pain, often described as a burning sensation (Stanghellini et al. 2016). Up to 75% of patients suffering from dyspepsia will have no underlying structural disease and thus will be classified as having functional dyspepsia. The rest fall under the structural

dyspepsia category, and further evaluation will depend on the presence of alarm features (weight loss, anorexia, vomiting, dysphagia, odynophagia, and a family history of gastrointestinal cancers), patient functional capacity, and goals of care (Mayer et al. 2013).

Rumination is characterized by the passive flow of ingested gastric contents into the oral cavity, followed by repeat mastication and swallowing or spitting out of the food bolus. It is not related to an anatomical alteration of the stomach, esophagus, or lower esophageal sphincter. The gastric distension by the food bolus triggers contraction of the stomach and simultaneous relaxation of the lower esophageal sphincter with subsequent rechewing of the food bolus. It is not associated with nausea (Stanghellini et al. 2016).

The traditional approach to evaluating and treating nausea and vomiting in serious illness is centered on understanding the etiology behind the symptom. Those with advanced malignancies, an etiology is identifiable in 75%, and in 25% there are multiple factors involved in the development of nausea and vomiting (Ang et al. 2010; Stephenson and Davies 2006).

In the typical elderly patient suffering nausea and vomiting, it is helpful to consider four broad categories: the primary disease, adverse effects related to disease directed therapy, frailty, and events brought on by unrelated comorbid conditions (Glare et al. 2011). Newly introduced cholinesterase inhibitors or opioid pain medications rather than the underlying disease may be the cause. Other potential etiologies include changes in bowel habits due to cancer, sytemic anti-neoplastic therapies, acute decompensation of chronic heart failure and uremia in those with advanced renal disease.

Assessment should ideally be carried out by a standardized tool such as the Edmonton Symptom Assessment System, the Memorial Symptom Assessment Scale, or the more recently introduced Integrated Palliative Care Outcome Scale. It is important to determine intensity, frequency, and associated symptoms, paying attention to descriptors and associated symptoms. These scales can be adapted to become a part of an electronic health record for patients, and permit quality improvement (Bruera et al. 1991).

3.1 Primary Disease Process

3.1.1 Gastroenterology (GI)

Acute onset of nausea (minutes to hours) should prompt one to exclude bowel obstruction, mesenteric ischemia, or myocardial infarction. Nausea associated with rapid onset of worsening colicky pain, in the setting of diminishing stool and flatus output with high pitched bowel sounds, will likely be related to bowel obstruction. An abdominal film will help differentiate bowel obstruction from other etiologies. If bowel obstruction emesis may lead to transient relief of nausea, and a strong feculent odor may be pervasive when dealing with a gastrocolic fistula. Distant and proximal etiologies of bowel obstruction will influence the volume and frequency of emesis. On physical examination, palpable periumbilical node can be suggestive of advanced intra-abdominal malignancy. Other important features in the clinical evaluation should include changes in stool consistency and frequency, as well as rectal examination, that may reveal a fecal impaction, or a palpable ridge found in some patients with advanced pancreatic, gastric, and lung cancer (Hussain et al. 2014).

If nausea has been present for weeks to months, the most common causes are: gastric stasis (cancer related such as carcinoma of the stomach, hepatomegaly with ascites) and dysmotility disorders (primary colorectal cancer, peritoneal carcinomatosis, ascites, adhesions, constipation, fecal impaction) (Glare et al. 2011; Stephenson and Davies 2006; Bentley and Boyd 2001).

3.2 Chemical and Metabolic Effects

Impaired gastric emptying should be suspected as the most likely cause when nausea and vomiting are intermittently present, with small volume of emesis and associated early satiety, abdominal distension, bloating and a feeling of fullness. Typical causes are anticholinergic medications, opioids, extrinsic compression of the gastric vault by ascites, and hepato- or splenomegaly (Ang et al. 2010). Diabetic gastroparesis occurs in frail

elderly patients with long-standing history of diabetes mellitus. Less often NSAIDs induce gastritis. In a series of 121 patients admitted to hospice, impaired gastric emptying was responsible for up to 44% of patient suffering from nausea and vomiting (Stephenson and Davies 2006).

Nausea and vomiting that are aggravated by sight and odors of food will typically be related to toxins, such as tumor necrosis or bacterial toxins. Digoxin and iron are medications that are linked with persistent nausea. Other common causes in advanced illness are liver metastases, hypercalcemia, and uremia with progressive renal dysfunction. This syndromic presentation can be identified in up to 40% of cases (Ang et al. 2010).

The presence of anxiety and/or personality changes and delirium will usually be caused by metabolic abnormalities such as hyponatremia, hypercalcemia, uremia, or adrenal insufficiency. Sepsis can also be linked to this clinical presentation.

Opioid-induced nausea and vomiting is present in up to 40% of cancer patients started on opioids (Campora et al. 1991). Mechanistic factors are constipation, gastroparesis, stimulation of the chemoreceptor trigger zone, and vertigo (Coluzzi et al. 2012). Opioid rotation has grade D evidence to suggest a switch from morphine to oxycodone, or hydromorphone benefits nausea. Subcutaneous use of methylnaltrexone has been reported to reduce nausea from methadone suggesting that the mechanism is peripheral (Yuan et al. 1999). Dopamine (D2) receptor antagonists such as haloperidol and prochlorperazine, as well as atypical antipsychotics such as olanzapine, have been utilized with varying degrees of success. Consideration of tapentadol as an alternative to oxycodone may also reduce the incidence of opioid-induced nausea and vomiting (Smith and Laufer 2014).

3.3 Neurologic Causes

Increased intracranial pressure as a cause behind nausea and vomiting (CNS metastatic disease, primary brain neoplasms, leptomeningeal disease) is associated with early morning headache and altered consciousness due to increased pressure on the reticular formation. Associated physical exam symptoms include 6th cranial nerve palsy, papilledema, and more ominously Cushing's triad of bradycardia, respiratory depression, and hypertension (Dunn 2002). This has been found in 2–8% of patients in palliative care (Ang et al. 2010; Glare et al. 2011).

Patients suffering from movement disorders and associated nausea and vomiting, typically with vertigo, are found in 2% or less of palliative care patients.

3.4 An Algorithmic Approach to Nausea and Vomiting Management

The decision to proceed with laboratory and imaging studies depends on the initial history and physical examination. In hospice evaluation may be perceived as excessively burdensome if the goals of care are to avoid aggressive interventions. Patients who suffer from acute dehydration will benefit from IV hydration. Measuring electrolytes will help identify potential culprits and lead to appropriate correction: sodium, potassium, calcium, creatinine, and blood urea nitrogen as well as albumin. Hypercalcemia is common with malignancies such as squamous cell carcinomas and multiple myeloma, hydration and bisphosphonates, or denosumab, a monoclonal antibody that binds to nuclear factor-kappa ligand (RANKL) will reduce calcium levels and nausea. Denosumab has become the preferred agent if renal impairment is present, or if hypercalcemia of malignancy has proven refractory to bisphosphonate therapy (Thosani and Hu 2015).

In patients with good performance status (defined as 2 or less on the Eastern Cooperative Oncology Group performance scale, >70% Palliative Performance Scale), an abdominal film will help differentiate bowel obstruction from severe constipation. If bowel obstruction is suspected based on KUB results, a computed tomography scan of the abdomen and pelvis may also be more specific for GI tract obstruction and is required if a surgery is being considered. In a similar fashion,

CT scan of the brain or magnetic resonance imaging helps clarify the role of stereotactic brain radiation and use of dexamethasone treatment for metastatic brain disease.

4 Pharmacology

4.1 Complementary and Alternative Medicine

The use of complementary and alternative medicine (CAM) is common in the general population. In 2012, the prevalence was 42% over the last year and 80% felt that CAM was helpful (Dossett et al. 2014).

Complementary and alternative medicine can be defined as a group of medical practices, such as herbs, acupuncture, chiropractic, and massage, among others, which are not in conformity with the standards of the medical community and may have fewer adverse effects than traditional treatments for nausea and vomiting in patients or may offer therapies that are more consistent with the patient's cultural or health care beliefs (Pan et al. 2000).

Most of the data about CAM in the treatment of nausea and vomiting are derived from studies that involve patients with CINV. In a small trial involving patients at the end of life, acupressure wrist band was not better than the placebo wrist band (Pan et al. 2000).

A systematic review in 2013 evaluated acupuncture in cancer pain found 11 trials that evaluated the effectiveness of acupuncture in the treatment of CINV. Eight trials were considered to have a high risk of bias, two were unclear. Only one positive trial in patients with breast cancer on high dose chemotherapy had a low risk of bias (Garcia et al. 2013).

Acupressure in the P-6 acupoint has been used in the treatment of postoperative nausea and vomiting. The intervention is considered effective; however, the quality of the data is considered low due to heterogeneity (Lee et al. 2015). Acupressure for the treatment of CINV has also been addressed. There have positive and negative trials. A recent trial comparing acupressure wristbands, sham acupressure, or antiemetics alone was a negative trial (Molassiotis et al. 2014).

Topical ABHR gel, a combination of lorazepam, diphenhydramine, haloperidol, and metoclopramide, has been reported in the use for refractory nausea and vomiting, especially for those unable to take medications by mouth in the hospice setting, despite the lack of absorption of these medications by that route. It is not currently recommended the use of topical ABHR gel as per the choosing wisely campaign from the American Board of Internal Medicine due to lack of benefits in well-designed studies (Currow and Abernethy 2013). Serum levels were unmeasurable (Gupta et al. 2014).

Therapeutic touch is reported to decrease the duration, frequency, and intensity of CINV compared to placebo. However, there was not description of the placebo intervention (Vanaki et al. 2016).

The impact of psychological factors on nausea and vomiting is widely acknowledged. Trials of relaxation training, coping preparations, imagery, music therapy, distraction techniques, or hypnosis demonstrate mixed results. Mind-body techniques are reported in the prevention CINV. Nevasic, which is an audio program, which uses specially constructed audio signals to generate an antiemetic reaction, did not reduced nausea and vomiting related to chemotherapy but did reduce the use of antiemetics (Moradian et al. 2015).

Ginger is commonly used to treat nausea, its potential mechanism of action as 5-HT3 antagonist. Ginger has anti-inflammatory properties and modulates gastrointestinal motility. Ginger reduces CINV and nausea associated to pregnancy. The studies are generally considered of low quality due to lack of standardized extracts, are poorly controlled studies with limited sample size (Marx et al. 2015).

In conclusion, CAM may be added to traditional care for the management of patients with nausea and vomiting associated to chemotherapy. CAM therapies can also give patients an added sense of control over the treatment of their symptoms. Little is known about the role of CAM in other causes other than CINV.

4.2 Conventional Pharmacological Approach

When considering best management practices for the pharmacologic treatment of nausea and vomiting in a palliative care setting, we can take a mechanistic or an etiologic approach. Given that even patients with advanced disease have potentially reversible causes for nausea and vomiting, following a therapeutic path based on the identification of a specific etiology and modifying or removing the offending cause of nausea is reasonable. This may not be feasible in very frail patients near end of life where an empiric antiemetic make more sense. There are no quality head-to-head studies comparing the two approaches. In the empirical approach, drug selection is based on single antiemetic agent efficacy based on clinical studies. Here, priority has been given to safety, efficacy, and pharmacokinetics shown in clinical studies. There is no convincing evidence that one approach is superior to the other (Bruera et al. 2004; Glare et al. 2004).

4.2.1 Prokinetic Agents

Given the prevalence of impaired gastric emptying in palliative care patients, and their low cost, these agents have traditionally been considered first-line agents in management of nausea and vomiting. As we consider the potential etiologic factors involved, they can enhance coordinated transit through the GI tract by promoting the release of excitatory neurotransmitters through activation of 5HT4 receptors in the enterochromaffin cells along the gut wall promoting peristalsis and intestinal tone, as well as by blocking central and peripheral 5 HT3 and D2 receptors and stimulating motilin receptors. Clinical considerations should include avoidance of these agents in the presence of complete bowel obstruction, GI bleeding, or during the immediate postoperative period (Glare et al. 2011).

4.2.2 Metoclopramide

Metoclopramide is a competitive dopamine 2 (D2) receptor antagonist; it is a benzamide derivative that primarily acts by blocking D2 receptors centrally and activating 5HT4 receptors resulting in release of acetylcholine mainly at the level of the lower esophageal sphincter, stomach, and proximal small bowel. Metoclopramide improves antroduodenal coordination and gastric emptying (Lee and Kuo 2010). At higher doses, it is a weak competitive 5HT3 blocker. According to the guidelines published by the Multinational Association of Supportive Care in Cancer/European Society of Medical Oncology (MASCC/ESMO) metoclopramide is the drug of choice for advanced cancer patients with nonchemotherapy related nausea and vomiting (Walsh et al. 2017). There have been two randomized control trials that showed moderate evidence in a with a small number of patients, and more recently a systemic review that determined moderate quality evidence for its clinical efficacy (Davis and Hallerberg 2010). Dosing is started as 5 mg every 8 h, and to maximize its absorption should be administered on an empty stomach, 30 min prior to meals. Drug half-life is 4–6 h, with an onset of action of 30–60 min when given orally, versus 1–3 min when administered intravenously. It can be given subcutaneously as a bolus or continuous infusion. Pharmacodynamically, it is more effective with continuous administration. In a retrospective assessment of cancer patients suffering from chronic nausea, patients tended to respond better and with less adverse effects to a continuous infusion up to 5 mg /hcompared to divided doses of immediate release metoclopramide. Tardive dyskinesia, akathisia, and other extrapyramidal reactions occur with higher doses (Grimes et al. 1982).

4.2.3 Domperidone

Domperidone is currently available in the United States only through the Federal Drug Administration's Expanded Access to Investigational drugs program. Please refer to ▶ Chap. 16, "Gastroparesis and Cancer-Related Gastroparesis" for more details.

4.2.4 Methotrimeprazine

Methotrimeprazine is a phenothiazine neuroleptic agent originally used in the management of schizophrenia that binds to multiple neurotransmitter receptor sites (Kennett et al. 2005). It has potent antagonist actions at a variety of drug target sites, including dopamine, histamine, adrenergic,

muscarinic, cholinergic and serotonin (5HT2 at the vomiting center) receptors. As a broad spectrum agent, it has potential application in patients with advanced disease due to likely multifactorial causes (Cox et al. 2015). Data on its effectiveness comes mainly from uncontrolled and observational studies (Eisenchlas et al. 2005; Dietz et al. 2013). It is effective in 60–80% of patients. Benze's review of chronic nausea and vomiting in palliative care patients found the level of evidence is low to moderate (level C), but deemed it an acceptable second- or third-line option (Benze et al. 2012). Methotrimeprazine via oral and subcutaneous route remains stable in a normal saline solution for up to 14 days. The preferred starting dose is 6.25–12 mg by oral route twice daily or 3.125–9.375 mg per 24 h via subcutaneous route. The oral dose can be increase up to 35–50 mg per 24 h (Amesbury et al. 2004; Eisenchlas et al. 2005). It may be considered in patients with underlying pain and nausea, as it has been described to possess analgesic benefits, particularly in neuropathic models of pain (Patt 1994). Monitoring for sedation, anticholinergic effects, as well as orthostatic hypotension are important considerations particularly in frail elderly patients. QT prolongation has been described, but is rarely encountered (Dahl and Refsum 1976).

4.2.5 Haloperidol

Haloperidol is considered a relatively potent butyrophenone neuroleptic that targets more specifically D2 receptors in the CTZ (Anchin et al. 1991; Helmeste and Seeman 1983; Sherman and Bolger 1988; Hardy et al. 2010). It has activity at sigma-1 receptors, and this activity has recently been linked to inhibition of pain hypersensitivity and facilitation of enhanced opioid antinociceptive effects (Romero et al. 2016; Entrena et al. 2009). Evidence of this benefit has recently been investigated in patients rotated from high-dose opioid regimens to methadone in combination with haloperidol (Salpeter et al. 2013). Concerns exist regarding the potential for QT prolongation with its administration via the intravenous route (Hatta et al. 2001). There have been no RCT published supporting the use of haloperidol as an antiemetic (Walsh et al. 2017). A moderate quality study that evaluated "ABH" topical gel concluded that the compound was comparable to placebo (Fletcher et al. 2014). An open-label trial showed clinical response in 20 of 33 evaluable patients, with 8 having a documented complete response. One trial suggested effectiveness of 65% (Lee and Kuo 2010). Dosing of haloperidol as an antiemetic is typically lower than its use as a neuroleptic. Starting dose is usually 0.5 mg every 6–8 h, and can be as high as 5 mg every 8 h via the oral route. Intravenously, usual doses are 0.5–2 mg every 8 h. Care should be taken when dosing in severe hepatic impairment, and in patients with advanced renal disease, it is recommended that starting doses be reduced by 50%. It should be avoided in patients suffering from Parkinson's disease, and those with narrow angle glaucoma and seizure disorders. Main adverse effects are extrapyramidal symptoms, and anticholinergic effects are possible. Drug-drug interactions occur via the CYP 3A4 system; care should be taken when using carbamazepine, phenytoin, and phenobarbital (Glare et al. 2011).

4.2.6 Olanzapine

This agent is classified as a thiobenzodiazepine atypical antipsychotic. Binding occurs at 5 HT-3, dopamine, histamine, and catecholaminergic receptors, and may be an alternative to those who do not respond to single antiemetics such as haloperidol and ondansetron. Evidence for its use comes primarily from trials evaluating chemotherapy-induced nausea and vomiting (Passik et al. 2004; Navari and Brenner 2010; Navari et al. 2007). It has been incorporated into both MASCC/ESMO and NCCN guidelines for CINV. A recent single-center study looked at 108 patients with advanced cancer at doses between 2.5 and 5 mg orally per day, with median treatment duration of 39 days (Kaneishi et al. 2016). Other uncontrolled series also showed evidence for difficult to control nausea and vomiting (MacKintosh 2016; Atkinson 2014; Passik et al. 2002). Dosing for CINV vary between 5 and 10 mg via oral route, ideally given at bedtime due to sedation. Desirable secondary effects in the palliative care setting are increased appetite and weight gain (Navari et al. 2008). Rare but

serious adverse events are insulin-resistant diabetes mellitus, a lowered seizure threshold and a prolonged QT interval. Common adverse events include somnolence, postural hypotension, constipation, dizziness, fatigue, dyspepsia, restlessness, and weight gain (Atkinson 2014; Chanthawong et al. 2014).

4.2.7 Prochlorperazine and Chlorpromazine

Both agents are widely used in both cancer- and noncancer-related palliative care settings. Like haloperidol, they block D2 receptors in the CTZ, as well as histaminergic, muscarinic, serotonergic, and alpha-adrenergic receptors. Doses for prochlorperazine range from 5 to 10 mg every 6 to 8 h by oral route, or 25 mg via rectal route 2–3 times daily. Chlorpromazine is typically given initially at 12.5 mg every 6 h usually to a maximum of 150 mg per 24 h. It can also be given intramuscularly at 25 mg 3–4 times daily. There are no quality studies looking at the effectiveness of prochlorperazine. Chlorpromazine has been evaluated in combination regimens with tropisetron and metoclopramide and found to be effective in only 20–30% of cases (Mystakidou et al. 1998). Chlorpromazine will typically have sedation as its most significant adverse effect, and thus tends to be more appropriate near end of life, particularly if delirium is part of the clinical picture. Other common adverse effects are anticholinergic effects, confusion, and extrapyramidal effects. Particularly with elderly males, glaucoma and benign prostatic hypertrophy can make them particularly susceptible to adverse events with these agents (Glare et al. 2011).

4.2.8 HT-3 Receptor Antagonists (5HT-2RA)

Serotonin antagonists target the 5HT-3 receptors found both in the periphery at vagus nerve terminals, and centrally in the NTS and CTZ (Aapro 2005). These agents have been used primarily in the setting of chemotherapy-induced nausea and vomiting (CINV). They are typically used in combination with corticosteroid and neurokinin-1 antagonist. A meta-analysis that looked at a total of 7808 patients concluded that all first-generation 5HT-3 RA are equally efficacious at preventing acute and delayed CINV following the use of highly emetogenic chemotherapy (Jordan et al. 2007) The evidence for its use in palliative care setting of nonchemotherapy-related chronic nausea is less robust. In one study, tropisetron was superior to metoclopramide and chlorpromazine in controlling chronic nausea in advanced cancer patients (Chanthawong et al. 2014). A different study demonstrated no difference when comparing ondansetron, metoclopramide, and placebo in the control of opioid-induced nausea among advanced cancer patients (Hardy et al. 2002). Doses recommended in the latest MASCC/ESMO guidelines are for ondansetron 8 mg or 0.15 mg/kg via IV route daily, or 16 mg daily orally. Granisetron is to be given in doses 1 mg IV (0.01 mg/kg) daily or 1–2 mg via oral route daily. Dolasetron 100 mg via oral route daily, tropisetron 5 mg IV via oral route daily, and palonosetron 0.25 mg IV or 0.5 mg via oral route (Roila et al. 2016). For palliative care patients being treated for pain with opioids, constipation as an adverse effect of5 HT-3 RA can be concerning. They also are known to prolong QT interval, and should be avoided when other QT-prolonging agents are used (Goodin and Cunningham 2002). In the palliative care setting, methadone can have a potentially additive pro-arrhythmic effect (Hafermann et al. 2011). They should thus be also avoided in patients with advanced cardiovascular disease. These are also very costly drugs which can be a limiting factor in a cost-conscious health system.

4.2.9 Antihistamines

There is a variety of antihistamine agents used in clinical practice for palliative care patients. Cyclizine, promethazine, and diphenhydramine are among some of the most common agents in this class. There is some evidence for their effectiveness in vestibular and chemical causes of nausea (Davis and Walsh 2000). Given their many potential drug-drug interactions via CYP2D6 pathway and significant anticholinergic adverse effects, these agents tend to be less frequently chosen for palliative care patients (American

Geriatrics Society Beers Criteria Update Expert Panel 2012). Evidence for their use is limited in the palliative care setting, and response rates reported in the range of 5–10% (Bentley and Boyd 2001).

4.2.10 Hyoscine

Hyoscine, also known as scopolamine, is an anticholinergic agent that binds preferentially to muscarinic receptors in the gastrointestinal tract, as well as blocking nicotinic receptors in a ganglion-blocking effect (Tytgat 2007). The drug is available in two formulations: butylbromide and hydrobromide. It is primarily reserved for management of refractory bowel obstruction symptoms near end of life, as it may reduce both GI secretions and smooth-muscle contractions that result in painful cramps. Evidence for its use comes primarily from experimentally-induced motion sickness-related nausea and vomiting in healthy volunteers (Pyykko et al. 1985). Statistically significant differences were found when the drug was compared to placebo in a series of 16 patients. The butylbromide formulation has low bioavailability, and is usually administered via subcutaneous infusion with doses ranging from 80 to 120 mg over 24 h. The hyoscine hydrobromide formulation is typically used in transdermal formulation in the US, ranging from 1.5 to 3 mg, but can also be used via oral (0.1 to 0.4 mcg every 4 h) and parenteral (0.6 to 2.4 mg administered over 24 h) routes (Glare et al. 2011). Particularly in patients with underlying delirium, dementia, it will be more likely to worsen confusion, and in the elderly, anticholinergic effects can be particularly troublesome: dry mouth occurred in up to 67%, and drowsiness in approximately 16% of subjects. Other adverse effects reported much less frequently are dry eyes, eye pain and eye pruritus, and blurred vision, and is contraindicated in narrow-angle glaucoma (Clissold and Heel 1985).

4.2.11 Octreotide

Octreotide (OCT) has a role primarily in the treatment of malignant bowel obstruction (MBO) in patients who have not responded to specific oncologic disease-targeted therapies, and deemed poor surgical candidates. Octreotide main mechanism of action is akin to somatostatin. It decreases splanchnic blood flow, inhibits release of serotonin, secretin, vasoactive intestinal peptide, among others, thus reducing intestinal and pancreatic fluid secretion as well as gastrointestinal motility (Glare et al. 2011). Most studies investigating the efficacy of OCT in a palliative care setting have significant limitations due to flawed design, power, and drop-out rates. One study evaluated OCT at doses ranging from 300 to 600 mcg/day in combination with haloperidol. Nausea, vomiting, along with thirst and need for IV hydration, were improved, with a reduction in total nasogastric output (Lee and Kuo 2010; Hisanaga et al. 2010). A prospective trial including 22 cases from 2006 to 2009 looked at assessing the clinical efficacy of OCT for vomiting in advanced gynecological malignancies not amenable to surgical interventions. Overall response rate was 82%, in 14 patients who had nasogastric tubes placed the response rate was 93% (Watari et al. 2012). Main adverse effects reported are diarrhea, abdominal pain, headache, fatigue, and malaise. Special consideration should be given to those patients with evidence of prolonged QTc interval, as well as those with significant bradycardia.

4.2.12 Cannabinoids

Currently available in the US in two formulations: dronabinol and nabilone. Both are approved by the US Food and Drug Administration for use in CINV refractory to first-line therapy. Both act via peripherally via CB1 receptors reducing intestinal motility in the gut, and may also act centrally on the dorsal vagal complex (Pertwee 1999; Parker et al. 2011). Dronabinol was compared to ondansetron and placebo in an RCT that showed a response rate 71%, ondansetron 64%, and placebo 15% for placebo. This study used lower doses than previous trials, resulting in less adverse effects and more compatible with current clinical practice (Meiri et al. 2007). A meta-analysis evaluated 13 RCT, 5 included dronabinol and 6 nabilone. Comparators used were prochlorperazine, alizapride, chlorpromazine, or domperidone. Dronabinol showed superiority over the comparator ($p = 0.03$, NNT 3.4,) while

nabilone showed no statistically significant difference ($p = 0.21$) (Machado Rocha et al. 2008). Doses with dronabinol are 2.5–5 mg by oral route three times daily, and with nabilone 1–2 mg twice daily, up to 6 mg daily. Most commonly reported adverse effects are somnolence, feeling of a "high" and sedation. Dizziness was reported significantly more frequently with cannabinoids when compared to metoclopramide and domperidone (Smith et al. 2015). Dysphoria was the most common cause for discontinuation of either medication among clinical trial patients, cited by 11% of patients withdrawing from treatment (Slatkin 2007).

4.2.13 Corticosteroids

Most of the evidence comes from the study of corticosteroids, particularly dexamethasone is in management of CINV. It has been suggested to work by various potential cellular mechanisms. Besides its known anti-inflammatory effect, it can have a direct central action by activation of glucocorticoid receptors at the level of the NTS in the medulla (Ho et al. 2004; Ho et al. 2004). There is also a possible interaction with 5 HT-3, tachynins NK1 and NK2, as well as alfa-adrenergic receptors (Andrews and Sanger 2014). Other clinical scenarios where dexamethasone has been included in treatment algorithms include malignant bowel obstruction and nausea due to raised intracranial pressure (Gralla et al. 1999). Doses have ranged from 4 to 8 mg per day, maximum doses of 16 mg over 24 h have been used in selected cases of malignant bowel obstruction (Glare et al. 2011). General recommendations are for limited trials to limit their potential adverse effects. Most concerning in the advance cancer population tends to be the risk for serious, life-threatening infections, as well as potential to induce hyperglycemia in diabetic patients, as well as delirium and sleep disruption in elderly patients, and those suffering from dementia. Efficacy rates vary significantly, and seem to be maximized at up to 75% when combined with metoclopramide (Bruera et al. 1996).

4.2.14 NK-1 (Tachykinin) Receptor Antagonists

This class of antiemetics are used primarily in the treatment of chemotherapy-induced nausea and vomiting (CINV). Specifically, these agents are recommended in the prevention of acute and delayed nausea in moderately to highly emetic risk chemotherapy regimens based on MASCC/ESMO and NCCN guidelines (Hardy et al. 2002). Agents currently available include aprepitant, fosaprepitant (parenteral formulation of aprepitant), netupitant, and rolapitant. Recommended doses for acute and delayed emesis are: aprepitant 125 mg on the day of chemotherapy followed by 80 mg daily for 2 days after chemotherapy, fosaprepitant 150 mg i.v. once on the day of chemotherapy; rolapitant 180 mg via oral route once on the day of chemotherapy and netupitant/0.5 mg palonosetron orally once on the day of chemotherapy. A recent systematic review looked at 17 trials, with a total of 8740 patients, assessing the role of NK-1 RA added to standard antiemetic treatment (5 HT-3 RA plus dexamethasone) for the prevention of CINV. NK-1 RA increased the likelihood of complete response (OR 0.51, 95% CI 0.46–0.57; 13 trials; $\mathbf{I}^2 = 12\%$) with a reduced need to use rescue antiemetic, as well as the reported frequency of nausea and vomiting. This benefit was found to be statistically significant for both highly emetogenic (OR 0.46, 95% CI 0.40–0.53) and moderately emetogenic OR 0.59, 95% CI 0.51–0.67) (dos Santos et al. 2012). The most common adverse effects experienced tend to be diarrhea and singultus; others include asthenia, alopecia, anorexia, and headache.

4.3 Nonpharmacological Management

Malignant bowel obstruction is described as the association of clinical and imaging evidence of bowel obstruction beyond the ligament of Treitz with incurable intra-abdominal cancer or extra-abdominal primary cancer with intraperitoneal

spread. The most common intra-abdominal cancers to cause malignant obstructions are ovarian and colorectal cancer. Meanwhile, breast cancer and melanoma are the most common extra-abdominal cancers to cause malignant bowel obstruction (Laval et al. 2014).

Nausea and vomiting usually result from malignant obstruction due to a combination of mechanical impedance, motility dysfunction, aggregation of secretions, diminished intestinal absorption, and inflammation (Teriaky et al. 2012). Medical management is therefore based on the use of steroids, antisecretory management, gastric antisecretory drugs, somatostatin analogues, and antiemetics (dos Santos et al. 2012), and nonpharmacological interventions generally include surgery (resection or palliative colostomy), stent placement, and decompression therapy (NGT, venting gastrostomies) (Dolan 2011).

The role of surgical versus nonsurgical management of patients with malignant bowel obstructions in patients with gynecologic and colorectal cancer is controversial. The management is basically empiric and there are marked variations in clinical practice. Retrospective cases showed wide variation in success rates, reobstruction and postoperative morbidity and mortality. There were no data about quality of life (Cousins et al. 2016).

The traditional surgical approach for treating malignant lower bowel obstruction (MBO) is associated with high rates of morbidity, mortality, and stoma formation. Less invasive alternatives such as colonic stents represent an option to overcome the high cost of hospital stays and poor quality of life associated with complications from surgery. Self-expanding metallic stents (SEMS) are expandable metallic tubes that are advanced to the site of obstruction along a guidewire in a collapsed state, under fluoroscopic and/or endoscopic guidance. Once deployed, the stents slowly expand radially to their maximum diameter under their own force, thereby achieving patency of the obstructed anatomy. They are generally well tolerated by patients with only conscious sedation, or no anesthesia. They are considered a less-invasive strategy than surgery, but complications still occur. Rates of stent migration, perforation, and reconstructions have been reported as 11%, 4.5%, and 12%, respectively, that limits its long-term efficacy (Watt). Stents treatment is associated with shorter length of stay, reduced ICU admissions, fever stoma formation, and shorter time to initiation of adjunct chemotherapy. The studies lack of information about quality of life and cost effectiveness. The shorter interval to chemotherapy and significant lower rates of 30-day mortality and short-term complications suggest that stents maybe reasonable alternative for treating patients with extensive metastatic disease or who are poor operative candidates due to severe comorbid conditions (Zhao et al. 2013).

Percutaneous endoscopic gastrostomy PEG tubes have been used commonly to supply alimentation since first described in 1980. A less common indication for PEG tubes is to be a long-term alternative to NGT in decompressing the gastrointestinal tract in benign and malignant diseases (Shaw et al. 2013). Patients with advanced malignancies who present with small bowel obstruction resistant to medical treatment and intractable vomiting have a very poor prognosis and end-stage palliation is usually sought, as the risk of surgery generally outweighs the benefit. Survival after venting gastrostomy placement is usually measured in weeks (Diver et al. 2013; Teriaky et al. 2012; Brooksbank et al. 2002). But a single center reported a mean survival of 135 ± 347.9 days (Issaka et al. 2014). Venting gastrostomy can facilitate the transition of these patients to home hospice. Improvements in nausea and vomiting are reported and it can also sometimes allow patients to eat small amounts of food for pleasure (DeEulis and Yennurajalingam 2015).

Some authors suggest that the time to place PEG is probably late in patients with malignant obstruction and that early PEG placement may lead to better outcomes (Laval et al. 2014).

Most venting gastrostomies are performed endoscopically. Reported complications include PEG occlusion and infection. Infections are particularly more likely in patients who have ascites.

The predictors of complications after PEG placement in the first 30 days were those with American Society of Anesthesiology (ASA) scores of 4, 4E, and 5E. Multivariate analysis revealed ASA scores >4, elevated WBC count, and advanced tumor stage to be independent predictors of mortality in the first 30 days and INR >1.5 and venting indication for PEG were independent predictors for overall mortality (Richards et al. 2013).

Ascites is commonly considered a relative contraindication for venting PEG placement in patients with malignant GI obstruction for the following reasons: the fluid can make puncturing the anterior wall of the stomach more difficult, the development of ascites between the stomach and the abdominal wall can increase the intraperitoneal catheter length and may predispose to tube dislodgement; and finally, ascites may prevent maturation of a tube track, thus facilitating pericatheter leakage of ascites and or gastric contents, which may result in skin breakdown and or peritonitis.

Fluoroscopic-guided placement of a PEG is feasible in most patients with malignant bowel obstruction and ascites, with a technical success rate of 72% and 77.4%. Ascites is managed with paracentesis and most frequently with intraperitoneal catheter (Shaw et al. 2013).

Gastroparesis can affect patients with serious illnesses, especially those with a history of diabetes and can also affect patients with cancer (Barkin et al. 1986). It can present with nausea and vomiting in addition to early satiety, postprandial fullness, and upper abdominal pain. It is better explained as a syndrome of objectively delayed gastric emptying in the absence of a mechanical obstruction. Opioid therapy can cause delayed gastric emptying and this should be considered before assuming a diagnosis of gastroparesis. The treatment usually consists of fluid, electrolyte, and nutritional support, optimization of glucose levels, and postpyloric feedings if there is evidence of unintentional weight loss of more than 10% during a period of 3–6 months, and or repeated hospitalizations for refractory symptoms. The use of prokinetics (metoclopramide) is indicated at the lowest effective dose.

Gastric electric stimulation can be considered for compassionate treatment of diabetic or idiopathic gastroparesis who present with refractory nausea and vomiting despite conventional therapy – prokinetics, fluid, electrolyte, and nutritional support, per open label studies. Complications from the device such as local infection or lead migration, as well as complications related to surgery, may occur in up to 10% of patients implanted (Camilleri et al. 2013; O'Grady et al. 2009).

Surgical options for the treatment of gastroparesis are: gastrojejunostomy, pyloromyotomy, and completion or subtotal gastrectomy. Major gastric surgery can relieve distressing vomiting from severe gastroparesis and improve quality of life in patients with a high risk for renal failure and poor life expectancy (Ejskjaer et al. 1999; Watkins et al. 2003).

In conclusion, nausea and vomiting from bowel obstruction are associated with a short-term survival. Pharmacological therapies are not always effective. Palliative venting gastrostomies and colonic stents are alternatives for symptomatic relief for patients with high surgical risk. However, these interventions are not without risk. Further research is needed to evaluate the benefit of early palliative interventions in the disease trajectory.

5 Summary General Guidelines

Initial assessment of the patient suffering from nausea and vomiting should identify those patients who are imminently dying. Here rapid optimization of symptom control should be the priority, and an empiric approach may be the most reasonable. Initial choice in advanced cancer based on the existing evidence would be metoclopramide, unless signs of bowel obstruction are present. Alternative agents can be haloperidol, levomepromazine, or olanzapine. Refractory symptoms at the end of life may lead to the consideration of palliative sedation.

In those patients who have a more extended prognosis, a more concerted effort to find reversible causes may be more appropriate. In patients

with advanced COPD and heart failure, a closer look at medications such as methylxanthines and digoxin may be warranted (Barr et al. 2003). Patients with uncontrolled diabetes mellitus may present with hyperglycemia. Correction with insulin and appropriate IV fluid administration should be considered. Hyponatremia may also be a contributing factor in patients with end-stage liver, kidney, or heart disease. Collaboration with an endocrinologist may be appropriate. Patients with liver failure may also present with symptomatic ascites leading to increased abdominal pressure. Therapeutic paracentesis and placement of an indwelling intraperitoneal tunneled catheter should be considered. If bowel obstruction or opioid bowel syndrome is suspected, a flat plate of the abdomen should be obtained. Confirmation of bowel obstruction should lead to insertion of a nasogastric tube, the initiation of around the clock octreotide plus haloperidol as first-line agent, based on MASCC recommendations. If this combination proves ineffective, anticholinergic antisecretory agents, such as scopolamine butylbromide, and/or dexamethasone can be added. In those expected to survive weeks to months, placement of a percutaneous endoscopic gastrostomy (PEG) tube should be considered. If a fecal impaction is present, a cotton seed enema may be administered.

Patients presenting with suspicion for raised intracranial pressure, CNS metastatic disease, should be managed up-front with dexamethasone. Those suspected of opioid-induced nausea and vomiting should be considered for opioid rotation. Antiemetics may be helpful, though no clear guideline exist to recommend one agent over another. Prophylactic treatment has not been shown to be effective.

Poor response to a single antiemetic should prompt treatment with a combination regimen. Here, medications that have complementary mechanisms of action may be more effective (e.g., choosing a prokinetic or haloperidol in combination with a 5 HT-3 RA). Failure of first- and second-line treatment options (metoclopramide, haloperidol respectively) should prompt consideration of broad spectrum of agents such as levomepromazine or olanzapine.

Nonpharmacologic options should always be considered in combination with any antiemetic regimen. Drug-drug interactions need to be considered before selecting a specific drug. Minimization of polypharmacy and frequent clinical reassessment are cornerstones of good palliative management of nausea and vomiting.

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Gastroparesis and Cancer-Related Gastroparesis

16

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_114

Abstract

Gastroparesis is an underrecognized cause of nausea, vomiting, early satiety, postprandial fullness, and weight loss in advanced cancer. Causes for gastroparesis include reduced pyloric compliance and mobility, impaired duodenal contractions, widespread neuropathy, and selective loss of interstitial cells of Cajal. Patients with cancer may develop gastroparesis because of chemotherapy-induced neuropathy, immunosuppression followed by opportunistic viral infections involving the gastrointestinal tract, procedures such as celiac blocks, paraneoplastic neuropathy or myopathy, and as a sequalae of graft-versus-host disease after allogeneic bone marrow transplant. The symptoms of gastroparesis do not correlate with the degree of impairment observed in gastric emptying studies. Treatment includes prokinetics such as metoclopramide, erythromycin, azithromycin, and domperidone. Symptoms may respond to mirtazapine, granisetron, and acupuncture. Gastric electrical stimulation and pyloromyotomy procedures have been reported to reduce symptoms, but there are no randomized trials to validate either procedure. In those failing to respond to medical management, a percutaneous endoscopy-placed gastric tube for decompression with a jejunal extension feeding tube (PEG-J) can be used to reduce symptoms and provide nutrition.

1 Introduction

Gastroparesis is defined as a delay in gastric emptying without mechanical obstruction (Camilleri 2016). Symptoms of gastroparesis are nonspecific and include nausea, vomiting, postprandial fullness, early satiety, and dyspepsia with a subset experiencing upper abdominal pain (Pasricha and Gastroparesis Clinical Research Consortium 2016). The three most common published causes of gastroparesis in the literature are idiopathic, a diabetic, and postsurgical. Gastroparesis associated with malignancies has been reported only in patient reports or small series (Pasricha and Parkman 2015; Leung and Silverman 2009). How frequently gastric paresis occurs in patients with cancer is not known. The pathophysiology of gastroparesis in non-cancer patients appears to be heterogeneous and consists of impaired fundus accommodation, visceral hypersensitivity, autonomic dysfunction, lack of compliance of the pylorus, and duodenal dysmotility (Nguyen and Snape 2015). The standard test for gastroparesis, gastric emptying by scintigraphy after a test meal, correlates poorly with symptoms of gastroparesis and quality of life (Pasricha and Parkman 2015; Borges et al. 2013). The principles to managing gastroparesis include: excluding gastric outlet obstruction, evaluating for iatrogenic causes (such as medications and surgery), and a trial of prokinetic medications (Camilleri 2016). The differential diagnosis includes functional dyspepsia,

which has similar symptoms, but can be associated with accelerated gastric emptying. Functional dyspepsia is also associated with impaired gastric accommodation and gastroduodenal hypersensitivity to distension. The rumination syndrome may superficially resemble gastroparesis and consists of repetitive regurgitation of gastric contents usually within minutes after a meal which is mistaken for vomiting. Effortless regurgitation in the rumination syndrome is preceded by a sensation of the need to belch which lasts 1–2 h. Treatment of the rumination syndrome is behavioral modification and not prokinetic medications. Finally, bulimia associated with anorexia nervosa may resemble gastroparesis associated with weight loss. Anorexia nervosa occurs in young women as does gastroparesis. In advanced bulimia, gastric emptying can be delayed (Camilleri 2016; Mascolo et al. 2016).

2 Diagnosis

Nausea and vomiting of all symptoms correlate the best with the degree of objective gastroparesis, but these symptoms are nonspecific for gastroparesis as are early satiety and postprandial fullness. Symptom tools like the Gastroparesis Cardinal Symptom Index (GCSI) have frequently been used in clinical trials and can be helpful in symptom assessment (Stanghellini and Tack 2014). A second patient questionnaire, the Patient Assessment of Gastrointestinal Symptoms (PAGS), has also been used in studies (Malik et al. 2015; Rentz et al. 2004). Objectively the retention of 10% of a test meal at 4 h measured by scintigraphy is the cardinal objective measure of gastroparesis. The 4 h gastric emptying test uses a ^{99m}Tc sulfur colloid-labeled egg sandwich as the test meal (Shin and Camilleri 2013; Camilleri et al. 2013; Abell et al. 2008). A wireless motility capsule (WMC) that measures pH, pressure, and temperature can also be used to assess gastric emptying as measured by the acidic gastric residence time of the capsule. There is a high correlation between the WMC capsule test and scintigraphy gastric emptying study. A third test, the ^{13}C-octanoate breath test, has also been approved for the same purpose by the FDA (Saad 2016; Nguyen et al. 2013).

3 Pathophysiology

3.1 Pyloric Compliance and Motility

Endoscopic functional luminal imaging probe investigations of pyloric function found reduced pyloric compliance and narrowed luminal diameter in a subset of patients with gastroparesis, early satiety, and postprandial fullness (Malik et al. 2015; McMahon et al. 2005). In another study, reduced fasting pyloric compliance was associated with objective gastroparesis, gastroparesis-related symptoms, and reduced quality of life (Gourcerol et al. 2015). In a third study, increased pyloric pressures measured by endoscopic functional luminal imaging probes were associated with impaired gastric emptying. This occurred in 42% of those with delayed gastric emptying and was associated with nausea and vomiting (Snape et al. 2016). The findings of reduced pylori compliance and increased pressures have led to the use of such modalities as intrapyloric injections of botulinum toxin, pyloric stenting, pyloroplasty, and other procedures directed toward the pylorus as a way of improving gastroparesis (Friedenberg et al. 2008; Arts et al. 2006; Clarke and Snape 2015; Khashab et al. 2013, 2015, 2017).

3.2 Impaired Duodenal Contractility

Impaired duodenal contractility rather than impaired antral contractility has been associated with gastroparesis measured by the GCSI (Barshop et al. 2015).

3.3 Widespread Neuropathy

Diabetic gastroparesis is associated with widespread autonomic and sensory neuropathy as measured by reduced heart rate variability, visceral hypersensitivity, and increased incidence of

sensory neuropathy. Unfortunately, though glycemic control is recommended by guidelines, tight glycemic control does not improve gastroparesis. Diabetics with retinopathy have a greater prevalence of gastroparesis (Softeland et al. 2014; Bharucha 2015a, b; Bharucha et al. 2015a, b). Symptoms normally associated with gastroparesis (nausea, vomiting, early satiety, and postprandial fullness) can occur in diabetics with normal gastric emptying. Unfortunately, the four symptoms which cluster in gastroparesis do not differentiate diabetics with and without gastroparesis (Bharucha 2015a, b; Bharucha et al. 2015a, b).

3.4 Loss of Interstitial Cells of Cajal

Interstitial cells of Cajal (ICC) are the pacemaker cells of the gastrointestinal tract and are lost in gastroparesis. A subset of macrophages (M2) act as "protectors" of ICC. Loss of gastric M2 cells is associated with loss of ICC and gastroparesis (Bernard et al. 2014; Choi et al. 2010).

3.5 Malignancy-Related Gastroparesis

Now, we do not know the prevalence of gastroparesis in patients with cancer; it is likely that the cause is heterogeneous. Reports of gastroparesis in patients with cancer are largely based on individual patient case reports or case series. Malignancy-associated gastroparesis can present clinically at initial diagnosis and is often associated with nausea, vomiting, and nutritional failure (Vaidya et al. 2014; Kelly et al. 2014). The differential diagnosis includes the possibility of pre-existing gastroparesis particularly in a diabetic who has developed pancreatic cancer. Individuals may have pre-existing idiopathic gastroparesis made worse or clinically apparent with the onset of cancer or with the development of chemotherapy neuropathy, surgical complication from an upper abdominal procedure, or the use of opioids. Post-viral infections cause gastroparesis in the immunosuppressed or from graft-versus-host disease. Paraneoplastic polyneuropathies are associated with gastroparesis (Pardi et al. 2002). Cancers can directly invade the myenteric plexus or mesentery, interrupting connections between extrinsic and intrinsic enteric neurons, causing a "functional bowel obstruction." A celiac block and abdominal radiation are known causes of gastroparesis (Iftikhar and Loftus 1998; Layer et al. 1986). Calcium channel blockers for co-morbid hypertension or arrhythmias cause gastroparesis independent of the cancer and can be mistaken as malignancy-related gastroparesis. Tricyclic antidepressants used as adjuvant analgesics delay gastric emptying. Amyloid infiltrates visceral smooth muscle or enteric neurons resulting in symptoms of gastroparesis and weight loss (Lee et al. 2016). Pancreatic cancer which invades the duodenum may present as idiopathic gastroparesis (Cengia et al. 2016). Loss of mesenteric artery blood flow by tumor compression or invasion causes ischemic gastroparesis (Liberski et al. 1990; Meneghini et al. 2008). Gastroparesis is reported after bone marrow transplant and may be the cause of prolonged nausea and vomiting after transplant (Johansson et al. 2003; Eagle et al. 2001). Individuals with intra-abdominal cancers which invade or cause ischemia to the celiac plexus may cause gastroparesis. Individuals with extra-abdominal cancers (most frequently breast, Hodgkin's lymphoma, and small cell cancers) are more likely to have paraneoplastic gastroparesis than individuals with intra-abdominal cancers (Pardi et al. 2002; Hejazi et al. 2009; Nguyen-tat et al. 2008; Donthireddy et al. 2007; Moskovitz and Robb 2002; Lucchinetti et al. 1998; Lautenbach and Lichtenstein 1995).

Management of gastroparesis associated with cancer is largely based on small case series and based on little to no evidence from randomized trials. There are no published guidelines established for managing gastroparesis associated with cancer but there are recommendations based on expert opinion. In regard to management, hydration and electrolyte replacement should be done initially (Leung and Silverman 2009;

Donthireddy et al. 2007). Gastric emptying scintigraphy is rarely done in individuals with cancer nausea, vomiting, early satiety, or postprandial fullness. Most recommend excluding gastric outlet obstruction. Dietary changes as recommended for non-malignant gastroparesis have not been tested in individuals with malignancy-associated gastroparesis (Shone et al. 1995). Metoclopramide has the greatest evidence base for treating nausea and vomiting in advanced cancer and is noted to improve tumor-associated gastroparesis (Davis and Hallerberg 2010; Shivshanker et al. 1983). A trial of metoclopramide should be over 2 days. Alternative prokinetics such as low-dose erythromycin and domperidone, though not reported in the management of malignancy-related gastroparesis, can be tried. If prokinetics fail to improve nausea and vomiting, an alternative antiemetic, either haloperidol or a phenothiazine, should be empirically tried. If this fails, then an NG tube is placed, and if the patient's symptoms respond, then a percutaneous endoscopic gastrostomy (PEG) with a jejunal feeding tube (PEG-J) is placed (Watson et al. 1997). Alternatively, if the patient has a short expected survival and is not expected to benefit from palliative feeding due to a short expected survival, a PEG external drainage with or without hydration may be offered.

4 Management of Non-malignant Gastroparesis

4.1 Diet

Low-fat liquid diets are better tolerated than high-fat liquid, low-fat solid, and high-fat solid diets (Homko et al. 2015). Small-sized particles are better tolerated than roughage (Olausson et al. 2014). There are foods which are poorly tolerated: orange juice, fried chicken, cabbage, oranges, pizza, sausage, peppers, onions, tomato juice, lettuce, coffee, salsa, broccoli, bacon, and roast beef. Better tolerated foods include ginger, gluten-free diet, tea, white potatoes, sweet potatoes, pretzels, white fish, clear soups, salmon, popsicles, white rice, and applesauce (Wytiaz et al. 2015).

4.2 Prokinetics

Prokinetic drugs enhance and coordinate gastrointestinal motility improving transit. It is assumed that the symptoms associated with dysmotility and that with improved smooth muscle contraction and coordination, symptoms will improve. However, as mentioned above, there is a poor correlation between dysmotility and the symptoms of gastroparesis, so it is an assumption that remains unproven (Janssen et al. 2013). Prokinetics increase acetylcholine release from primary motor neurons in the myenteric plexus which increases muscular contraction. Other transmitters which improve motility and are targeted by different classes of prokinetics include substance P and its receptor, motilin and its receptor, and ghrelin and its receptor. Serotonin improves motility through 5HT4 (5-hydroxytryptamine-4) receptors (Acosta and Camilleri 2015). The pathophysiology of gastroparesis includes not only gastric dysmotility but other abnormalities such as impaired pyloric sphincter, reduced capacitance, duodenal dysmotility, as well as other gastrointestinal hormones which adversely influence motility (cholecystokinin and peptide YY) (Kumar et al. 2008; Khoo et al. 2010). It is likely that prokinetics will only benefit a subset of patients with gastroparesis because gastric dysmotility accounts for only a subtype of gastroparesis (Stanghellini and Tack 2014; Malik et al. 2015; Gourcerol et al. 2015; Barshop et al. 2015; Stanghellini et al. 1997).

4.3 Metoclopramide

Metoclopramide is the only prokinetic drug approved by the US Federal Drug Administration (FDA) for treatment of gastroparesis which can also be given for greater than 12 weeks. Metoclopramide blocks dopamine D2 receptors and is an agonist for 5HT4 receptors (Albibi and McCallum 1983). At high doses (>120 mg) metoclopramide blocks 5HT3 receptors (Marty et al. 1990; Sanger and Alpers 2008). D2

receptors in the area postrema may be one of the mechanisms for nausea associated with hypomotility. It is likely that activation of peripheral 5HT4 receptors is the primary mechanism behind metoclopramide's prokinetic benefits (Broad et al. 2014; Sanger 2014a). Multiple studies with the primary objective of gastric emptying have demonstrated metoclopramide benefits in improving gastric emptying. Open label studies demonstrated symptom responses (Shivshanker et al. 1983; Lata and Pigarelli 2003; Seibert et al. 1989; Trapnell et al. 1986; Ricci et al. 1985; Snape et al. 1982; Muls and Lamberigts 1981; Malagelada et al. 1980; Hartong et al. 1977; Longstreth et al. 1977). A recent randomized trial which compared oral and intranasal metoclopramide with placebo found that symptoms improved in all three trial arms as measured by the GCSI (Parkman et al. 2015). This study illustrates that symptoms related to gastroparesis are subject to placebo responses. However, in this trial, women responded better to metoclopramide than placebo, indicating that benefits may be gender related. Metoclopramide can be given orally, intranasally, per rectum, subcutaneously, or intravenously. Initial oral doses are 5 mg three times daily with titration up to 40 mg per day (Camilleri et al. 2013). Doses are usually given prior to meals and at bedtime. Metoclopramide elixir may be better tolerated than the tablets. Side effects include involuntary movements, akathisia, dystonia, and tardive dyskinesia. Side effects are more frequent in women, children, and at higher doses and are less prevalent in those individuals getting continuous infusion of metoclopramide rather than oral bolus doses (Cavero-Redondo et al. 2015; Bateman et al. 1985). Metoclopramide is metabolized through CYP2D6 and has potential drug interactions as it reversibly inhibits CYP2D6. Metoclopramide has been associated with a prolonged QTc interval (Livezey et al. 2014; Sarganas et al. 2014). Doses will need to be reduced in renal and hepatic failure (Siddique et al. 2009; Lehmann et al. 1985; Albani et al. 1991).

5 Motilin Agonists

5.1 Erythromycin

Motilin agonists directly activate smooth muscle and interact to a lesser extent with enteric neurons. At low doses (50–100 mg), erythromycin enhances cholinergic activity and facilitates smooth muscle contraction. At high doses (200 mg), erythromycin causes non-propagating smooth muscle contractions and atropine-resistant non-cholinergic dependent segmental contractions (Broad and Sanger 2013; Broad et al. 2012). Low-dose erythromycin does not cause tachyphylaxis or down-regulate motilin receptors and is less likely to cause nausea or vomiting than high doses (Broad et al. 2012; Sanger 2012, 2014b; Sanger et al. 2013a; Cuomo et al. 2006). An open label study found that symptoms improved in 83% of those who received erythromycin 50–100 mg four times a day (Dhir and Richter 2004). Clinical responses appeared to be sustained over weeks. In a systematic review of oral erythromycin, five studies were reviewed whose primary outcome was gastric emptying with a demonstrated improvement in 43% (23/60 patients) and a symptom response in 48% (11/23 patients). Studies were methodologically flawed, participants were few, and there were significant risks of bias in these studies (Maganti et al. 2003). Recommended doses range from 3 mg/kg IV every 8 h to 50–100 mg orally before meals and at bedtime (Camilleri et al. 2013; Janssens et al. 1990; Tonelli et al. 2009). Erythromycin is an inhibitor of CYP3A4 and thus has significant risks for drug interactions. Erythromycin also prolongs the QTc interval which can lead to arrhythmias (Pal and Mitra 2006; Freeman and Platt 1997).

5.2 Azithromycin

Azithromycin has been compared with erythromycin during small bowel manometry in 30 patients with gastroparesis. Doses of erythromycin were

250 mg IV and azithromycin 250–500 mg. Azithromycin at these doses had similar improvement in motility. The promotility effects of azithromycin lasted longer than erythromycin. Two observational studies found that azithromycin had clinical benefits equivalent to erythromycin with fewer drug interactions and less effect on QTc intervals. However, there are no randomized trials comparing the two macrolides (Potter and Snider 2013; Larson et al. 2010; Moshiree et al. 2010).

5.3 GSK962040 (Camicinal)

Camicinal is a motilin agonist which is not a macrolide. It does not appear to produce tachyphylaxis. Camicinal improves gastric emptying in type 1 diabetics and accelerates gastric emptying in normal volunteers. In a phase II trial, camicinal improved diabetic gastroparesis (Chapman et al. 2016; Hellstrom et al. 2016; Hobson et al. 2015; Barshop and Kuo 2015). In a randomized trial involving ventilated patients who were intolerant of gastrointestinal feeding, 50–75 mg of camicinal improved gastric emptying measured by the ^{13}C-octanoate breath test (117 vs. 76 min), increased glucose absorption, and reduced gastric residual volumes (Chapman et al. 2016).

6 Dopamine Blockers

6.1 Domperidone

Domperidone is a D2 receptor antagonist which does not cross into the CNS and thus has limited extrapyramidal side effects. It is not licensed in the United States but can be made available through a compassionate clearance under the FDA. Domperidone chemical structure is based on butyrophenones. It has a low oral bioavailability (15%) but a high affinity for gastrointestinal D2 receptors (Van Nueten et al. 1978). Domperidone improves antroduodenal coordination via interactions with specific dopamine receptors located on nervous structures in the gut wall (Schuurkes and Van Nueten 1984). Dopamine-induced gastric relaxation is prevented by dopamine antagonists. D2 antagonists exert gastric stimulatory effects and improve gastroduodenal coordination (Schuurkes and Van Nueten 1984; Van Nueten and Schuurkes 1984; Schuurkes et al. 1985). In a study involving 125 patients, domperidone 10 mg was given 3–4 times daily in a group of patients, most of whom had idiopathic gastroparesis. Assessment was done 2–3 months after initiating therapy. Forty-five of the patients have had moderate improvement in their symptoms as measured by the GPGAS. Nausea and vomiting as well as postprandial fullness improved. Side effects included headache, tachycardia, palpitations, and diarrhea (Schey et al. 2016). Domperidone has potential drug interactions through CYP3A4 and can prolong the QTc which can lead to arrhythmias (Youssef et al. 2015; Templeton et al. 2016; Ioannou et al. 2016).

7 Serotonin Receptor Agonists

7.1 Prucalopride

Prucalopride is a highly selective 5HT4 agonist which does not have the cardiovascular risks of cisapride (Briejer et al. 2001). Prucalopride is licensed outside of the United States for chronic idiopathic constipation. Preliminary evidence suggests prucalopride could improve symptoms of gastroparesis and gastric emptying. Prucalopride at low drug levels ($3 \times 10(-7)$ M) enhances the electrically evoked release of acetylcholine in gastric circular muscle (Leclere and Lefebvre 2002). In normal healthy individuals, prucalopride accelerates gastric emptying and reduces gastric residual volumes measured at 120 min (Kessing et al. 2014). Prucalopride improves nausea, vomiting, and early satiety relative to placebo in patients with idiopathic gastroparesis. A large phase III study is presently open to accrual. The ability of prucalopride to block cardiac repolarization is 20-fold less than

that of cisapride and hence clinically safe (Potet et al. 2001). However, prucalopride has poorly defined pharmacokinetics. Prucalopride may reduce the efficacy of oral contraceptives. Miscarriages have been reported in clinical trials. Prucalopride should not be taken during pregnancy (Prucalopride 2011).

7.2 Ghrelin Analogs

Motilin and ghrelin receptors are members of the same subfamily of G-protein-coupled receptors. In fact, there is a 52% amino acid identity between the two receptors. However, the receptors do not bind the same ligands. Ligands are in different areas of the gastrointestinal tract. Ghrelin is located within gastric oxyntic cells, whereas motilin is located within antral and duodenal villous epithelial cells (Sanger 2013). Ghrelin stimulates gastric motility and appetite mostly via vagus-dependent pathways. Ghrelin does not appear to improve gastric emptying or symptoms and neither does the ghrelin analog TZP-102 (Sanger et al. 2013b; McCallum et al. 2013). Relamorelin is a potent ghrelin receptor agonist which is a pentapeptide amide. It has a half-life of 4.5 h and clinically is injected twice daily. In a randomized phase II controlled trial, twice daily relamorelin 10 mcg accelerated gastric emptying and reduced vomiting frequency and severity relative to placebo in adults with diabetic gastroparesis. There was also improvement in nausea, bloating, and early satiety as a composite outcome compared with placebo (Lembo et al. 2016). Side effects were like those of placebo. There were no QTc interval changes noted. Requirements of injections twice daily are a drawback, perhaps less so for diabetics on insulin.

8 Symptom Management

8.1 Granisetron

Transdermal granisetron has been used in a prospective observational study involving 51 patients with gastroparesis. The study was 2 weeks in duration and used the GCSI to measure the primary outcome. Most the participants had idiopathic gastroparesis. Thirty-one (76%) had improvement in nausea and vomiting. Early satiety, postprandial fullness, loss of appetite, and upper abdominal pain also improved. Side effects included erythema at the patch site, pruritus, and constipation (Midani and Parkman 2016). There are no randomized trials which compare granisetron to other antiemetics.

9 Antidepressants

9.1 Tricyclic Antidepressants

Nortriptyline has been compared to placebo in a randomized trial (Parkman et al. 2013). The outcomes were not better than placebo. A randomized comparison between placebo, amitriptyline, and escitalopram over 10 weeks found that amitriptyline improved ulcer-like pain symptoms associated with gastroparesis. However, there was no improvement in dysmotility-like symptoms (Talley et al. 2015).

9.2 Mirtazapine

Mirtazapine is an indirect 5HT1a receptor agonist; an inverse agonist at 5HT2c; and an antagonist to histamine (H1), 5HT2, 5HT3, and alpha-2 adrenergic receptors. Mirtazapine improves gastric emptying in diabetics but does not accelerate gastric emptying in normal individuals (Kim et al. 2006; Yin et al. 2014; Gooden and Takahashi 2013; Choung et al. 2008; Tack et al. 2016). Mirtazapine has been effective in improving symptoms associated with functional dyspepsia and weight loss. However, there are no randomized trials of mirtazapine in patients with gastroparesis. Mirtazapine has minimal inhibitory effects on CYP1A2, CYP3A4, and CYP2D6 in vitro. Little is known about its interactions with other drugs (Owen and Nemeroff 1998). Mirtazapine has a significantly lower risk of cardiovascular adverse events and drug reactions than other antidepressants (Spindelegger et al. 2014).

10 Complementary Approaches

10.1 Acupuncture

In annulus, acupuncture improves gastric emptying through stimulation of the vagus nerve (Ouyang et al. 2002). Acupuncture increased the regularity of slow waves in the stomach and improved gastric arrhythmias. Acupuncture points include pericardium 6 (Pc6), stomach 36 (ST36), and stomach 44(ST44) (Lin et al. 1997). Electroacupuncture (EAP) and transcutaneous electroacupuncture (TEAP) have frequently been used in various studies. In a short randomized controlled trial of 2 weeks, EAP improved symptoms in a group of patients with diabetic gastroparesis (Wang 2004). In the second randomized trial involving patients in critical care who had delayed gastric emptying, acupuncture was superior to prokinetic in improving gastric emptying (Pfab et al. 2011). TEAP has been compare to sham TEAP in a group of patients with functional dyspepsia. TEAP improved gastric accommodation and the power of gastric slow waves relative to sham (Xu et al. 2015). A large study of 712 patients compared a prokinetic agent (itopride), placebo, and acupuncture in patients with functional dyspepsia. Acupuncture improved symptoms and quality of life than either placebo or the prokinetic drug (Ma et al. 2012). The advantage of TEAP is that patients can be taught self-administration and apply TEAP at home. TEAP is a low risk procedure but does require skill.

10.2 *Zingiber officinale* (Ginger)

Ginger reduces nausea associated with pregnancy, in the postoperative setting, and nausea associated with motion sickness. It has also been used to reduced chemotherapy-related nausea with mixed results (Ding et al. 2013; Giacosa et al. 2015; Lete and Allue 2016; Montazeri et al. 2013; Palatty et al. 2013; Ryan et al. 2012; Thomson et al. 2014). Ginger blocks serotonin receptors as the proposed mechanism of its antiemetic action. Ginger in a dose of 1200 mg as a single dose has been demonstrated to accelerate gastric emptying in patients with functional dyspepsia (Hu et al. 2011; Wu et al. 2008; Lazzini et al. 2016). However, there are no randomized trials of ginger in the management of gastroparesis (Leung and Silverman 2009).

11 Non-pharmacological Therapies

11.1 Gastric Electrical Stimulation

Transcutaneous and endoscopy placed leads with gastric electrical stimulation (GES) has been used as a means of improving gastroparesis. In non-randomized studies, gastric stimulation has reduced nausea and vomiting and total symptom burden (Shah et al. 2017). In a systematic review, there were five studies reviewed with randomly allocated patients to periods with or without GES. Total symptom severity scores did not differ when the electrodes were on or off (0.17 [95% confidence interval: −0.06 to 0.4]; $P = 0.15$). In 16 open label studies of GES, there was a significant decrease in symptoms (2.68 [2.04–3.32]; $Q = 39.0$; $P < 0.001$) (Levinthal and Bielefeldt 2017). Improvement seen in studies when the current was off suggests that a significant number of responses seen in the open label studies could have been placebo responses. Randomized trials are needed before adopting this approach.

11.2 Procedures Directed at the Pylorus

Pyloromyotomy, pyloroplasty, pyloric stenting, botulinum toxin injections into the pylorus, and per-oral endoscopic antropyloromyotomy have been reported to improve gastroparesis in case series (Snape et al. 2016; Clarke and Snape 2015; Khashab et al. 2015; Gonzalez et al. 2017; Lebaras and Swanstrom 2016; Mancini et al. 2015; Soares and Swanstrom 2015). These procedures have not been subject to randomized trials and should be considered experimental until

further evidence as to benefits or lack thereof emerges (Camilleri et al. 2013).

12 Percutaneous Endoscopically Placed Gastric Drainage Tube with a Jejunal Feeding Tube Extension (PEG-J)

A PEG-J should be considered in patients who failed to improve with medical management. Nausea and vomiting can improve and patient nutritional failure can be reversed with a PEG-J. It has been suggested that a trial of NG suctioning should be done before placing a PEG-J to see if symptoms do improve. Minor complications from the procedure occur in 57% and serious complications in 13%. Serious complications include gastric perforation, bleeding, infections, wound leakage, hematoma, gastric ulceration, and cellulitis (Table 1).

Table 1 Recommendations for gastroparesis

1	Suspect gastroparesis in anyone with intractable nausea, vomiting, postprandial fullness, early satiety, abdominal pain, and GERD-like symptoms who does not have a gastric outlet obstruction
2	Exclude iatrogenic diseases and medications (opioids, anticholinergics, cyclosporine, cannabinoids, GIP-1 analogs)
3	Exclude thyroid disease; control hyperglycemia in a diabetic (blood glucose <275 mg/dl)
4	If significant weight and/or reduced performance score, consider an underlying malignancy and an abdominal CT scan
5	Review previous abdominal surgeries
6	Do a standard 4 h gastric stimulation test
7	Correct fluid deficits and electrolyte abnormalities
8	Diet should be low fat and small particle. Certain foods may be better tolerated than others
9	Metoclopramide is the drug of choice; start with 5–10 mg before meals and at bedtime. If in the hospital or unable to take orally, start metoclopramide at 40 mg/d IV in divided doses or as a continuous infusion
10	Alternative drug therapy includes domperidone at 5–10 mg before meals and at bedtime or erythromycin 50–100 mg orally before meals and at bedtime
11	Symptom medications include granisetron, mirtazapine, amitriptyline (depending on the symptom cluster) and ginger
12	Butyrophenones (haloperidol), phenothiazines, and atypical antipsychotics (olanzapine) could be used for nausea but should not be combined with metoclopramide. Olanzapine may be tolerated by individuals who have extrapyramidal adverse effects from metoclopramide or haloperidol
13	Gastric electrical stimulation and acupuncture could be considered in those not responding to medical management
14	If symptoms are intractable, consider a PEG-J tube

13 Summary

Gastroparesis is a common disorder in the population. The frequency of gastroparesis in cancer is not known. Malignancy-associated gastroparesis likely has a several etiologies which will likely influence responses to therapy. Management of malignancy-associated gastroparesis is guided by therapies developed in populations with non-cancer gastroparesis and the meager evidence derived from published literature. Future studies are needed to clarify the incidence and management of malignancy-associated gastroparesis.

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Cachexia/Anorexia and Feeding Difficulties

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_16

Abstract

Symptoms related to anorexia (loss of appetite), cachexia (muscle loss and wasting) and dysphagia (reduced ability to eat) are devastating for a person with a palliative illness and their families. They are common, especially as illness advances, and occur in both malignant and non-malignant illness. Not only do the conditions serve as a visual reminder of the chronic disease, they also affect the psychology governing the social aspects of eating. For many years, anorexia, cachexia and dysphagia as distinct conditions were overlooked by healthcare professionals and researchers as the focus was on the primary chronic illness instead (Fearon et al., Understanding the mechanisms and treatment options in cancer cachexia. Nat Rev Clin Oncol 10(2):90–99, 2013). Clinical research, particularly in the field of cancer cachexia, has gained new insight in the pathogenesis and management of the conditions including anorexia and dysphagia. This chapter will define the conditions and outline the epidemiology, etiology and pathophysiology and assessment and management of these symptoms.

1 Introduction

Cachexia is a complex metabolic syndrome characterized by the profound reduction of lean body mass (LBM) and adipose tissue and involuntary loss of more than 10% of premorbid weight and is associated with anorexia (loss of appetite), asthenia (physical weakness) and changes in body image (Del Fabbro et al. 2006). Cachexia comprises a complex interplay of inflammatory and metabolic imbalances, compromised immune system responses (with increased susceptibility to infections), and associated changes in glucose, lipid and protein metabolism (Macciò et al. 2012). Cachexia may occur in up to 80% of patients with advanced cancer and is a marker for poor prognosis (decreased adherence to treatment, lengthy hospital stays and increased mortality) and the main cause of death in 20% of patients (Inui 2002). Cancer cachexia is more common in patients with solid tumors, in children and in elderly patients. Cachexia is also common in acquired immune deficiency syndrome (AIDS), chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF) and other chronic illnesses, such as dementia, tuberculosis, malaria, chronic kidney disease, liver disease and rheumatoid arthritis (Del Fabbro et al. 2006). "Weight gain" may come in the form of ascites or edema and may mask the progression of cachexia, and so can obesity, which may have underlying muscle wastage (Fearon et al. 2013). The management of major contributors to this syndrome, such as chronic nausea, constipation, early satiety, taste alteration, anemia, dyspnea, deconditioning and depression, may result in significant improvement. Megestrol or corticosteroids are current pharmacological treatments which predominantly stimulate appetite. Nutritional supplementation and appetite stimulation alone cannot overcome muscle mass wasting, and this makes cachexia difficult to treat and reverse (Del Fabbro et al. 2006). Cachexia is a significant burden to both the patient and families. Along with helplessness and fear, frustration sets in with some family members resorting to force-feeding their loved ones, hoping that the food would give them the energy to fight the cancer (Fearon et al. 2013). Dysphagia issues, which are common in head and neck cancer patients, include choking, dehydration, malnutrition, aspiration and a resulting loss of eating (Raber-Durlacher et al. 2012). Any treatment will require careful assessment and alternatives to oral administration. This chapter will use the latest literature to provide a comprehensive summary of

anorexia, cachexia and feeding difficulties that are experienced by cancer and noncancer populations.

2 Anorexia-Cachexia Syndrome

2.1 Definitions

Anorexia is clinically defined as the reduction or loss of appetite (Muscaritoli et al. 2010). There may be associated symptoms such as nausea and vomiting, early satiety and changes in taste and smell (Muscaritoli et al. 2010). Anorexia can be part of the anorexia-cachexia syndrome, but there are multifactorial causes for appetite and appetite-related problems.

Sarcopenia is characterized by loss of muscle mass and strength (Muscaritoli et al. 2010).

Cachexia is characterized by severe loss of body weight, fat and muscle and increased protein catabolism. The causes of cachexia are multifactorial and include the underlying disease, disease-related metabolic abnormalities and reduced availability of nutrients (Muscaritoli et al. 2010). A staging classification for cancer cachexia has been developed (pre-cachexia, cachexia, refractory cachexia) (Box 1) (Fearon et al. 2011).

Box 1

Pre-cachexia

- Anorexia
- Impaired glucose tolerance
- Weight loss ≤5%

Cachexia

- Weight loss >5% OR Body Mass Index (BMI) <20 and weight loss >2% OR sarcopenia and weight loss >2%
- Often reduced food intake and systemic inflammation

Refractory cachexia

- Low performance status (WHO score 3 or 4)

Box 1 (continued)

- Life expectancy <3 months
- Rapidly progressive cancer unresponsive to anticancer therapy

Source: Fearon et al. (2011)

2.2 Epidemiology

The occurrence of cachexia is not only limited to cancer but also found in other terminal conditions such as chronic heart and kidney disease, chronic obstructive pulmonary disease (COPD), neurological diseases, systemic inflammatory conditions and HIV/AIDS. It is estimated that around 0.5–1% of the global population suffers from cachexia (Haehling et al. 2016).

Table 1 summarizes the prevalence of cachexia in several chronic diseases based on US, Japanese

Table 1 Prevalence of cachexia in several chronic diseases based on US, European and Japanese populations[a] (Japan figures in brackets)[b]

Disease	Prevalence in population	Prevalence in the disease	1-year mortality rate (%)
Cancer	0.5	28–57 (advanced) (45.6) 50–80 (several types)	20–80
Chronic heart disease	2.0	13.6 (33) 16–42[c]	20–40
Chronic renal disease	0.1	30–60	20
COPD	3.5	27–35 (31–41)	15–25
Rheumatoid arthritis	0.8	18–67[c]	5
HIV/AIDs		10–35[c]	

COPD chronic obstructive pulmonary disease, *HIV/AIDS* human immunodeficiency virus/acquired immunodeficiency syndrome

[a]Haehling et al. (2016)

[b]Konishi et al. (2016)

[c]Farkas et al. (2013)

and European populations. Unfortunately, data outside these industrialized countries is scarce. Depending on the cachexia criteria used, the reported prevalence may vary (Haehling et al. 2016) as seen in the Japanese figures (in brackets below).

Due to changes in physiology of oral intake endured by head and neck cancer patients, a study showed a 42% prevalence of cachexia in newly diagnosed patients (Jager-Wittenaar et al. 2017). In advanced head and neck squamous cell carcinoma, cancer cachexia was identified in 6.1% and 18.7% of the enrolled patients at pretreatment and 12 months post treatment, respectively, with a higher probability of cancer-specific death, noncancerous death and overall death ($p < 0.05$) (Kwon et al. 2017). In Irish oncology outpatients, cachexia was highest in hepatobiliary (65.2%) and upper gastrointestinal tumors (64.3%) and was associated with poorer performance status, adverse global quality of life (QoL) ($P = 0.003$), poor appetite ($P < 0.001$) and nausea and vomiting ($P < 0.001$) (Cushen et al. 2015). In a systematic review of palliative care-related problems, anorexia was found to be prevalent (50% or more) in both cancer and noncancer patients (Moens et al. 2014). In patients who survived to the final phase of dementia, it was found that 53.2% were more likely to die from cachexia or dehydration (Koopmans et al. 2007). Although there have been improvements in antiretroviral therapies of HIV, wasting and anorexia continues to be a problem (Keithley and Swanson 2013).

Recent findings in COPD patients have discovered gene variations in the phenotypes of two muscle-wasting genes associated with cachexia (McDonald et al. 2014).

The burden of cachexia influences many facets of society including morbidity and mortality, impaired quality of life, and healthcare costs. In the USA, cachexia included an older cohort (average age 67.85 years), longer hospital duration (around double), loss of function in the "major" category (52.6%), and increased economic costs (around 66%), compared to non-cachexia patients (Arthur et al. 2014).

2.3 Clinical Assessment

Clinical assessment should evaluate appetite and related symptoms (changes in taste (hypogeusia) and smell (hyposmia), early satiety, nausea), food intake (including protein and calories), muscle mass and strength, factors promoting catabolism, and performance status (Fearon et al. 2011). Thus, anorexia may be diagnosed earlier than cachexia if the patient reports cessation of eating due to early satiety, nausea, and bloating caused by gastrointestinal delays (Davis et al. 2004). The effects of cachexia and its meaning from the patient's perspective should also be captured, and so the impact on their caregivers (Fearon et al. 2011). This might include the inability to undertake activities of daily living, understanding it as a flag of poor prognosis, feeling under pressure to eat, guilt, and altered mood. Families may constantly urge the patient to eat and express frustration when the person does not want to eat anything (Fearon et al. 2011).

The consideration of reversible causes, such as mucositis, unrelieved symptoms such as pain and breathlessness, constipation, and difficulty in sourcing meals, should be considered (Fearon et al. 2011). Referral to a dietician for a detailed dietary assessment may be appropriate.

Weight, weight loss history, current height and weight (to calculate BMI) and previous stable weight (to calculate percentage weight loss) are required (Fearon et al. 2011).

Systematic inflammation may be present and contribute to increased catabolism and may be evaluated by serum C-reactive protein (Fearon et al. 2011). Indirect indicators of a hypercatabolic state are the rate of progression of the cancer itself and/or non-responsiveness to anticancer therapies (Fearon et al. 2011).

The assessment of muscle strength and mass is advocated, and a range of methods are available, and consensus about which can be routinely used in clinical practice has not been reached (Fearon et al. 2011). Upper limb hand grip strength is useful to assess muscle strength, and muscle mass by cross-sectional imaging (CT, magnetic resonance imaging (MRI)), dual energy X-ray imaging (DEXA), and anthropometry (mid-arm

Table 2 Causes of anorexia

Peripheral *Tumor-producing*	Peripheral *Chemotherapy-producing*	Cytokine release	Central
Substances that alter food intake, e.g., increased lactate, tryptophan, or parathormone-related peptide Alterations in nutrients resulting in anorexia, e.g., low zinc levels result in hypogeusia Decreased ghrelin	Altered taste perception and causing nausea, vomiting, mucositis, abdominal cramping, bleeding, and ileus Dysgeusia	Increased: IL-1 IL-6 TNFα	Depression Pain Alterations in central neurotransmitters (e.g., serotonin and corticotropin-releasing factor (CRF)

muscle area) and bioimpedance (Fearon et al. 2011).

2.4 Pathophysiology

2.4.1 Anorexia

Anorexia results from the failure of appetite signals and much of this is governed by the hypothalamus. In animals, these are proposed to be caused by the reduced expression and release of ghrelin by interleukin (IL)-1 and reduction in neuropeptide Y expression and signaling (Davis et al. 2004). A recent study has shown that plasma ghrelin levels were associated with anorexia, but not cachexia, in patients with non-small cell lung cancer (NSCLC) (Blauwhoff-Buskermolen et al. 2017). The causes of anorexia can be classified as peripheral (due to the tumor (including cytokine release) and chemotherapy) and central causes. In humans, these causes are summarized in Table 2. Other proposed pathways include via neuronal nitric oxide synthase (nNOS), increased serotonin by IL-1, increased ciliary neurotropic factor, increased activity of anorexigenic neuropeptides (corticotropin-releasing factor (CRF) and melanocortin) and dynamin (Ezeoke and Morley 2015).

2.5 Cachexia

The pathophysiology of cancer cachexia is multifactorial consisting of heightened inflammatory responses, oxidative stress, negative protein and energy balance, hormonal imbalances, altered lipid and carbohydrate metabolism and gastrointestinal function, contributing to muscle wasting and fatigue (Kaasa et al. 2015). A summary of each contributing factor is given below and is shown in Fig. 1.

Inflammation*:* The inability of the immune system to definitively counteract tumor growth results in chronic cytokine activity (by both the host and tumor) with deleterious effects on cell metabolism, body composition, nutritional status and immune system efficiency. A complex interplay of proinflammatory cytokines including interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)-α, which are produced both by the activated immune system and by tumor cells, is implicated in the pathogenesis of cancer-related anorexia and cachexia syndrome and associated metabolic changes (Macciò et al. 2012).

TNF-α increases gluconeogenesis (generation of glucose from noncarbohydrate sources), lipolysis (breakdown of lipids and involves hydrolysis of triglycerides into glycerol and free fatty acids) and proteolysis (breakdown of proteins into smaller polypeptides or amino acids); decreases the synthesis of glycogen, lipids and proteins; induces the formation of IL-1; and stimulates the expression of uncoupling proteins (UCP) 2 and UCP 3 in cachectic skeletal muscle. The levels of IL-6 were observed to be higher in patients with cachexia (Aoyagi et al. 2015). C-reactive protein (CRP, prognostic combined with decreased plasma albumin) positively correlated with weight loss, the occurrence of cachexia, and recurrence in advanced cancer (Suzuki et al. 2013). STAT3 activation (implicated in muscle wasting) and fibrinogen are increased (Fearon et al. 2013). Elevated acute-phase protein response (APPR), which is correlated to elevated REE and reduced

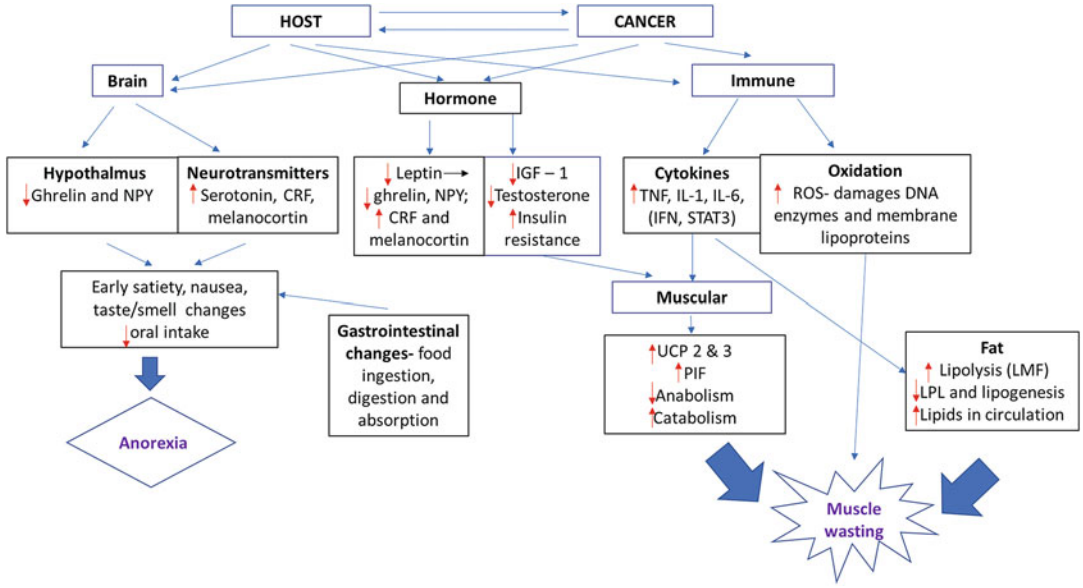

Fig. 1 Cancer-related cachexia mechanisms. *CRF* corticotropin-releasing factor, *IFN* interferon, *IGF* insulin growth factor, *IL* interleukin, *LMF* lipid-mobilizing factor, *LPL* lipoprotein lipase, *NPY* neuropeptide Y, *PIF* proteolysis-inducing factor, *ROS* reactive oxygen species, *TNF* tumor necrosis factor, *UCP* uncoupling proteins (Macciò et al. 2012; Aoyagi et al. 2015; Suzuki et al. 2013; Fearon et al. 2013; Inui 2002; Del Fabbro et al. 2006)

energy intake, has been seen in 50% of patients with solid epithelial cancers (Suzuki et al. 2013). Tumor-derived factors such as proteolysis-inducing factors and the recently discovered myostatin (which is upregulated) also play a central role in the pathogenesis of muscle wasting, through the activation of the ubiquitin-proteasome proteolytic pathway (Macciò et al. 2012).

Oxidative stress is characterized by increased levels of ROS due to the increased activity of the immune system. This damages DNA, enzymes and membrane lipoproteins, and its inadequate detoxification leads to muscle wasting (Macciò et al. 2012).

Altered protein metabolism may be influenced by tumor progression, comorbid conditions, old age, physical deconditioning, nutritional deficiency, drugs (especially those that target both tumor pathways and muscle protein anabolism), and medical interventions (Fearon et al. 2013). In patients with cachexia, the rate of muscle protein catabolism increases in cachexia, while anabolism of new proteins decreases (especially in times of reduced protein intake), resulting in net protein breakdown and subsequent muscle mass loss. Uncoupling proteins (particularly UCP 2 and UCP 3), which are associated with energy metabolism in skeletal muscle, are upregulated in the cachectic state. The proteins may increase resting energy expenditure (REE) which is also increased, and this is dependent on the tumor (Aoyagi et al. 2015).

The loss of skeletal muscle mass in cachectic cancer patients has been shown to correlate with the presence of a proteolysis-inducing factor (PIF) in the serum that is capable of inducing protein degradation, as well as inhibiting protein synthesis, in isolated skeletal muscle.

Gluconeogenesis, with a depletion of protein and lipid stores, results in weight loss (Macciò et al. 2012).

Hormonal: Starvation or a loss of body fat can lead to a decrease in leptin, a protein hormone marker of nutritional status, whereby food intake exceeds energy expenditure. In cancer cachexia, excessive decrease in leptin by cytokines results in the suppressed production of ghrelin, neuropeptide Y (NPY) and other appetite-stimulating

neuropeptides, and increased activity of anorexigenic neuropeptides such as corticotropin-releasing factor (CRF) and melanocortin. Low concentrations of testosterone and other anabolic hormones are major contributors to cachexia-related wasting of skeletal muscle. Insulin-like growth factor 1 is also down-regulated, which increases protein breakdown and induces muscle wasting via angiotensin II (Suzuki et al. 2013).

Carbohydrate metabolism undergoes changes to sustain the increasing macronutrient demands of the tumor (Inui 2002). Hypoinsulinemia and/or peripheral resistance to insulin results in the inability of the host cells to use newly formed glucose (Macciò et al. 2012).

Altered lipid metabolism includes enhanced lipid mobilization (via lipid mobilization factor: LMF), decreased lipogenesis and decreased activity of lipoprotein lipase (LPL), the enzyme responsible for triglyceride clearance from plasma. Cytokines prevent LPL from removing lipids from circulation for storage (Inui 2002).

Gastrointestinal dysfunction encompassing the mouth and the digestive tract, resulting from the disease or its treatment, may interfere with food ingestion, digestion and absorption (Inui 2002).

Although increased concentrations of cytokines in the plasma, peripheral tissues and central nervous system have been found in cachexia associated with other chronic diseases, there are also other characteristic features that differentiate the diseases (Seelaender and Batista 2014). Table 3 outlines the features, triggers and distinct characteristics of cachexia in other chronic diseases. Due to these differences, there are no common treatment options for anorexia and loss of lean body mass in these diverse and distinct disease states. In syndromes involving either cardiac or renal disease, cachexia may contribute to further damage of the other organ (Cicoira et al. 2011).

2.6 Prevention

Early assessment and routine monitoring of cachexia is vital to prevent or mitigate symptoms. Screening by quality-of-life questionnaires such as Malnutrition Universal Screening Tool (MUST) scores and CT assessment of body composition will identify at-risk patients and allow for prompt interventions in these patients (Cushen et al. 2015).

Malignancy-related cachexia has detrimental effects to physical function, which, in turn, reduces the tolerance of anticancer therapy and subsequently increases mortality. Thus, nutritional support to preserve energy and protein intake before or while concurrently treating the disease is an important factor in the prevention of cachexia and thus the survival of the patient. This was seen in a study of newly diagnosed, treatment naïve cancer patients with cachexia, whereby a patient-tailored nutrition therapy plan maintained body weight and improved survival rate (De Waele et al. 2015).

Through its anti-inflammatory effect, exercise has been shown to be effective at counteracting the muscle catabolism by increasing protein synthesis and reducing protein degradation, thus successfully improving muscle strength, physical function (cardiovascular fitness and decreasing fatigue) and quality of life in patients with non-cancer-related cachexia such as rheumatoid arthritis (Gould et al. 2013). Thus, it is suggested that exercise is included early in the treatment plan for cancer-related cachexia.

One physiological factor that occurs before a clinical diagnosis of cachexia is made is muscle wasting. In a Phase III study using enobosarm, a nonsteroidal selective androgen receptor modulator (SARM), subjects prior to receiving chemotherapy were eligible to apply, allowing the clinical trial to examine both prevention and treatment of the condition (Crawford et al. 2016). Given that the best outcome would be the prevention of muscle wasting, and hence cancer cachexia, future research should focus on both prevention and treatment of this condition.

2.7 Intervention

2.7.1 Nonpharmacological Therapies

To address malnutrition in the cancer patient, it is recommended that the nutritional regime should provide 30–35 kcal/kg/day, 1–1.2 g protein/kg/

Table 3 Characteristics of cachexia in other chronic diseases

	Chronic heart failure (HF) (Loncar et al. 2016)	COPD (Remels et al. 2013)	Chronic renal/kidney disease (CKD) (Laviano et al. 2010)	Chronic liver disease (Plauth and Schütz 2002)	Rheumatoid arthritis (RA) (Roubenoff 2009)
Features	Progressive tissue wasting; bone and fat compartments also affected	Pathological changes in intracellular mechanisms of muscle mass maintenance (i.e., protein and myonuclear turnover)	Leptin as an inflammatory cytokine and influencing appetite, energy homeostasis	Increased hypermetabolism and specific REE; portal hypertension	Loss of body fat-free mass often accompanied by increased fat mass and stable body weight Demonstration of increased metabolic syndrome in patients underlines complex interplay between fat mass, lean mass and insulin resistance
Triggers	Immune (increased circulating levels of proinflammatory cytokines combined with increased or reduced anti-inflammatory mediators), metabolic (reduced circulating testosterone and dehydroepiandrosterone sulfate), and neurohormonal consequences, which induce catabolic and anabolic imbalance. The overall net catabolic dominance provokes systemic tissue wasting Both epinephrine and norepinephrine can cause a catabolic metabolic shift, leading to a graded increase in REE	Oxidative stress, myostatin and inflammation	No renal update of leptin and ghrelin Thus, increased circulating levels	Pro- and anti-inflammatory cytokine-driven hypermetabolism	"Sarcoactive" molecules ((TNF)-α and IL-1β, IL-6, IFN-γ, transforming growth factor-β1 and MyoD), energy expenditure, protein metabolism, physical activity levels and hormones
Effects	Anabolic deficiency induces loss of skeletal muscle mass and function. GH/IGF-1 axis may impact the anabolic/catabolic balance in the wasting syndrome. Adiponectin, an adipokine with multiple metabolic actions, increases both locally and globally with HF severity and is highest in cachectic patients. The overactivation of the ubiquitin proteasome pathway (UPP) in the skeletal muscle has been attributed to increased oxidative stress	Peripheral muscle characterized by a fiber-type shift toward a more type II, glycolytic phenotype and an impaired oxidative capacity (collectively referred to as an impaired oxidative phenotype)	Leptin signaling, through the hypothalamic melanocortin receptors, may play an important role in the pathogenesis of inflammation-associated cachexia in CKD Increased ghrelin reduces appetite/food intake	Elevation of the activity of the adrenergic (e.g., epinephrine and norepinephrine) sympathetic system	Decreased body cell mass (BCM) and increased REE in patients

day, and 30–50% of fat covering the nonprotein calories (Nicolini et al. 2013). Although there is a component of malnutrition in cachexia patients, cachexia cannot be treated by nutrition alone (Konishi et al. 2016). In a systematic review evaluating dietary counseling given to cancer patients, the results showed no improvement in weight or energy balance in the different stages of cachexia (Balstad et al. 2014). This was reiterated in a meta-analysis of nutritional supplementation in COPD patients (Ferreira et al. 2000).

It is suggested that exercise (which can be classified as low-intensity balance training to high-intensity treadmill walking) may attenuate the effects of cancer cachexia via the modulation of muscle metabolism, insulin sensitivity and levels of inflammation. However, a Cochrane systematic review concluded that there was insufficient evidence to determine the safety and effectiveness in patients with cancer cachexia (Grande et al. 2015). Nevertheless, aerobic exercise training has been shown to counteract skeletal muscle wasting in patients with cardiac cachexia (Alves et al. 2015). However, it is envisaged that patients would need to exceed their dietary intake to counter the effects of anabolic resistance, and this could be difficult to achieve in already frail patients. For COPD patients, pulmonary rehabilitation is now a standard of care (Fearon et al. 2013).

2.8 Pharmacological Agents

For anorexia, corticosteroid use has strong evidence in patients with malignancies; however, a recent review could not recommend a corticosteroid or a dosing regimen. Methylprednisolone (125 mg iv) for 8 weeks showed promising results. On the contrary, corticosteroids have not demonstrated efficacy in end-stage nonmalignant disease (Miller et al. 2014). Corticosteroid resistance is reported in cachexia associated with COPD (Barnes and Celli 2009).

Megestrol acetate (MA) is approved in the USA for use in AIDS patients for weight gain and appetite stimulation (Ezeoke and Morley 2015). However, MA is associated with adverse effects, in particular, venous thromboembolism (Ruiz Garcia et al. 2013). Current evidence does not support the use of progesterone (viz., MA and medroxyprogesterone (Provera)) therapies for non-cancer cachexia in terms of weight gain. Its impact on symptoms such as appetite and HRQOL, however, is generally positive (Taylor and Pendleton 2016).

Synthetic delta-9-tetrahydrocannabinol (delta-9-THC) cannabinoid, dronabinol, sold as MARINOL®, has been approved by the FDA for AIDS-related anorexia and appetite loss (Food and Drug Administration 2004). However, trials for cancer anorexia have been inconclusive (Whiting et al. 2015).

Due to the multifactorial nature of cachexia, a variety of pharmacological agents have been trialed to alleviate inflammation, stimulate appetite and increase anabolic tone and decrease catabolic events (Anderson et al. 2017).

Table 4 outlines the pharmacological agents in their class category and their proposed mechanism of action on anorexia/cachexia. The latest literature on the pharmacological interventions and the findings has been summarized in Table 4. Note that much of the data published is from anorexia/cachexia in cancer patients.

Fish oil encompasses polyunsaturated fatty acids (PUFAs), omega-3-fatty acids, or *n*-3 fatty acids, namely, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (Ries et al. 2012), and most products deal with EPA and DHA in combination. *n*-6 Fatty acids are also present, and the ratio between the *n*-3 and *n*-6 fatty acids needs to be kept as high as possible due to the pro-inflammatory nature of the *n*-6 fatty acids (Colomer et al. 2007). The authors acknowledged that certain cancers responded better to PUFAs, namely, the gastrointestinal and pancreatic cancers. The relatively short length of the studies may not reveal significant catabolic changes which take many months to restore, and higher doses may need to be considered (Mazzotta and Jeney 2009). In newly diagnosed patients with NSCLC, 2.2 g of fish oil per day stabilized weight and muscle mass compared to standard care (Murphy et al. 2011). The study highlights the importance of initiating supplementation from the onset

Table 4 Proposed pharmacological agents and their mechanism of action in anorexia/cachexia

Anti-inflammatory	Mechanism of action
Corticosteroids	Inhibition of synthesis and/or release of proinflammatory cytokines such as TNF and IL-1, which decrease food intake directly or through other anorexigenic mediators, such as leptin, CRF and serotonin 4 Enhance NPY levels in the hypothalamus, which may increase appetite and food intake. NPY-induced feeding is known to be dependent on circulating glucocorticoid levels (Inui 2002)
Progestins	Action on cytokines, and its inhibiting effect on TNF from acting on fatty cells and their products (López et al. 2004)
NSAIDS	Nonselective blockers of the cyclooxygenase pathway and inhibiting production of prostaglandins that cause inflammation and pain (COX-2 pathway). Block formation of thromboxane A2 (TXA2) in platelets preventing aggregation (Solheim et al. 2013)
Thalidomide	Shown to downregulate the production of TNF and other proinflammatory cytokines (Gordon et al. 2005)
Fish oil known as PUFAs/EPA/DHA/n-3-FA	Prostaglandin E2 synthesis and suppression of proinflammatory factors, such as interleukin-1 (IL-1) and tumor necrosis factor (TNF) (Mazzotta and Jeney 2009)
Anabolic	
Ghrelin	Stimulates the synthesis of growth hormone and increases appetite through the production of neuropeptide Y (Mansson et al. 2016)
Anamorelin (ghrelin analogue)	Potent and selective GHSR-1α agonist (Temel et al. 2016)
Testosterone (and synthetic derivatives oxandrolone, nandrolone)	Increase muscle mass through upregulation of protein synthesis (through binding to the androgen receptor) and interaction with insulin regulatory system (Gullett et al. 2010)
SARMS, e.g., enobosarm	Induces conformational changes in the androgen receptor upon binding. This selectively alters the interaction of the receptor with proteins in different tissues and changes the receptor's ability to regulate gene expression (Dobs et al. 2013)
Antipsychotic	
Mirtazapine	Blockage of postsynaptic 5-HT1$_b$ and 5-HT$_2$ receptors with inhibition of release of neuropeptide Y, a brain peptide involved in appetite stimulation; blocks 5-HT$_3$ receptor (anti-nausea); blocks H$_1$ receptor; and alters serum levels cytokines (Riechelmann et al. 2010)
Olanzapine	5-HT$_3$ (anti-nausea) and 5-HT$_{2c}$ (may underlie appetite stimulation) receptor blockage (Braiteh et al. 2008)
Multimodal	
Cannabis/cannabinoids	Appetite stimulation via its action on the cannabinoid Type I receptors (CB1) in the hypothalamus, increasing the palatability of food via a complex biochemical cascade incorporating ghrelin, chime and digestive signaling hormones. Anti-inflammatory and antiemetic (Ezeoke and Morley 2015)
Espindolol	Reduced catabolism, through nonselective β receptor blockade; reduced fatigue and thermogenesis, through central 5-HT1$_a$ receptor antagonism; increased anabolism, through partial β2 receptor agonism (Stewart Coats et al. 2016)
Carvedilol	α1-/β1-/β2-receptor antagonist (Clark et al. 2017)

of first-line chemotherapy and continuing during treatment.

Along with the adverse effects below, ghrelin, a peptide of 28 amino acids, produced primarily in cells at the base of the stomach, had long-lasting effects such as altered liver function, headaches and bronchitis. In COPD patients, acute myocardial infarction and small intestine perforation were observed at 20 μg/kg of the synthetic ghrelin (Mansson et al. 2016).

In an earlier study, lower doses of olanzapine (up to 7.5 mg) stabilized or increased weight in 6 out of 14 patients with cancer, with improved appetite, Mini-Nutritional Assessment (MNA) and Karnofsky performance scores (Braiteh et al. 2008).

Testosterone and its derivatives such as oxandrolone have shown positive effects on body weight and LBM in HIV/AIDS and COPD cachectic patients (Gullett et al. 2010).

Although there are single studies that show positive results with vitamin, mineral and protein supplements, and rare adverse events, there was insufficient evidence to recommend their use in cancer cachexia (Cuhls et al. 2016) (Table 5).

2.8.1 Unproven Treatments

In cachectic patients with advanced cancer, oral melatonin (a hormone produced by the pineal gland that regulates sleep and wakefulness) 20 mg at night did not improve appetite, weight, or quality of life compared with placebo (Del Fabbro et al. 2013).

In a double-blind, randomized, placebo-controlled clinical trial, pentoxifylline (a TNF inhibitor) 400 mg, three times a day, did not have any effect in weight gain and arm circumference in cachectic patients. Although QoL was improved after 1-month treatment, 2-month treatment was not significantly different to placebo (Mehrzad et al. 2016).

Hydrazine sulfate, a TNF inhibitor, has shown limited evidence for its use in cachexia and anorexia (PDQ® Integrative 2017).

Cyproheptadine, a histamine antagonist with antiserotonergic properties, was shown to mildly enhance appetite but failed to negate weight loss in patients with advanced cancer (Kardinal et al. 1990).

Prokinetic drugs such as metoclopramide are used for gastroparesis and may relieve chronic nausea and early satiety which influence caloric intake. In particular, controlled-release metoclopramide (20–80 mg over 12 h) showed a 50% reduction in the severity of vomiting, with some improvement in appetite and bloating (Wilson et al. 2002).

2.8.2 Combinational Treatments/ Interventions

In cancer cachexia patients, a fish-oil-enriched supplement (2 g of EPA and 600 kcal daily) resulted in increased lean tissue mass and functional ability compared to relative weight stability produced by fish oil or EPA alone and no effect from nutritional supplementation alone (Barber 2001).

In a Phase II open-label study in pancreatic and lung cancer patients, a multimodal intervention consisting of exercise, anti-inflammatories and energy-dense nutritional supplements combined with dietary advice showed improved weight compared to standard cancer care (Kaasa et al. 2015). It has been noted that dietetics and exercise compliance is an issue in patients who are unfit and at an advanced stage of their cancer (Forget et al. 2014). Taken together, the results indicate that a multimodal treatment approach personalized to the patient should include early assessment of the symptoms and combines non-pharmacological (e.g., nutritional support, exercise) and pharmacological interventions (e.g., orexigenic, anabolic, anti-catabolic and anti-inflammatory) required to address the underlying pathophysiology (Zhang and Garcia 2015; Dev et al. 2017).

In a Phase III randomized study, the most effective treatment in terms of all three primary efficacy endpoints LBM, REE and fatigue, and the secondary endpoints appetite, IL-6, Glasgow Prognostic Score (GPS) and Eastern Cooperative Oncology Group performance status (ECOG PS) score was the combination regimen that included medroxyprogesterone (500 mg/day) or megestrol acetate (320 mg/day); oral supplementation with eicosapentaenoic acid; L-carnitine (4 g/day); and thalidomide (200 mg/day) agents (Mantovani et al. 2010).

3 Feeding Difficulties

Dysphagia (swallowing difficulty) can be caused by many conditions which alter the normal function of the mouth, pharynx, larynx and esophagus. It can be associated with painful swallowing, known as odynophagia. Dysphagia is classified from an anatomical point of view as either oropharyngeal and esophageal, or by pathophysiology (structural or physiological) (Clavé and Shaker 2015). Oropharyngeal dysphagia occurs when there is difficulty or inability to form or

Table 5 Summary of literature of pharmacological agents examined for anorexia and cachexia in chronic disease

Drug	Disease	Dose	Adverse effects	Outcome
Methylprednisolone dexamethasone Betamethasone (Miller et al. 2014) *R*	Anorexia	Orally, iv (with dexamethasone equivalent doses ranging from 3 to 25 mg per day)	Hyperglycemia and gastrointestinal bleeding Higher doses may contribute to increased side effects	All studies showed improvement in appetite with the corticosteroid used, however not always statistically significant
Megestrol acetate (MA) (Ruiz Garcia et al. 2013) *R*	Cancer cachexia, anorexia Approved for AIDS	Varying doses: 100–1600 mg	Impotence in men, edema of the lower limbs, deep vein thrombosis, gastrointestinal Intolerance, death	Improves appetite and is associated with slight weight gain in cancer, AIDS, and in patients with other underlying pathology. Higher doses more related to weight improvement than lower doses
Indomethacin (I), celecoxib (C) (Solheim et al. 2013) *R*	Cancer cachexia	I: 400 mg 3 × daily; C: 200 mg × 2	None, although known side effects include gastrointestinal ulcers/ hemorrhage and cardiac events at higher NSAID dosage	Improved weight, physical performance, self-reported quality of life and inflammatory parameters. Evidence is too frail to recommend NSAID for cachexia outside clinical trials
Thalidomide (Gordon et al. 2005)	Pancreatic cancer cachexia	200 mg	Peripheral neuropathy, rash, daytime somnolence, constipation	Improvement in physical functioning correlated positively with weight gain
PUFAs (Mazzotta and Jeney 2009) *R*	Anorexia-cachexia Cancer	EPA: 170 mg–4.9 g DHA: 115 mg–3.2 g	None	No dose-response effect of EPA and DHA on weight, lean muscle mass, symptoms, QoL, or survival
Fish oil (Ries et al. 2012) *R*	Cancer cachexia	12 g per day tolerated	Abdominal discomfort, fish belching, fish aftertaste, nausea and diarrhea	Likely that the anti-inflammatory effects of n-3 FA are not effective in refractory cachexia
Ghrelin (Mansson et al. 2016) *R*	Cancer, heart failure, COPD cachexia	Variable: 2, 8, 13 μg/kg/ day iv	Stomach rumble (borborygmus), body heat, somnolence, thirst, nausea constipation; hematoma at the site of administration, increased frequency of evacuations, fatigue, atrial fibrillation	Positive effect on growth hormone plasma levels, weight gain, increases in lean mass, and reductions in loss of adipose tissue

Anamorelin (ghrelin analogue) (Temel et al. 2016)	NSCLC Cachexia/anorexia	100 mg	Hyperglycemia (up to 1%) as grade 3–4	Increased LBM, but not handgrip strength; improvements in symptoms such as appetite and food intake
Oxandrolone (Orr and Singh 2004) *R*	HIV-AIDS, COPD	Up to 200 mg/day	Hepatic dysfunction. Take note of virilizing effects and cholesterol changes	Improvements in body composition, muscle strength and function, status of underlying disease or recovery from acute catabolic injury and nutritional status
Enobosarm (Dobs et al. 2013) *R*	NSCLC, colorectal, non-Hodgkin's lymphoma, chronic lymphocytic leukemia, or breast cancer cachexia	1 and 3 mg	Generally same between groups	Improved LBM, physical function, and QoL
Mirtazapine (Riechelmann et al. 2010)	Cancer cachexia/anorexia	15–30 mg po/day	Moderate confusion, dizziness and blurred vision, mild dry mouth and drowsiness	24% improved appetite and gained 1 kg or more; 6% health-related QoL
Olanzapine (Naing et al. 2015) *R*	Cancer cachexia/anorexia	2.5–20 mg po/day	Somnolence, pancreatitis, extrapyramidal symptoms, nausea/vomiting (all grade 2)	Changes in metabolic cytokines and body weight did not correlate. Trend toward attenuation of weight loss (not statistically significant)
Cannabis/cannabinoids (Lutge et al. 2013) *R*	HIV Anorexia	2.5–20 mg/day	Concentration difficulties, fatigue, sleepiness, or sedation, mood-altering effects, reduced salivation, and thirst	Stabilization or increase in weight
Espindolol (Stewart Coats et al. 2016)	NSCLC or colorectal cancer cachexia	10 mg × 2 daily	Treatment emergent (>10% of patients): anemia, cough, dyspnea	Significantly reversed weight loss, improved fat-free mass, and maintained fat mass
Carvedilol (Clark et al. 2017)	Cardiac Cachexia	3.125–25 mg × 2 daily	None reported	Prevented weight loss; promoted weight gain

COPD chronic obstructive pulmonary disease, *DHA* docosahexaenoic acid, *EPA* eicosapentaenoic acid, *FA* fatty acids, *NSAID* nonsteroidal anti-inflammatory drugs, *iv* intravenous, *LBM* lean body mass, *NSCLC* non- small cell lung cancer, *po* by mouth, *PUFAs* polyunsaturated fatty acids, *QoL* quality of life, *R* review

move a food bolus safely from the mouth to the esophagus, whereas esophageal dysphagia is where the food bolus fails to pass through the esophagus.

Oropharyngeal dysphagia can be associated with regurgitation, coughing, oropharyngeal aspiration (entry of food and liquids or secretions into trachea or lungs) and choking (Clavé and Shaker 2015). Esophageal dysphagia can be associated with regurgitation and odynophagia, but respiratory symptoms are less common unless advanced or untreated (Clavé and Shaker 2015).

3.1 Epidemiology

Dysphagia is common in people with head and neck diseases and neurological or neurodegenerative diseases and older people (Clavé and Shaker 2015). Oropharyngeal dysphagia is reported in up to 40% of older people, due to neural and muscular changes characteristic of aging, which is then compounded by multi-morbidity, medications and frailty (Clavé and Shaker 2015). High prevalence rates in dementia of 80–100% and Parkinson's disease of 60–80% also are reported, in particular, in advanced disease (Clavé and Shaker 2015).

The prevalence of dysphagia in head and neck cancers pretreatment has been reported to be 28% in patients with stage T2 or more oral cancer, 51% in pharyngeal cancer and 28% in laryngeal cancer (Clavé and Shaker 2015; Raber-Durlacher et al. 2012). Prevalence varies depending on tumor stage and site, which impact differently on motility or structures involved in swallowing (Raber-Durlacher et al. 2012). Acute dysphagia is common in patients receiving concurrent chemoradiation or radiotherapy to the chest region, with rates of 20–40% seen (Raber-Durlacher et al. 2012).

3.2 Etiology

Swallowing is a complex biomechanical and physiological process by which food and drink passes and is cleared through the oral cavity, pharynx and esophagus to the stomach at an appropriate rate (Clavé and Shaker 2015; Raber-Durlacher et al. 2012). The oral phases of swallowing are voluntary, followed by a highly coordinated involuntary reflex controlled by the medulla and cerebral cortex, involving 6 cranial nerves and over 25 muscles (Fig. 2). The process of swallowing is altered to cater for different volumes and viscosity of the food bolus (Raber-Durlacher et al. 2012).

Causes (Clavé and Shaker 2015; Raber-Durlacher et al. 2012; Cook 2009) include:

- Structural – malignancy (esophageal, gastric, thyroid, mediastinal, larynx, pharynx, oral cavity)
- Neurological – cerebrovascular disease, brain tumors, Parkinson's disease, dementia
- Poor dentition
- Medications which reduce saliva (opioids, tricyclic antidepressants, atropine, hyoscine)
- Radiotherapy to the head and neck, mediastinum, or lung
- Surgical procedures to the head and neck
- Acute and chronic graft-versus-host disease
- Mucositis

3.3 Approach to Assessment

An assessment of swallowing includes clinical evaluation, swallow trials and, in some cases, instrumental evaluation (Raber-Durlacher et al. 2012). On history, key symptoms include difficulty swallowing liquids or solids, food getting stuck, coughing, choking, regurgitation, avoidance of particular food consistencies and poor oral intake. The possible causes of dysphagia should be considered in the past medical history.

Examination requires inspection of the oral cavity for dental status, dryness, mucositis and other abnormalities; strength, motion, symmetry of the tongue, lips, cheeks and soft palate; and evidence of aspiration pneumonia on chest examination. The level of consciousness and neurological examination are also crucial. There may be also dysarthria (motor speech disorder) and dysphonia (inability to produce a voice) present (Raber-Durlacher et al. 2012).

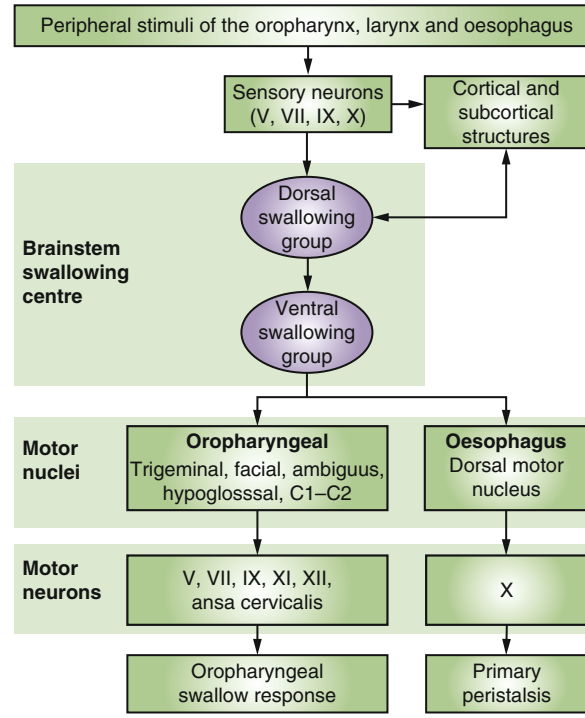

Fig. 2 Oropharyngeal swallow response and primary peristalsis (Clavé and Shaker 2015 - reproduced with permission)

An observed swallowing test may also be conducted if deemed safe, and one may try various food and fluid consistencies. Videofluoroscopy, to allow radiographic assessment of the dynamics of swallowing, may be required for objective assessment (barium or gastrografin) (Raber-Durlacher et al. 2012). Endoscopy may offer visualization of the pharynx, larynx, or esophagus (Raber-Durlacher et al. 2012). A chest radiograph may be required if aspiration pneumonia is suspected.

3.4 Approach to Management

The management of dysphagia aims to ensure adequate nutrition and hydration, maximize swallowing function, minimize risk of aspiration, and maintain the enjoyment associated with eating and drinking a range of foods and fluid. A multidisciplinary approach is needed, and input may be required from speech and language pathologists, ear nose and throat specialists, radiologists, neurologists, gastroenterologists, dieticians and geriatricians (Clavé and Shaker 2015).

Recommendations may include increasing chewing of food and number of swallows for each food bolus. A modified diet may be required, which includes soft or pureed foods and thickened fluids. This risk of aspiration and poor nutrition needs to be balanced carefully with the goals of care and impact of modified diet on quality of life, and shared decision making with the patient and their caregiver is critical. Some patients may choose to accept a risk of aspiration, for the quality of life associated with being able to eat normal food. Strategies can be used to increase the safety of swallowing, such as advice related to position, eating when fully alert, and moving food bolus to the stronger side of the mouth in case of tongue unilateral paralysis. Oral hygiene is important, and so is ensuring appropriate fit of dentures to allow adequate chewing. It is also important to consider transdermal and subcutaneous routes for essential medications, if difficulty in swallowing medications is occurring (Mercadante 2017).

In most cases, oral-assisted comfort feeding, where patients are offered food by mouth, is appropriate (Lembeck et al. 2016). Enteral feeding should be considered in the context of the

progression of the underlying disease and evidence-based nutritional support to improve nutritional or functional status in that clinical situation, goals of care of the patient, and reversibility of the swallowing problem. Enteral feeding does not reduce the risk of aspiration pneumonia. Nasogastric tubes can cause bleeding, trauma, nasal discomfort, esophageal perforation, and aspiration and can be displaced. In longer-term situations, a percutaneous gastrostomy tube may be appropriate, which, in most cases, can be inserted endoscopically. Complications include bleeding, skin infections, peritonitis and tube leakage. When discussion and recommendation is to avoid enteral feeding, it is important that careful communication about the quality of life associated with comfort feeding and the adverse effects that are being avoided is relayed. Attention is required to understand the cultural, social and individual meaning that appetite loss and dysphagia play.

Local interventions may be appropriate for esophageal strictures and malignant obstruction, including dilatation, endoscopic ablation, stent placement and radiotherapy (Glen 2016). In esophageal cancer, radiotherapy can be given in a single dose or a short-fractioned course over 1–2 weeks, and there is increasing evidence that brachytherapy may give better palliation than stenting (Glen 2016). Laser ablation can be helpful if there is concurrent bleeding (Glen 2016). Self-expanding metal stents can provide good palliation within a single procedure that can be tolerated in very unwell patients, but are less suited for high esophageal tumors (Glen 2016). Fully or partially covered stents are the ideal in palliation as they have patency advantages due to the metal preventing ingrowth (Glen 2016). The complications of stent placement can include esophageal bleeding, stent migration, stent obstruction, pain and gastroesophageal reflux (especially in low or junctional cancers). After stent placement, approximately two-thirds of patients can return to a normal diet. Re-intervention may be needed for migrated partially or fully covered stent or tumor regrowth (Glen 2016).

Proton pump inhibitors and prokinetic medications (such as metoclopramide) for concurrent gastroesophageal reflux can also be helpful.

4 Conclusion and Summary

Anorexia, cachexia and dysphagia are all multifactorial conditions correlated to poor outcomes and quality of life which require careful assessment. Along with defective appetite signaling characteristic in anorexia, both anorexia and cachexia encompass a complex pathophysiology that includes inflammation, anabolism and changes in hormonal status. In addition, appetite (encompassing taste and smell), feeding and swallowing difficulties (resulting in decreased oral nutritional intake), gastrointestinal support (e.g., nausea, decreased motility of food, early satiety), physical exercise, pain, current treatment (chemotherapy, radiotherapy, surgery) and psychosocial and psychological assessment will need to be considered in patients with cachexia. A multimodal treatment plan which includes early and routine screening, nutritional support, targeted pharmacological treatment counteracting the mechanisms of the disease (if possible, concurrently with cancer treatment) and appetite stimulation needs to be personalized for the patient. Furthermore, caregivers need to be included in the conversation to provide better understanding and support to the patient. More data is required for anorexia, cachexia and dysphagia in non-cancer chronic diseases.

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Swallowing Difficulties

18

Prudence Ellis and Jacqui Allen

Contents

Abstract

In the many considerations that arise during end-of-life care, swallowing problems are common and may have a disproportionately large impact on the patient and family. Inability to eat safely or tolerate diet results in nutritional challenges, difficulty maintaining physiological reserve and resilience, and isolation from social activities. The latter may in fact be the most troubling aspect for those wishing to optimize remaining precious time, given that most social interactions are based on meals and deglutition. A clinician providing care and support in a palliative care setting must recognize the risk of swallowing impairment and should actively query the presence and degree of problems encountered.

Many interventions and strategies are available to mitigate swallowing difficulties and are best managed in a team setting with input and

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_19

feedback from all team members in conjunction with the patient. This chapter will cover key aspects of deglutition, how it may be altered in unwell patients, and available interventions that may be appropriate for those receiving palliative care.

1 Introduction

Humans are social animals and nearly all our social situations revolve around conversation and food. This presents a real problem when you have swallowing difficulties when it can be embarrassing, unsafe, or anxiety-provoking to consider a meal with friends and family. When patients face limited time, these situations become even more acute, and quality of life (particularly with eating and drinking) is of paramount consideration.

Problems with swallowing can develop for many reasons in patients nearing the end of life. These include the direct effect of the illness, effects of treatment or management, cognitive issues, medication effects, deconditioning and fatigue, change in taste, loss of saliva, mood disorders, and inanition. The clinician should be particularly cognizant of deglutitive changes and inquire about these directly as they often impact quality of life and, in many cases, there are options to ameliorate symptoms. Managing swallowing problems is a multidisciplinary challenge. Teamwork can be the critical factor in preventing life-threatening complications and long-term morbidities and in offering support and timely intervention. Regular and clear communication between team members and the patient can relieve anxiety, provide education, and optimize function.

In this chapter, we will review the importance and impact of deglutition and swallowing dysfunction in the environment of palliative care. This will provide a practical platform for clinicians who care for those receiving palliative care which includes anticipating possible problems, recognizing symptoms and signs of swallowing disorders, and identifying management strategies and options.

2 Swallowing

Swallowing is a complex process requiring a series of muscles to work in synchronicity to perform a relatively short movement. Some movements are voluntary, and others reflexive, but they are codependent (Logemann 1998).

2.1 The Normal Swallow

It should first be noted that the "normal" swallow shows great variability among healthy individuals. Deglutition involves 30 muscle pairs, 5 cranial nerves and accessory nerves, coordinating with cortical, subcortical, and medullary respiratory centers and the swallow central pattern generator (Shaw and Martino 2013). The complexity of deglutition and its need to coordinate precisely with respiration results in a series of protective airway reflexes and responses. Disordered deglutition is an airway risk and may result in significant morbidity and mortality. Understanding neurologic control points enables better management of patients with swallowing problems. A summary of cranial nerve function involved with swallowing is provided below. Deglutition has been arbitrarily divided into phases. However, in reality, it is a continuous process, and many aspects occur simultaneously within a predetermined sequence. Recent research indicates the interdependent aspects of deglutition should be treated as a continuum, rather than in separate phases. Nonetheless, historically swallowing has been divided into four phases (oral preparatory, oral, pharyngeal, and esophageal).

Assessment of all aspects is required to understand swallowing ability and dietary/nutrition risk.

The swallow begins with a person being alert and able to sense food. It is common practice to include both the oral preparatory phase and oral phase under a single heading in an assessment, namely, the oral phase. This is considered the voluntary stage/s of the swallow where bolus may be voluntarily ejected from the oral cavity.

Food is placed in the mouth and the lips are closed to prevent anterior spillage. The food or

fluid in the mouth is then masticated (chewed) and mixed with saliva to create a cohesive bolus. The bolus is held between the tongue and the anterior hard palate. Mastication is in a lateral rotary movement, and the tongue manipulates the bolus to the back of the mouth. The bolus is held in place by contraction of the soft palate against the base of the tongue and contraction of the buccal muscles. Dentition influences deglutition by contribution to bolus breakdown, allowing salivary enzymes to begin digestion, tastants to be sensed, airway closure to begin, and lubrication to be provided to form a cohesive bolus.

The tongue begins to move the bolus toward the back of the mouth, against the hard palate. Negative pressure is created by muscle contraction, and the bolus moves toward the faucial pillars.

Innervation is predominantly via the trigeminal nerve (CNV), the facial nerve (CNVII), and the hypoglossal nerve (CNXII). The vagus nerve (CNX) innervates the palatoglossus muscle. CNVII innervates the muscles of the face, while CNV innervates those muscles used to chew, elevate, and lateralize the mandible. The intrinsic and extrinsic muscles of the tongue are innervated by CNXII (other than the palatoglossus). Finally, the soft palate is innervated by CNV and CNX (Drake et al. 2010; Moore 2010). Sensation is provided by the lingual nerve (a branch of CNV) and the glossopharyngeal nerve (CNIX) with special taste senses provided by the chorda tympani (branch of CNVII, hitchhiking with the lingual nerve) and CNIX. Sensation of the valleculae is via CNX, superior laryngeal nerve. This nerve is critical in guarding the larynx and mediating laryngeal closure and airway protection when bolus or secretions are identified.

The swallowing reflex is initiated as the bolus passes the faucial arches triggering the pharyngeal phase of the swallow, which is stereotyped, involuntary, and centrally coordinated. Total pharyngeal transit time in adults is usually less than 1.5 s and must encompass airway closure, laryngeal elevation, pharyngeal peristalsis, and pharyngoesophageal segment (PES) opening. This requires coordination with the respiratory system.

The soft palate retracts to close the velopharyngeal port. The bolus passes over the base of the tongue, which retracts toward the posterior pharyngeal wall. The pharyngeal muscles create peristaltic waves traveling at approximately 15 m/s, which carry the bolus through the pharynx. Simultaneously, the epiglottis deflects the bolus laterally to protect the laryngeal vestibule and retroverts which smoothes the valleculae. The aryepiglottic folds, false and true vocal folds all contract to achieve airway closure and prevent penetration and aspiration. The hyoid moves anterosuperiorly (approximately the distance of one vertebra) which acts as a drawstring to assist in distension of the upper esophageal sphincter (UES). Cessation of tonic UES contraction occurs within 0.3 s after suprahyoid muscular contraction starts to ensure an open sphincter when the bolus arrives. Bolus size influences duration of hyolaryngeal elevation and airway closure duration, with larger volumes resulting in greater opening duration and displacement.

The vagus nerve transmits pharyngeal sensory information via pharyngeal and superior laryngeal branches and is the key mediator of the airway closure reflex (adductor reflex). Afferent information converges at the nucleus tractus solitarius (NTS) of the medulla and then travels through interneurons to the nucleus ambiguous (NA) which produces efferent (motor) output. Motor signals return to the pharynx via vagal branches (pharyngeal plexus and recurrent laryngeal nerve), with additional input from the dorsal motor nucleus (DMN) of the vagus (inhibitory). The DMN input likely prevents mis-sequencing. Vagal outflow also initiates airway protective mechanisms, and accessory nerve and C1 and C2 nerves produce hyoid elevation (Drake et al. 2010; Moore 2010).

Relaxation of the upper esophageal sphincter occurs and lasts less than 1 s. In reality this is a cessation of tonic contraction, rather than an active relaxation (Allen 2016; Miles et al. 2016). The UES then contracts to protect the pharynx from regurgitated material and to limit air swallowing. The bolus is carried via esophageal peristalsis (circular and longitudinal muscle contractions) to the lower esophageal sphincter (LES)

(Shaw and Martino 2013). Once the LES has relaxed, the bolus moves into the stomach. The process of transportation through the esophagus takes from 8 to 20 s for liquid but may be as long as 60 s for pills or solids (Logemann 1998; Miles et al. 2015, 2016).

CNX mediates UES function allowing bolus into the esophagus during deglutition (Drake et al. 2010; Moore 2010). Esophageal peristalsis is under vagal and myenteric control through the NA and DMN of the vagus combined with sympathetic and parasympathetic neural networks. Differential latencies and a pool of inhibitory vagal neurons enable a sequential waveform to occur from proximal to distal within the esophagus.

2.2 The Disordered Swallow

The "normal" swallow demonstrates variability which, at times, can be difficult to differentiate from disordered deglutition. Physical trauma, tumors, neuromuscular conditions, surgery, medicines, and aging all contribute to changes in a swallow.

2.2.1 Common Features of Swallowing Dysfunction

Change to the musculature or innervation of the swallow may result in disordered deglutition. Ultimately, the purpose of a swallow is to pass food and fluids from the mouth to the stomach via the pharynx and esophagus. Given the interdependence of the swallow phases, it follows that disruption to any stage may result in dysphagia (swallowing problems) (Table 1).

Altered oral sensation may yield anterior spillage of a bolus, incomplete mastication, oral incompetence, and delayed initiation of a swallow (if a swallow is initiated at all). Problems with lateralization of the jaw, or rotary mastication, or damaged dentition may give rise to an incompletely masticated or two-phase/piecemeal bolus, which poses a risk of aspiration. A cohesive bolus is required for safe transportation throughout a swallow, as a piecemeal bolus heightens the risk of pooling, residue, and material breaking away into the laryngeal vestibule. A two-phase bolus may compromise airway closure mechanisms due to differential bolus velocities and therefore confusion over appropriate airway closure duration.

Table 1 Common contributors to swallow impairment

Contributor	Effect	Complaint
Mass or tumor	Deflect bolus incorrectly Obstruct deglutitive pathway Neural compromise – sensory and motor Pain – reduced effort and mobility of pharynx Loss of airway protection	Solid and liquid dysphagia Pill dysphagia Lump in the throat Cough Loss of appetite Choking
Dryness (xerostomia, xerophagia)	Mucosal irritation (abrasion) Thick mucus Reflux Impaired bolus cohesion and transit	Pain Cough and hawking Acid or bile taste, burning pharynx/chest pain Food sticking or spitting out food
Medications	Dryness Drowsiness Loss of appetite Constipation	Solid food dysphagia Loss of appetite Weight loss Early satiety
Cognitive issues	Reduced urge to eat Depression – loss of appetite Fear of choking	Weight loss Low mood No interest in food
Deconditioning	Loss of muscle tone and strength Loss of compensatory reserve	Solid and liquid dysphagia Weight loss Fatigue Reduced volume of food intake

Saliva is critical in mastication, helping to achieve a cohesive bolus, providing lubrication, initiating digestion, enabling tastant dissolution, mechanically flushing the oral cavity, and protecting dentition and mucosal lining. One need only see a patient following radiotherapy with xerostomia and its significant impact on oral bolus control and dental health to appreciate the benefit of saliva.

If oral incompetence is present, bolus transit may be affected, either with anterior loss (i.e., from the lips) causing skin irritation and embarrassment or inappropriate posterior spillage into the pharynx with potential for airway soiling. Velopharyngeal incompetence will also affect oral transit, as the bolus may escape North into the nasopharynx. Loss of the stable velopharyngeal diaphragm impairs pressure generation and ability to provide impetus to the bolus in the oropharynx. Residue may be observed in the valleculae or tongue-base regions or pyriform apices and intra-deglutitive or post-deglutitive aspiration of residue may occur.

From the time that bolus contacts the tongue dorsum, airway closure begins. Once the bolus reaches the posterior third of the tongue, the involuntary swallow is triggered. A coordinated sequence of events occurs. This begins with three-level airway closure, hyolaryngeal elevation and consequent epiglottic retroversion, and pharyngeal constrictor peristalsis. Cessation of upper esophageal sphincter contraction enables distraction of the UES and generation of negative pressure in the pharyngoesophageal segment which combine to effect bolus transit. This all occurs in approximately 1.5 s, and even slight mismatching of event timing may have significant ramifications. Consequences include misdirection of bolus +/− airway violation, incomplete bolus transit with residue which may then be aspirated, and anatomic changes such as development of a diverticulum. Poor sensation due to neurological disease, surgical distortion, and post-radiotherapy damage or injury will prevent the SLN from identifying incoming bolus in a timely fashion. Airway closure may then be late or absent and aspiration may occur. Loss of strength in pharyngeal musculature reduces impetus of the bolus and means it must rely on gravity and tongue pumping to coincide with UES opening and allow bolus flow. Anterosuperior hyoid elevation and cessation of tonic UES contraction result in a distracting effect, opening the UES. If hyolaryngeal elevation is present, this may be enough to permit bolus transit, but if there is poor elevation or mistiming of bolus arrival at the UES, then penetration and aspiration will ensue. At times only part of the bolus may traverse the UES leaving bolus remnants in the pyriform fossae. Given that the larynx descends post-deglutition and protective airway constriction relaxes, this can expose the airway to misdirected bolus. Surgical tethering of tissue and radiation fibrosis often limit hyolaryngeal elevation. Stroke or progressive neurologic disease frequently impairs pharyngeal strength and results in reduced UES opening duration and diameter.

If material enters the laryngeal vestibule, then penetration has occurred. When material passes the vocal folds into the airway, aspiration has occurred. Either incident may be associated with a response to eject the material, and in many cases bolus penetration is simply cleared during the swallow by the closure of the airway "squeezing" bolus out of the larynx. If there is no response, then aspiration is deemed "silent." This presents the greatest risk as bolus may remain lodged in the lower airways and produce pneumonitis, lung abscess, pneumonia, or death.

UES constriction persists after bolus passage to ensure no retrograde movement of the bolus into the pharynx (esophagopharyngeal reflux, EPR). Poor peristaltic wave in the esophagus may impair bolus transport and risk reflux of the material into the pharynx. This may prompt compensatory UES hyperfunction as a protective mechanism to prevent pharyngeal transgression. In some patients this is felt and described as a lump on the throat or globus sensation. If mechanical obstruction is present in the esophagus (e.g., unfolded or stiff aorta; peptic, malignant, or caustic stricture; Schatzki's rings; or external compression), bolus may also be impeded at that site.

Assessment of esophageal function may be performed by various individuals and varies between centers. For example, in Australia, it is

formally the domain of the gastroenterologist. However, in New Zealand, otolaryngologists, gastroenterologists, radiologists, and speech pathologists may assess and comment on the esophageal phase of swallowing.

Aspiration and Penetration

Aspiration and penetration describe entry of bolus material into the larynx. Penetration occurs when bolus crosses the plane of entry of the laryngeal vestibule (a line following the aryepiglottic folds to the epiglottic tip), and aspiration when the bolus passes beneath the vocal folds. A response may occur in either situation, e.g., a cough to clear; however, if a response is lacking, then silent aspiration has occurred. This is a major risk factor for pulmonary problems as bolus remains within the lower airways. Rosenbek and colleagues described the penetration-aspiration scale (Rosenbek et al. 1996) which categorizes the degree of airway violation and whether a response is seen (Table 2). This is one of many forms of categorizing severity of penetration and aspiration.

A major goal of dysphagia management is to prevent adverse consequences of aspiration, namely, fever, decreased oxygen saturation, chest infections, aspiration pneumonia, decreased quality of life, increased length of stay, and death. It is also important to note the additional financial burden that dysphagia imparts on the healthcare system. Although no data is available for palliative care, international data estimates that the cost of dysphagia per person, within 1 year of ischemic stroke, is $4510 more than those without dysphagia (Bonilha et al. 2014). Additionally, Sutherland, Hamm, and Hatcher (2010) estimated the mean cost of treatment for a person with aspiration pneumonia to be $17,000. Although these figures do not dictate the management of a person with dysphagia, it is an important administrative fact in advocacy for early dysphagia management.

Table 2 Penetration-aspiration scale[a]

Score	Description of events
1	Material does not enter the airway
2	Material enters the airway, remains above the vocal folds, and is ejected from the airway
3	Material enters the airway, remains above the vocal folds, and is not ejected from the airway
4	Material enters the airway, contacts the vocal folds, and is ejected from the airway
5	Material enters the airway, contacts the vocal folds, and is not ejected from the airway
6	Material enters the airway, passes below the vocal folds, and is ejected into the larynx or out of the airway
7	Material enters the airway, passes below the vocal folds, and is not ejected from the trachea despite effort
8.	Material enters the airway, passes below the vocal folds, and no effort is made to eject

[a]Rosenbek et al. (1996)

2.3 Swallow Dysfunction in Selected Conditions

Although aging alters swallow physiology, many older adults maintain functional swallows well into their tenth decades. Certain high-risk illnesses are associated with increased swallowing problems, and management is determined by the underlying causes, patient factors, and resources. Some of these conditions are discussed in the following sections.

2.3.1 Head and Neck Cancer

Representing around 5% of all cancers in Australasia, head and neck cancer is most commonly squamous cell carcinoma (HNSCC) arising from the epithelial lining of the upper aerodigestive tract. There is also a contribution from skin-related carcinoma which may involve deeper structures and thyroid carcinoma which is intimately related to the recurrent laryngeal nerve putting the voice and swallow safety at risk. Risk factors for head and neck cancer include male gender, age >60 years, smoking, alcohol intake (and a combination of the two), and human papilloma virus (HPV) infection. Subsites within the head and neck vary as to which causative factor is most commonly responsible; e.g., oropharyngeal carcinoma is associated with HPV infection in >80% of cases now (Gillison et al. 2015). There is variation in treatments of sites, responses to treatment, and subsequent

functional deficits that follow treatment. This is seen most starkly in the differential treatment response of HPV-positive carcinoma of the head and neck vs non-HPV positive carcinoma. In the last decade, HPV has been identified as a major contributor to disease in younger, nonsmoking, nondrinking individuals. The upside to this early onset disease is that it is typically far more responsive to treatment and demonstrates a greater cure rate. This has now led to trials in which therapy is being de-escalated to evaluate whether oncologic control can be achieved with a lower treatment burden. The aim is to reduce treatment-related morbidity such as dysphagia, voice change, osteoradionecrosis, and secondary malignancy (Mirghani et al. 2015; Masterson et al. 2014).

Malignancy at any subsite of the head and neck affects deglutition. Oral cavity lesions create pain on tongue motion; affect sensation, taste, and oral competence; and disturb mastication. Oropharyngeal malignancy may be obstructive and painful and reduce superior laryngeal nerve sensation leading to increased risk of aspiration. Hypopharyngeal tumors often result in obstruction of the pyriform apex or PES and may reduce vocal fold mobility compromising airway protection. Laryngeal cancer impairs airway protection reflexes and cough efficiency. Dysphonia is often an early sign in glottic-level tumors (Figs. 1 and 2) but may not be seen in supraglottic malignancy until advanced disease is present.

Most importantly in head and neck cancer patients, the treatment is also highly likely to impair both deglutition and phonation. Whether the treatment is surgical resection, radiation/chemoradiation, or a combination of surgery and postoperative radiotherapy, vital structures will be in the "line of fire" at all times. Achieving cure of the cancer does not guarantee a functional swallow or voice. In many patients, swallowing parameters deteriorate in the 5 years following completion of treatment for HNSCC regardless of cancer eradication. Radiation-induced xerostomia and osteoradionecrosis are unique complications seen only following HNSCC treatment, not from the tumor itself. Xerostomia exposes dentition to increased risk of caries, periodontal disease, and tooth loss, further impairing oral bolus control and mastication. Radiation may also induce trismus such that mouth opening is grossly reduced and fitting food or a toothbrush into the oral cavity can be difficult. Resection of tongue or pharyngeal tissue may create sumps, insensate regions, and poor mobility even if reconstruction occurs.

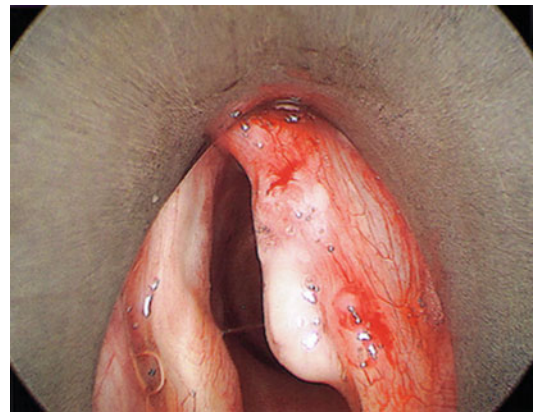

Fig. 1 Endoscopic clinical photograph of right vocal fold squamous cell carcinoma

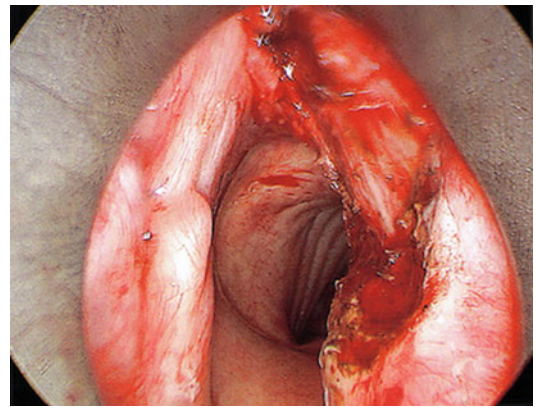

Fig. 2 Endoscopic clinical photograph of right vocal fold post-resection of squamous cell carcinoma

2.3.2 Neuromuscular Diseases

Conditions that affect cortical control, brainstem coordination, peripheral neural pathways, or the neuromuscular junctions of the muscles of the swallow yield changes in deglutition. This increases the risk of penetration and aspiration.

Motor Neurone Disease

As deterioration of the upper and lower motor neurons occur, the response of the muscles to stimuli decreases. This can affect all muscles relating to the swallow. It may present as difficulty initiating a swallow, reduced hyoid elevation, poor epiglottic deflection, and incomplete relaxation of the UES. This might also affect the peristaltic wave, and therefore a person may show difficulty with solid consistencies earlier than liquid consistencies. As noted by Langmore, Grillone, Elackattu, and Walsh (2009), "virtually all patients experience swallowing problems at some point in the disease if they live long enough." Prevalence of dysphagia is estimated at 81% at the time of death (Hardiman 2000).

Cerebrovascular Accident

Both cortical cerebrovascular accidents (CVAs) and brainstem strokes will affect swallowing. Dysphagia is present in 27–30% of persons with traumatic brain injury, and from 8.1 to 80% of those with acquired brain injury, with an average of 50% for those with stroke (Langdon et al. 2007; Takizawa et al. 2016; Ramsey et al. 2003). Presentation of dysphagia in these cohorts varies, with symptoms in stroke relating to the area of lesion. Presentation in those with TBI or executive function impairment includes nonmechanical symptoms of dysphagia, for example, overfilling the mouth and drinking/eating too quickly or slowly. A large proportion will improve spontaneously but this may be over months. Brainstem lesions tend to fair worse as it is more likely that cranial nerves IX–XII will be affected creating a combined swallowing insult. Both impaired motor (poor hyolaryngeal elevation, weak pharyngeal constriction, incomplete airway closure, uncoordinated pharyngoesophageal segment function) and sensory (inability to feel bolus and trigger airway protection and patterned swallow phases) function is found. Screening of all individuals presenting with CVA is vital. Many screening tools have been proposed including bedside assessments and questionnaires. Unfortunately, these tools will miss a significant proportion of impaired swallowers – those with silent aspiration. Instrumental assessment is the most reliable way to assess swallow safety but requires additional resources and time and is not always appropriate in the palliative care setting. Disordered deglutition post stroke is associated with worse outcomes, longer hospital stay, increased likelihood of readmission, and pneumonia within the first 3 months (Ramsey et al. 2003). Early rehabilitation can greatly enhance swallow recovery and protect against complications.

Parkinson's Disease

Parkinson's disease may affect both the motor and non-motor aspects of the swallow. It is noted that dysphagia occurs in a high proportion of people with Parkinson's disease. This figure ranges from 33% (based on subjective bedside assessments) to 80% (based on objective assessments) (Kalf et al. 2012). Dysphagia in Parkinson's disease is more prevalent in males; however, it is also linked with the duration of the disease and the presence of dementia (Cereda et al. 2014). As with other cohorts, dysphagia may be evident with reduced efficiency of mastication, poor base-of-tongue contraction, poor hyoid elevation, and pharyngeal residue, all of which pose a risk of penetration and aspiration.

It should be particularly noted that only a small proportion of people with dysphagia and Parkinson's disease are able to identify symptoms of swallowing problems. This figure is estimated to be between 20 and 40% upon questioning and only 10% reporting dysphagia spontaneously (Bird et al. 1994; Suttrup and Warnecke 2016). This is significant, as pneumonia is the most common cause of death in the population of people with Parkinson's disease (Morgante et al. 2000).

Multiple Sclerosis

Oropharyngeal dysphagia occurs in over 30% of multiple sclerosis cases (Prosiegel et al. 2004). As with all other forms of oropharyngeal dysphagia, this entails risk of aspiration and penetration and subsequent pneumonia. Persons with MS are also noted to have insufficiency of velopharyngeal elevation, which leads to the presence of hyper +/− hyponasality (Vitorino 2009). This could also increase the risk of nasal regurgitation, given the

role of the soft palate in preventing bolus entry into the nasopharynx.

Dementia

It is estimated that around 45% of persons with dementia also present with dysphagia (Horner et al. 1994). Others report prevalence as high as 80% (Wasson et al. 2001) and 84% (Horner et al. 1994).

Dysphagia may present differently depending upon the particular dementia experienced (Easterling and Robbins 2008). For example, persons with Alzheimer's disease may forget to eat, be unable to chew, forget to swallow, and show poor pharyngeal clearance (Horner et al. 1994), while persons with frontotemporal dementia may experience an increase in appetite and change in food preferences, have larger bite sizes, and eat nonedible items (Easterling and Robbins 2008). Furthermore, persons with vascular dementia show difficulty chewing and coordinating a swallow (Gallagher 2011).

2.3.3 Gastric Conditions

Gastroesophageal reflux disease is highly prevalent, with estimates of 14% of adults reporting weekly reflux symptoms (Eusebi et al. 2017). Therefore, a large proportion of those receiving end-of-life care will experience reflux as a pre-existing comorbidity. Factors related to the terminal disease and its treatment may further impact this and increase reflux related irritation. These include medications, radiotherapy, body position, saliva production, and surgery. In patients who receive narcotic analgesia, there is a diminution of the spontaneous swallow rate, and oral dryness can be a medication side effect – a combination which can produce swallow issues. Loss of saliva increases reflux irritation due to loss of buffer, lubrication, and mechanical flushing protection. In rare cases impingement on the esophagus or gastric inlet by malignant disease may impair bolus throughput, and certainly esophageal and gastric cancer can produce marked feeding difficulties both through direct obstruction and loss of appetite.

Stomach emptying typically occurs within 90 min. Medication can slow this process and result in induced gastroparesis. Symptoms reported are early satiety and loss of appetite resulting in smaller meal volumes.

2.3.4 The Aging Swallow

As we age, our swallow naturally changes. These changes may not result in direct swallow impairment but may reduce physiological reserve when the swallow is challenged. This has been termed "presbyphagia" to indicate the relationship to the aging process.

Logemann et al. (2013) noted significant changes in the swallow, including a change in the method of propelling the bolus from the front to the back of the mouth increasing duration of the oral stage. There is also a delay in the triggering of the swallow reflex (and subsequent pharyngeal phase), with a delay in the hyoid and larynx returning to the pre-swallow position (older persons have a slower refractory period). An increased number of penetration events are also noted, but in the absence of aspiration. In a recent normative study, quantitative oropharyngeal and esophageal swallowing parameters remained fairly constant in those up to 80 years after which there was an appreciable increase in oropharyngeal and esophageal transit times and reduction in pharyngeal constriction (strength) (Miles et al. 2016).

2.4 Summary

Swallowing problems are present in many individuals nearing their end-of-life with wide-ranging and overlapping causes but are poorly reported and subsequently may not receive enough attention. Swallowing comprises a series of interconnected phases, whereby disruption can occur at any stage. The greatest risk of swallow impairment is penetration and aspiration with development of chest infection and its associated mortality.

Dysphagia can occur in any person, whether it is part of the natural aging process, brain injury, or a neuromuscular disorder. Given the complex nature of deglutition, we recommend that people who are deemed at risk of dysphagia by a health

professional (due to diagnosis or reported symptoms) should undergo swallow screening and assessment. This would then determine the need for diagnostic assessment. This will be further expanded in the next section.

3 Assessment

In order to prevent the consequences of swallowing problems, it is crucial to be able to identify those at risk or with impairments who need expert management. Complete swallow assessment is time-consuming, so initial screening tools have been proposed to allow a more targeted approach.

3.1 Screening

Screening for swallowing problems is recognized as the first part of a holistic swallow assessment. Screening can usually be completed by any health professional and is mandatory within 24 h in some locations for all people who have had a stroke (Cichero et al. 2012).

Screening is not intended as a substitute for a comprehensive assessment. It is intended to identify symptoms of dysphagia and signs of swallow impairment and therefore identify those who may require comprehensive assessment by a speech pathologist (Martino et al. 2009).

Various screening tools are available within the literature. Broadly speaking, these cover areas which can be examined by any health professional (Cichero et al. 2009; Martino et al. 2009; Stewart 2003). Speech Pathology Australia, the Australian SP representative body, suggest the inclusion of:

- Diagnosis: Determining if the person's diagnosis heightens their risk of dysphagia (e.g., stroke, neurodegenerative condition, head and neck cancer).
- Interview: This involves discussing the person's history of swallowing, presenting symptoms (e.g., frequency of overt signs of aspiration, chest infections, feelings of food being stuck).
- Symptoms: Symptoms of slurred speech, facial weakness, drooling, coughing on saliva, weak/absent cough (note: gag reflex is not a predictor of swallowing impairment and is excluded from screening) (Martino et al. 2009).
- Sip test: Where appropriate, patients are given a sip of thin water, and observations are made for coughing, throat clearing, change in voice quality, drooling, and change in respiration. Some debate exists about the validity of water-sip tests, but screening with water-sip tests where appropriate is still recommended in the Speech Pathology Australia Dysphagia Guideline (Cichero et al. 2012; Osawa et al. 2013).

Various local health districts have designed their own adapted version of these screening tools; however, the content remains largely similar. Screening tools are also part of the usual admission process for residential aged care facilities (both high- and low-level care) and often form part of acute-care policy for initial admission screening.

Those who "fail" the screening (i.e., demonstrate signs suggestive of aspiration or other risk factors for swallowing problems) are referred to speech pathology for comprehensive assessment of swallowing, leading to accurate diagnosis and targeted management.

3.2 Comprehensive Assessment

Comprehensive assessment of dysphagia most commonly begins with a functional assessment. This involves an extensive case history, cranial nerve examination, oromotor examination, and food/fluid trial (where appropriate) at the bedside. Further assessment with instrumental measures such as fibreoptic endoscopic evaluation of swallowing (FEES) or videofluoroscopic swallowing studies (VFSS) may be performed although this is not always possible in every setting.

3.2.1 Functional

A speech pathologist begins examination with an extensive case history. Examination of the medical file, previous SP intervention, comorbidities

and medications, current diet/fluids, palliative care phase/PCOC stage, concerns about eating, and recent chest history are reviewed. Preliminary hypotheses are then formed about a person's likely presentation.

Bedside Assessment

The first part of the assessment is determining if a more in-depth assessment is warranted.

Patient Presentation

First and foremost, a patient must be sufficiently alert for assessment. It would be inappropriate to attempt an assessment on a person who is delirious, unable to maintain eye contact, and unable to stay awake to sufficiently swallow a bolus (e.g., 2 min). The lack of alertness will make assessment unreliable and increase risk of aspiration. The decision must be made for each individual by the supervising clinician. Similarly, it may be inappropriate to perform a full assessment on someone with severe pain, and assessment may need to be deferred until pain is controlled.

A patient is observed for their ability to manage their own secretions, the presence of tubes (e.g., nasogastric, nasojejunal, tracheostomy), and their ability to cooperate with an assessment (Cichero et al. 2012).

Cranial Nerve Examination/Oromotor Examination

To begin the physical examination, the speech pathologist observes the oral cavity. Assessment includes the health of the oral mucosa (e.g., pink), moisture, health of the soft tissue (e.g., presence of oral thrush), and dentition (presence of dentures/own dentition, cleanliness of teeth). The odor of the mouth may be observed, and quality of the secretions (e.g., stringy, clear), as well as the pre-existing anatomy of the oral cavity.

A cranial nerve examination will assess those nerves innervating muscles throughout the swallow. The speech pathologist will request the patient to perform a series of movements and will observe symmetry, deviation, range/rate of movements, strength of movements, and sensation. If the patient is unable to follow instructions, the speech pathologist may complete the movements in front of the patient so that they may copy their movements.

- CNV – observe the jaw for range of lateral and opening/closing movements, strength of jaw, strength of masseters, and mandibular sensation, tongue sensation, and taste.
- CNVII – observe the face for closure at rest, droop, sensation to upper face, lip rounding, lip speed during "oo-ee" said in quick, repetitive succession, strength of facial movements, and lip retraction.
- CNIX and CNX – observe the soft palate for symmetry of elevation, and observe nasal emission, voice quality, pitch variation, volume control, and respiration.
- CNXII – examine tongue movement, range and strength of movement, fasciculations, weakness, or atrophy.
- Observe a volitional cough for strength and productivity. Cough reflex testing may also be performed at bedside in some settings (see below).
- Observe and palpate the hyoid for dry swallow strength and perceived range of movement.
- The gag reflex is no longer consistently recommended as part of the assessment as it is innervated by a different nerve than the larynx and pharynx and does not have predictive value (Cichero and Murdoch 2006).

It should be noted that not all parts of the assessment will always be possible. In palliative care, a patient may be highly distressed and only able to tolerate small amounts of oral intake or remain alert for very short periods. In this case, a cranial nerve examination may not be possible in a formal, structured way, and priority may be given to ensuring the person's comfort.

Food/Fluid Trial

If deemed appropriate, the speech pathologist may commence a food and/or fluid trial to determine the most appropriate recommendations.

Positioning

Ideally, a person would be positioned upright for assessment. Recent evidence suggests that sitting at 90 degrees upright may not be best for those

with poor sitting balance or trunk control, as this places undue pressure on their respiration, and that 45 degrees is adequate for this population (Park et al. 2013).

Self-Feeding

It is most useful to assess a person as close to their natural abilities as possible, particularly if the person is at home or will return home. It is important to determine if the person feeds themselves and if they use any prescribed or specific cutlery or other utensils.

To begin, the speech pathologist instructs the subject to take a single bite or mouthful of drink or food. The attending speech pathologist will determine if the food and fluids should be those which the person is already receiving or the safest oral diet (e.g., puree and extremely thick, in most cases).

As the person consumes the food or fluids, observations are made for the oral preparatory/oral phase and the pharyngeal phase. The esophageal phase is not assessed at bedside.

Oral Phase

Observation of the presence of any anterior spillage, oral pooling, bolus control, mastication, oral transit time, and anterior-posterior movement of the bolus is made.

Pharyngeal Phase

Pharyngeal phase: observation of the timing of the swallow, effort required for the swallow, laryngeal movement, voice quality post swallow, coughing, throat clearing, nasal regurgitation, and swallows per bolus are documented. Aspiration may be suspected based on cough response, cervical auscultation, or change in oxygen saturations. Laryngeal movement is not objectively assessed at bedside, but is assessed via palpating the hyoid during the swallow. Assessment of timing of a swallow is not possible at bedside, as the true location of the bolus for swallowing is unknown.

At bedside, the speech pathologist may also try compensatory strategies with the food and fluids, which may allow different recommendations to be made.

In many cases, a bedside examination is all that is available to a speech pathologist for assessment. Though objective measures are considered the "gold standard," these are not necessarily appropriate for someone receiving palliative care or for someone in a subacute facility. It may cause them unnecessary inconvenience, may tire them, and may yield no changes to their management.

3.2.2 Instrumental

Additional ancillary assessments may be considered on a case-by-case basis.

Cervical Auscultation

As part of a comprehensive assessment, a speech pathologist may utilize cervical auscultation to provide aural information about the swallow. It is not suitable as a stand-alone assessment, but can be useful for supporting hypotheses as an adjunct to additional assessments. Cichero and Murdoch (2006) provide an exemplary summary of this method.

Cervical auscultation utilizes a standard stethoscope. Some speech pathologists prefer pediatric stethoscopes, as they better fit under the neck with a firm seal and account for additional skin surface area.

The speech pathologist places the stethoscope with a firm seal, just below the cricoid cartilage and in a central location (Hirano et al. 2001). The patient performs a swallow of saliva, and the speech pathologist observes the normal sounds of the swallow. Usually, two clicks signify (1) the closure of the laryngeal valve and the projection of the base of the tongue to the posterior pharyngeal wall and (2) the opening of the upper esophageal sphincter and the pharyngeal stripping wave (Cichero and Murdoch 2006). Pharyngeal residue may be audible, as well as multiple swallows per bolus. The sounds of swallowing become longer as we age, and this may be perceived by the ear (Cichero and Murdoch 2006). During the observation of quiet respiration, the speech pathologist can often hear the clarity of the breath sounds and if there is any fluid, food, or saliva sitting in the airway.

Pulse Oximetry

The measure of oxygen saturation is another useful adjunct to assessment. Again, this is not suitable for use as a stand-alone assessment but provides useful information about suspected aspiration.

To utilize pulse oximetry, a pulse oximeter is placed on the person's index finger while a food and fluid trial takes place. The baseline oxygen saturation is observed, as well as the usual fluctuations in saturation for that person. The value is observed for change during assessment, and a drop of 2% is significant for indicating the presence of aspiration (Lim et al. 2001). However, most devices have a 2% error rate, so information must be used in conjunction with other clinical indicators to determine the outcome of assessment. As oxygen saturation does not drop immediately at the time of aspiration, monitoring of saturation is necessary for several minutes after the trial.

Cough Reflex Testing

Current research is analyzing the effectiveness of screening patients in acute care utilizing cough reflex testing to assist with identification of silent aspiration at bedside. This is completed with a standard nebulizer mask with free-flow output of 8 L and restricted flow of 6.6 L/min and 0.4–0.8 mol/L of citric acid (Miles et al. 2013). This assists with identification of silent aspiration at bedside. This is useful as an adjunct to assessment to assist with identification of those at risk of silent aspiration. However, the application of this measure may not be appropriate in all settings, particularly in palliative care.

Manometry and Electromyography

Manometry can be used to examine the pharyngeal contraction during a swallow and is conducted by a gastroenterologist. A small tube is passed through the nasal passage into the esophagus. Electromyography is performed with electrodes placed on the skin over muscles of interest or directly into the muscles themselves (Cichero and Murdoch 2006).

With these measures, pharyngeal and esophageal contractions are measured for effectiveness. Again, this may be a useful adjunct for some assessments, but application in palliative care and subacute settings is limited due to the absence of radiological machines and the patient status (i.e., invasive investigations may not be appropriate).

Fibreoptic Endoscopic Evaluation of Swallowing (FEES)

Fibreoptic endoscopic evaluation of swallowing (FEES) is an instrumental evaluation technique that can be performed at bedside but requires specialized equipment and a trained clinician familiar with endoscopy. Also known as functional endoscopic evaluation of swallow, this involves the insertion of a flexible endoscope (fiberoptic or videoscope) passed per naris Assessment is made of anatomy, function, secretions, and sensation alongside evaluation of penetration, aspiration, and regurgitation when the subject is given food or fluid or swallows saliva. The study can be tailored to the individual's needs and abilities, and the clinician must have clear goals for the study and appreciate the anatomy and function of the laryngopharynx when performing this evaluation.

FEES can provide invaluable information about laterality of deficits, secretion management, compensatory strategies, and swallow safety. It is quick to perform and usually well tolerated. There is no exposure to ionizing radiation and FEES may be performed in both adults and children. Impediments to utilizing FEES include the cost of equipment and need for training, patient discomfort and nasal access issues, difficulty in performing in those with poor cognition, "whiteout" effect wherein the view is obscured mid-deglutition as the pharynx constricts around the endoscope, and ability to clean and disinfect endoscopic equipment. FEES may also be used as a training tool through biofeedback wherein the patient can watch the video screen and practice maneuvers that alter swallows. Examination can be recorded to video files allowing review at leisure and by clinicians not present during the performance of the study.

With the advent of efficient battery-powered endoscopes, FEES is more accessible than

previously and may represent the instrumental evaluation that is easiest to achieve in a palliative setting, given the difficulty in moving ill patients to radiology suites for videofluoroscopic evaluations.

Videofluoroscopic Swallow Study (VFSS – Also Known as Modified Barium Swallow, MBS)

VFSS (previously termed modified barium swallow – MBS) is a dynamic, real-time videofluoroscopic swallow evaluation. Ionizing radiation is administered to obtain images through a fluoroscope, and therefore this must be performed in a radiological facility by a speech pathologist or medical radiation technologist +/− a radiologist (Figs. 3 and 4).

The VFSS utilizes barium sulfate (either powder or liquid) as a contrast agent which is then mixed with food and fluids.

The patient is positioned upright for assessment, and contrast is consumed. On VFSS, the following areas are visible (in addition to those seen at bedside):

- Base of the tongue to the posterior pharyngeal wall contraction
- Bolus cohesion
- Soft palate retraction and elevation
- Contraction of the pharyngeal constrictors
- Deflection of the epiglottis (Fig. 3)
- Elevation and anterior movement of the hyoid
- Opening of the upper esophageal sphincter
- Passage of the bolus through the pharynx to the esophagus and stomach
- Airway violation (aspiration) (Fig. 4)
- Residue or bolus oscillation

On VFSS, some anatomic abnormalities may be observable. These include osteophytes, diverticula, and cricopharyngeal bar. VFSS provides an excellent overview of the swallowing function from the oral cavity to stomach. It delivers a raft of information which can inform management and allows testing of any potential rehabilitation and compensatory strategies, as well as the safest food and fluid consistencies. By using quantitative measures, further data may be extracted from VFSS (Leonard and Kendall 2014; Leonard et al. 2000; Miles et al. 2015, 2016) and compared to well-documented normative data for age and

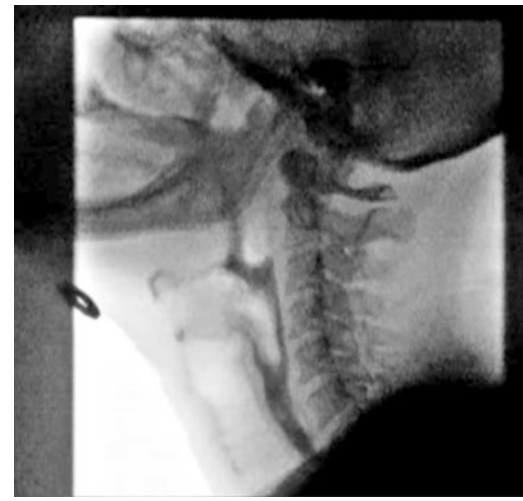

Fig. 3 Lateral fluoroscopic view mid-swallow demonstrating retroflexed epiglottis outlined by barium bolus with hyoid elevation and closed airway anteriorly and bolus flowing through the open pharyngoesophageal segment posteriorly

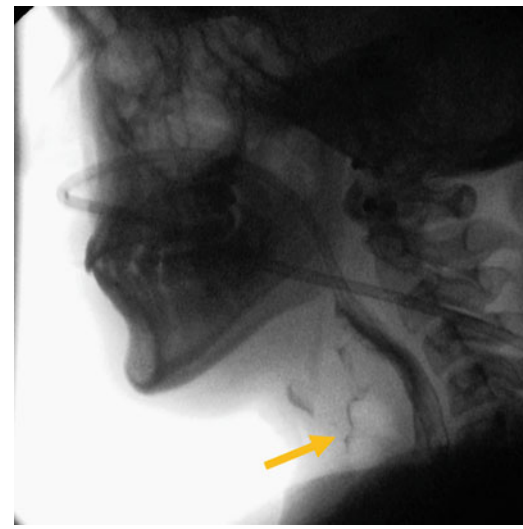

Fig. 4 Lateral fluoroscopic view mid-swallow demonstrating aspiration of bolus into the airway anteriorly (*short arrow*) with majority of the bolus passing posteriorly through the pharyngoesophageal segment. Note a nasogastric tube is in situ

gender. As exposure to ionizing radiation occurs, it behoves the clinician to maximize the value of the study. VFSS should not be considered a binary test of aspiration alone.

4 Intervention

The combination of functional and instrumental assessments allows the multidisciplinary team to make recommendations for diet and management. The SP provides recommendations regarding the safest oral diet (if any), environmental support, behavioral strategies, and rehabilitation and may support discussions regarding choice making for quality of life. Otolaryngologists, physicians, oncologists, and supervising medical personnel can provide additional advice regarding surgical options and pharmacological treatments.

4.1 Non-pharmacological

Non-pharmacological interventions are most commonly guided by a speech pathologist. These vary from compensatory techniques (behavioral strategies, food/fluid modification, environmental modification, and symptom management) to rehabilitative exercises and to a quality-of-life approach which places the emphasis on choice-making.

4.1.1 Compensatory

Behavioral Strategies

Behavioral strategies are those designed to optimize the safest oral diet by teaching a person to perform an action before, during, or after a swallow. It should be noted that these may be conservatively used in palliative care, and only under the direction of a speech pathologist and medical team. This might involve the following:

- Head tilt/rotation – tilting the head or turning it to the side of weakness, directing the bolus to the stronger side (Logemann 1998; Logemann et al. 1989).
- Chin tuck – tucking the chin in toward the chest to widen the pharyngeal space (Logemann 1998).
- Body posture – this may involve side lying to the stronger side, allowing a person to swallow and clear residue with the aid of gravity (Sura et al. 2012).
- Supraglottic swallow – a swallow is performed followed by an immediate cough; the cough is *not* preceded by breathing in (intended to clear material in the airway) (Martin et al. 1993).
- Super-supraglottic swallow – a supraglottic swallow is performed with the addition of an effortful swallow (Martin et al. 1993).
- Multiple swallows – several swallows to ensure clearance of a bolus and any remaining pharyngeal residue.
- Effortful swallow – swallowing as hard as you can to increase hyolaryngeal excursion, oral and pharyngeal pressures, and subsequent movements (Kahrilas et al. 1991).

This is not an exhaustive list of all behavioral strategies, but those most commonly utilized and those that may apply to the palliative care setting. More rigorous approaches (such as neuromuscular electrical stimulation – NMES) are not appropriate for the palliative care setting (Xia et al. 2011).

Food/Fluid Modification

Food and fluid modification is designed to ensure a person is able to adequately manipulate, form, and swallow a bolus with minimal residue and minimal entry into the airway. Thicker viscosities may slow the bolus transportation; softer foods make it easier to chew or moister to allow for better cohesion.

The names and definitions of food textures vary across the globe; however, they generally involve:

- Full/normal – unmodified food.
- Soft/texture A – food with lumps up to 1.5 cm in size. Food should be well cooked, moist, and fork mashable (some networks break this further into two levels of soft diets).

- Minced/texture B – has small lumps (up to 0.5 mm), which are moist and soft. Lumps should be tongue mashable.
- Puree/texture C – smooth, lump-free food that holds its shape on a spoon.

Fluid consistencies also vary, but they are generally:

- Thin/normal – unmodified fluids
- Mildly thick/level 150/nectar/level 1 – runs through the prongs of a fork in a continuous stream
- Moderately thick/level 400/honey/level 2 – runs through the prongs of a fork slowly in large drips
- Extremely thick/level 900/pudding/level 3 – sits on a fork and does not run through

Given the numerous labels of each classification, as well as the variety across the world, Cichero et al. (2013) sought to develop standardized classification for terminology. The "International Dysphagia Diet Standardisation Initiative" (IDDSI) recommends a total of ten textures, on a continuum labeled from 0 to 7. Most noticeably, there has been a suggested addition of "slightly thick" and "liquidized" diet. Slightly thick refers to fluids which naturally occur and are thicker than normal fluids, and liquidized foods refer to smooth, lump-free and liquid food (moderately thick). The latter is a very useful diet in palliative care (as well as in other settings), particularly for those that prefer drinking to eating (such as those with MND, dementia, or esophageal cancers).

There remains a great variety in the application of recommended diets. Standardization is not yet mandatory, and communication between speech pathologists is vital to prevent incorrect diet and fluid provision. This standardization project shows great promise for improving the continuity of modified diets and fluids across the world, reducing confusion, and improving quality of life for patients.

Free-Water Protocol

A speech pathologist may recommend modified diet and fluids, but may also make suggestions for a "free-water protocol" to assist with hydration and maintenance of quality of life.

The Frazier Free Water Protocol involves the provision of as much thin water as desired to a patient (Panther 2005). Criteria for recommended use of this protocol include nil excessive choking and subsequent physical stress, waiting for 30 min after a meal, use of any recommended swallowing strategies, diligent oral care, medications with thickened fluids/fruit puree, and family education. Karagiannis and Karagiannis (2014) provided additional criteria of good mobility and cognition, resulting in nil significant increase in rates of aspiration pneumonia and significantly improved quality of life of participants. Research remains inconclusive about the overall effectiveness in increasing hydration, and implementation should be at the discretion of the supervising clinicians.

Environmental Modification

In addition to the above strategies, environmental modification may be utilized to aid safe swallowing without requiring the person to change their behavior. Environmental modification may involve altering the method of feeding, distractions, and the local environment. For example:

- Use of a straw or spout cup – moderates the bolus flow and amount and assists with poor upper limb control.
- Use of adapted cups (e.g., cutout cup) – moderating the amount that can flow from the cup with the maximum tipping of the cup.
- Use of finger foods – useful for those who eat well with their hands but not with cutlery or other utensils.
- Reduction of local distractions – ensuring a person is focused on their meal by turning off the television and reducing the number of people in the room (Kyle 2012).
- Eating with the patient to provide a model of eating behavior (also often useful for those with dementia).
- Providing six smaller meals instead of three large meals to reduce the burden of eating large meals.
- Dentition may affect texture choices. Ill-fitting dental appliances can be an impediment and

cause xerostomia. Loss of dentition may make eating solid foods impossible, and input of a dentist may help in some cases.
- Lubrication is crucial to deglutition. Saliva helps form the bolus, initiates digestion, protects the mucosal lining and dentition, provides antibodies and antibacterial molecules, mechanically flushes oral and pharyngeal spaces, and dissolves tastants in food. Xerostomia is a common consequence of disease treatment, particularly radiotherapy and medications. It must be considered and compensated as far as possible with introduced hydration, minimizing drying medications, moisturizing food, and meticulous dental hygiene (see ▶ Chap. 20, "Mouth Care").

Feeding Strategies

Feeding strategies may be useful with presenting symptoms. These can be implemented by carers and professionals and for those persons who require full assistance with feeding. As always, a person should only be fed when they are alert and able to swallow.

- Alternate between food and fluids to assist with washing away oral and pharyngeal residue.
- Alternate between tastes, textures, and temperatures (Easterling and Robbins 2008).
- Alternate between bolus and an empty spoon – light pressure on the tongue with the spoon may assist with initiating a swallow.
- Gentle touch may increase nutritional intake and attention to the meal (Eaton et al. 1987).
- Discuss the food taste, smell, and color (Wasson et al. 2001).

Independence is always encouraged and, for the most part, yields better swallowing. However, feeding strategies assist with swallow stimulation for someone whose initiation is compromised.

Symptom Management

In some cases, it may be appropriate to recommend rehabilitative exercises to improve the function of a swallow. These are rarely used in palliative care and are most commonly recommended in a rehabilitation setting.

4.1.2 Rehabilitative

- Masako – this involves placing the tongue between the upper and lower teeth and holding it in position while swallowing. The Masako improves the base of the tongue to posterior pharyngeal wall contraction (Fujiu and Logemann 1996).
- Mendelsohn – this involves raising the larynx and consciously inhibiting the lowering of it for a sustained period. The Mendelsohn assists with opening the upper esophageal sphincter (McCullough et al. 2012; Mendelsohn and McConnel 1987).
- Shaker – this involves lying in supine, keeping the shoulders on the bed, and lifting the head to look at the toes, thereby improving the anterior movement of the larynx and the opening of the UES (Shaker et al. 1997).

4.1.3 Choice Making

Above all, the primary consideration of the speech pathologist for the person receiving palliative care is their ability to choose what they wish. A speech pathologist may make recommendations which are believed to be the safest based on available evidence, but the person may at any time elect their preferred diet and fluids.

At the forefront in all forms of healthcare is the necessity to treat each person as an individual. A person may wish to accept the risks and consequences of aspiration, or they may wish to take a more conservative approach. They may choose to have a combination of approaches or implement the Frazier Free Water Protocol.

It is the role of the speech pathologist and the multidisciplinary team to educate the patient and family, ensure they feel able to make a choice, and assist them in carrying out their wishes to ensure their quality of life is maximized.

4.2 Pharmacological

Medication is part of holistic care of the terminal patient. They may require analgesics and regular medication for comorbid conditions. In addition they may receive treatment-specific medication such as chemotherapy. All medications may

have side effects, some of which can impair deglutition. As mentioned, drying of the pharyngeal lining impairs swallow and can result in pain or opportunistic infection, particularly *Candida* spp. Careful consideration should be given to current medications and their risk benefit profile, as well as any new proposed or introduced medications.

Pharmacological therapies that may offer benefit for swallow disorders include lubricants (artificial saliva, lozenges (sugar-free), gum (sugar-free), and alginates), antacids (H2 blockers, proton pump inhibitors, binders/alginates), analgesics which allow swallow without pain, prokinetic agents (domperidone, metoclopramide, erythromycin) which enhance esophageal function and help secretion control, anti-inflammatories (non-steroidal and steroidal), and antifungals. Each medicine should be carefully evaluated and considered in conjunction with other current medicines to avoid drug interactions. There are no specific medications to "treat dysphagia," and use of medicines will be determined by symptoms and comorbid disease. Rarely should drying medications be used as these typically result in thickening of sputum and make it more difficult to clear. In specific cases amitriptyline given at 10 mg nocte may reduce overall saliva production without severe side effects, but all medications should be discussed with the supervising clinicians.

4.2.1 Surgical

Rarely is surgery appropriate in palliative care, although a terminal illness is not a complete contraindication to targeted surgery. Again, each individual case will require appropriate consideration. For example, airway protective procedures such as injection laryngoplasty or medialization may be very helpful in preventing choking and aspiration. This improves quality of life and communication during a patient's final days. For some, an injection laryngoplasty may be performed in the clinic under local anesthetic, obviating the need for general anesthesia and speeding recovery. There are several other procedures to protect the airway such as laryngeal framework surgery (arytenoid adduction), tracheostomy, laryngeal suspension, or laryngotracheal separation; however, these are increasingly invasive and often not appropriate in a palliative care setting.

Dilatation of aerodigestive sphincters, strictures, rings, or bars may be appropriate as these can often be accomplished under local anesthetic or sedation and may improve bolus transit and reduce residue that predisposes to airway violation. Feeding tube placement such as percutaneous endoscopic gastrostomy (PEG) may be undertaken during treatment and in place when patients transition to palliative care. These can be invaluable as a medication delivery system and to provide adequate hydration but have not been shown to significantly reduce mortality associated with aspiration. Nutritional supplementation can also be provided but must be undertaken after careful discussion with a dietitian and palliative care consultant. Cricopharyngeal myotomy or botulinum toxin injection of the cricopharyngeus muscle may improve swallow in patients with obstructive pharyngoesophageal segments. Onabotulinum toxin can also be utilized for laryngeal spasm or cervical dystonia and has been used to reduce saliva output from the submandibular glands in some cases.

5 Conclusion and Summary

When an individual is approaching the end of their life and is aware of a terminal diagnosis, the ability to communicate and to be part of social events with family and friends is of the utmost importance. Nearly all social situations include eating, and when this is impaired, there can be a significant decrement in the quality of life for the individual. Many patients will experience swallowing difficulties as a result of their disease process, the treatment of the disease whether it be surgical or medical, and of increasing frailty and deconditioning. Palliative care teams should be aware of the high prevalence of swallow impairment and should directly inquire about symptoms and observe for signs of disordered deglutition. Early and frequent assessment by speech pathologists can provide a marked improvement in swallow function and reduction in risk associated with

poor swallowing. Limiting pulmonary soiling is vital in maintaining health, and a competent swallow is at the heart of this.

Simple dietary and behavioral measures can be employed to facilitate swallowing. Careful medication management will minimize xerostomia and reduce pain. Targeted surgical procedures may minimize airway violation or treat strictures. Non-oral feeding can maintain nutrition but deprives the individual of the pleasure of food. Even taking a small amount of oral diet or liquid for pleasure should be considered, particularly in the terminally ill. At times, the risk of aspiration may be accepted where the overall quality of life gain from eating outweighs the swallow risk – a decision that only the patient can make. The most important approach is to involve all team members and the patient to individualize the treatment plan so that each patient receives the options most suited to their needs. Education of the individual and their family around safe eating practices, food preparation, and compensatory strategies can go a long way to mitigating swallow risks. It also empowers the patient and their support network allowing them to plan day-to-day life. At all times the patients' wishes and preferences must be at the core of recommendations and management strategies.

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Mucositis

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Emma Bateman, Richard Logan, Rachel Gibson, and Dorothy Keefe

Contents

Abstract

Mucositis is an inflammatory reaction of the mucosa of the alimentary tract (AT) caused by chemotherapy, radiotherapy, and targeted therapy for cancer. It presents a significant burden not only to patient quality of life but also may result in diminished tumor control (through dose reductions) and increased treatment costs (due to extended hospital stays and supportive care). Mucositis symptoms may vary not only due to the treatment modality but also according to genetic predispositions of the patient toward developing toxicity (toxicogenomics). Management of mucositis is at present supportive only, with treatments that reduce incidence, severity, and duration of clinical symptoms, but do not prevent or cure mucositis altogether. A great deal of current research into the mechanisms involved in development and progression of mucositis is also being carried out; it is hoped that a clear understanding of mucositis pathophysiology, along with comprehensive toxicogenomics, will enable more preventative treatments to be developed.

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_17

Abbreviations

5-FU	5-fluorouracil
AT	alimentary tract
BF	Bayes factor
CAM	complementary and alternative medicine
CT	chemotherapy
GI	gastrointestinal
GLP	glucagon-like peptide
H_2BT	hydrogen breath test
HSCT	hematopoietic stem cell transplantation
IL	interleukin
LIL	low-intensity laser
LLLT	low-level laser therapy
MASCC/ISOO	Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology
mAb	monoclonal antibody
MMPs	matrix metalloproteases
mTOR	mechanistic target of rapamycin
NCI-CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
NF-κB	nuclear factor kappa B
OM	oral mucositis
PRO	patient-reported outcome
QOL	quality of life
RCT	randomized controlled trial
RT	radiotherapy
SBS	short bowel syndrome
SBT	^{13}C-sucrose breath test
TAT	targeted anticancer therapy
TBI	total body irradiation
TKI	tyrosine kinase inhibitor
TLR	toll-like receptor
TNF	tumour necrosis factor
WHO	World Health Organization

1 Introduction

Mucositis is a common side effect of cancer treatment and affects the entirety of the alimentary tract (AT). It occurs in 50–100% of cancer patients (Gibson and Stringer 2009) receiving cytotoxic treatment including chemotherapy (CT), radiotherapy (RT), targeted anticancer therapy (TAT), and combinations thereof. It presents with various signs and symptoms, including ulceration, xerostomia, pain, nausea, vomiting, and diarrhea. These clinical symptoms significantly impact not only patient quality of life (QOL) but may lead to treatment reduction or cessation, which severely impacts the effectiveness of cancer treatment (Lalla et al. 2014). Furthermore, the fiscal burden of mucositis is substantial, costing approximately 25,000 US dollars per cycle of chemotherapy in increased hospital stays due to complications (such as infection, malnutrition, and dehydration) and supportive care resources (Carlotto et al. 2013). The importance of mucositis prevention and intervention is paramount and is contingent upon a firm understanding of the underlying pathophysiology.

Mucositis literally means "inflammation of the mucosa," with factors including (but not limited to) ulceration, pain, and diarrhea manifesting as clinical symptoms, rather than distinct conditions. However, mucositis is often used as a blanket term to describe both the cause and the symptoms (Keefe 2006). Mucositis is also often used to refer solely to oral mucositis (OM); however, it can occur in any region of the AT; care must therefore be used regarding terminology in this field (Keefe 2006).

Slight structural and functional differences delineate the distinct regions of the AT (Keefe 2004). It is these divergences that may underlie the development of distinct clinical symptoms specific to certain regions, for example, xerostomia occurring in the oral cavity and diarrhea occurring in the lower GI tract (Keefe 2004; Sonis 2011). It is also apparent that different cancer treatments can cause distinct conditions, a finding made evident with increasing use of targeted anticancer therapy (TAT, such as TKIs, mAbs, and mTOR inhibitors), whereby symptoms of mucositis are ostensibly observed, but with possibly different underlying mechanisms and responses to treatment than those caused by CT or RT (i.e., aphthous ulcers with mTOR inhibitor use (Peterson et al. 2016; Van Sebille et al. 2015)). This is most probably due to the difference in therapy targets (and consequent off-target effects)

(Keefe and Bateman 2012) but is no doubt compounded by regional characteristics of the AT (Keefe 2004; Van Sebille et al. 2015).

Recent studies in our laboratories (Van Sebille et al. 2015; Bowen 2014; Bowen et al. 2014) have suggested TAT, in particular ErbB tyrosine kinase inhibitors, induced diarrhea in very different ways. This comes from a preclinical model demonstrating no significant histopathology in the small and large intestines of rats following TAT treatment for up to 28 consecutive days, despite developing consistent diarrhea (Bowen 2014; Bowen et al. 2014). In contrast, our findings in traditional preclinical chemotherapy and radiotherapy models have demonstrated significant damage throughout the gastrointestinal tract associated with diarrhea and other clinical indicators of mucositis including diarrhea (Gibson et al. 2003; Bowen et al. 2006; Gibson et al. 2005; Logan et al. 2007a; Yeoh et al. 2007; Bateman et al. 2012).

Current understanding of the underlying pathophysiology of mucositis is based largely upon preclinical animal models, made useful by the fact that observation and sampling of patient tissue can be difficult, particularly with GI mucositis. The findings of these animal models lead to the development of Sonis' widely accepted five-phase model of mucositis (Sonis 2004) (Fig. 1). These phases are essentially a biological sequence of dynamic events that depends on effective communication between the epithelium and the mesenchyme; Fig. 1 shows each stage and the linked yet divergent nature of CT/RT-induced mucositis versus TAT-induced mucositis. Stage IV, which is the loss of epithelial integrity, is the symptomatic phase, and the phase against which the vast majority of treatments are used to assuage symptom severity and duration. However, the most effective interventions would be those targeting earlier stages, in order to prevent or reduce the development of mucositis.

While the AT has several distinct regions (oral, gastrointestinal, colorectal) that manifest distinct clinical symptoms in response to injury, the AT mucosa is also a continuum, whereby symptoms of injury are often underpinned by similar pathophysiologies (Al-Dasooqi et al. 2013) and do not occur in isolation. Applications of distance matrices are beginning to answer some crucial questions regarding toxicity clustering, such as whether severity of clustered toxicities are also linked, whether risk for one implies risk for another, and whether certain toxicities occur more frequently together than others. Bayesian analysis of retrospective patient data compares pairs of toxicities and whether the toxicities are related. The strength of association is known as Bayes factor (BF), and BF >1 shows some evidence of association, BF >3 supports a strong evidence of association, and BF >7 provides decisive evidence in favor of association. The limitation with Bayesian analysis for toxicity clustering is that it can only detect a link between one other toxicity; Markov network, based on Bayesian analysis, can detect more than one link and allows for development of closed loops or clusters of related toxicities. Recent studies (Aprile et al. 2008, 2009) have generated toxicity clusters and loops for common toxicities experienced by 300 adult colorectal patients receiving chemotherapy using Bayesian and Markov analysis, showing that many toxicities heretofore treated as discreet can be clustered together due to strong associations. These clusters may have a common pathobiology which may lead to a common treatment, reducing the incidence, severity, and duration of the entire cluster, which would greatly improve QOL and possibly increase cancer cure. Nevertheless, more work is needed to show if this holds for other cancers and other treatments.

Effective treatment needs to be similarly multidisciplinary yet holistic, as it is becoming increasingly evident that cancer treatment toxicities exist in clusters (Aprile et al. 2008; Walsh and Rybicki 2006). In the burgeoning field of toxicogenomics, patients are being profiled not only for suitability of a cancer treatment to maximize tumor control but also for the treatment that also will elicit the least toxic response.

1.1 Diagnosis and Assessment

The assessment of oral mucositis is relatively straightforward as the oral cavity can be easily

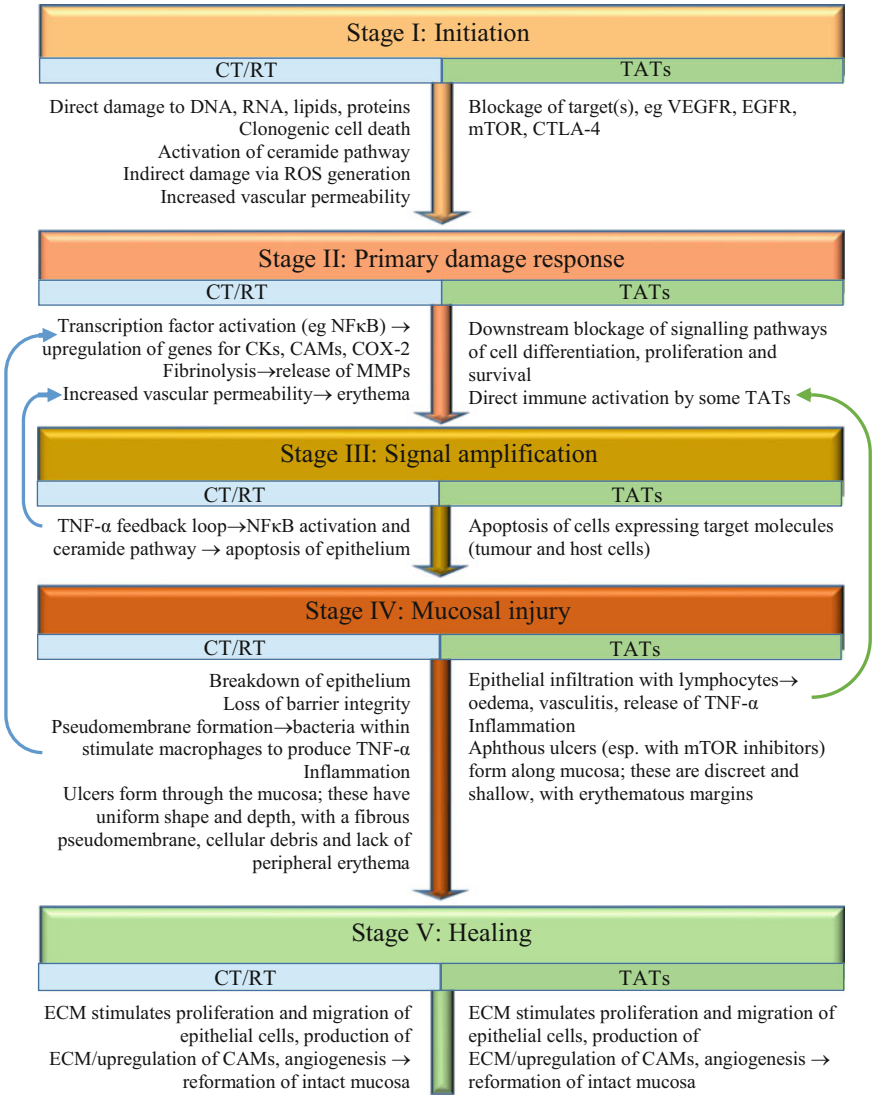

Fig. 1 The five-phase model of the pathophysiology of mucositis (Modified from Keefe and Bateman in press)

visualized and, for many patients undergoing cancer treatment, the development of oral mucositis is predictable. For example, patients undergoing conventional head and neck radiotherapy for oral squamous cell carcinoma will most often start to develop mucositis in the form of oral pain and erythema within the field of radiation early in their course of treatment. Subsequently, this will usually progress to obvious oral ulceration that continues throughout the remainder of their radiotherapy and begin to resolve on the completion of the treatment. Likewise, the majority of patients undergoing hematopoietic stem-cell transplantation (HSCT) will develop mucositis along with many other oral complications in the course of their treatment (Elad et al. 2015). Different chemotherapy regimens are associated with different risks of the development of mucositis depending on the drugs that are used; furthermore, a combination of chemotherapy with radiotherapy also increases the risk (Al-Mamgani et al. 2013). Improvements in the provision of radiotherapy (e.g., intensity-modulated radiotherapy) have

allowed a treatment to be more targeted; however mucosal toxicity still occurs (Hoffmann et al. 2015).

Oral mucositis can present as a spectrum of changes that are evident clinically, dependent on the timing of cancer treatment. Initially it can present as areas of mucosal erythema accompanied by pain (Fig. 1). This evidentially develops into more widespread, confluent areas of ulceration (Fig. 1) associated with significant pain. This is associated with increasing functional problems including the need for parenteral nutrition in some patients and, in the "worst case" scenario, the need to suspend treatment. This has implications for the effectiveness of the cancer treatment and is a major reason why mucositis needs to be effectively managed.

The clinical diagnosis of oral mucositis, while generally straightforward, can be made more complicated by other adverse effects that can affect the oral cavity, including salivary gland hypofunction, oral infections (e.g., candidiasis), dysgeusia, increased dental caries, and osteoradionecrosis. Furthermore, the increasing use of chemotherapy regimens with newer targeted agents have resulted in the occurrence of other toxicities that manifest in the mouth, including osteonecrosis and risk of hemorrhage. Accordingly, it is important that assessment by a dentist or health professional with experience in assessing the oral mucosa is undertaken, in order for patients to have optimal oral health prior to the commencement of their cancer treatment, and it is also important for a dentist to be available to monitor their oral health and function as they proceed through their treatment. This enables patients to have the optimum treatment and also the optimum quality of life during their treatment (Elad et al. 2015; McGuire et al. 2006).

Unlike the oral cavity, the remainder of the alimentary tract is not easily visualized clinically, and assessment is therefore difficult, relying on patient-reported symptoms. Endoscopic evaluation of patients is often complicated by other factors including increased risk of infection from myelosuppression and also thrombocytopenia. Recent reviews have highlighted the potential for tests that indirectly indicate gut damage that can be used to assess the degree of gastrointestinal mucosal injury occurring as a result of cancer treatment (Tooley et al. 2009; Gibson and Bowen 2011). Ideally, this would be done prior to the development of gastrointestinal symptoms of abdominal bloating, pain, and diarrhea so that these can be prevented or managed before they become so severe that treatment regimen modification or cessation is required. Alternatively, the use of biomarkers could indicate the extent of intestinal damage so that patients can be appropriately provided additional support (e.g., parenteral nutrition) on the basis of objective assessment criteria (Herbers et al. 2010).

The measurement of plasma citrulline levels has been promising as a marker for small intestinal damage (Herbers et al. 2010; Lutgens et al. 2003). Physiologically, citrulline levels in the plasma provide a surrogate marker for small intestinal epithelial cell mass (Lutgens and Lambin 2007). In the setting of radiation damage from total body irradiation as part of treatment for hematological malignancies (Lutgens et al. 2005) or abdominal fractionated radiotherapy (Lutgens et al. 2004), plasma citrulline levels correlated with clinical toxicity grading. Furthermore, plasma citrulline levels have been shown to be able to differentiate between different myeloablative chemotherapy regimens and the degree of intestinal damage between regimens (Herbers et al. 2010). Another factor that is important from a clinical perspective is that the use of citrulline as a marker of regimen-related intestinal damage has also been demonstrated in a pediatric population (van Vliet et al. 2009).

Noninvasive tests have also been examined with respect to the assessment of intestinal damage with respect to small intestinal function. Examples of these tests include the hydrogen breath test (H_2BT) and the ^{13}C-sucrose breath test (SBT) (Howarth et al. 2006). Both tests are simple breath tests that are noninvasive, assess small intestinal function, and pose essentially no risk to patients (Tooley et al. 2009). H_2BT does have some limitations in that it relies on the presence of hydrogen-producing bacteria residing in the colon and can be influenced by diet and antibiotic use (Tooley et al. 2009). The SBT is an

indicator of sucrase activity and integrity of brush border and enterocyte function, and in the context of gastrointestinal mucositis, small intestinal sucrase activity is reduced (Tooley et al. 2009). Both animal and clinical trials have demonstrated its potential effectiveness as a marker of intestinal damage in chemotherapy-associated small intestinal mucositis (Tooley et al. 2009; Pelton et al. 2004). While promising, SBT, like H_2BT, has limitations. The timing required to implement the test requires multiple tests every 15 min over a period of 2 h, which for some patients may not be practical. Furthermore, the lack of availability of specialized equipment required for the analysis of samples may also preclude its use in some centers (Gibson and Bowen 2011).

Despite these limitations, the need for a noninvasive marker to assess intestinal damage in patients undergoing cancer is important in order to effectively monitor and manage these patients during treatment, before clinical symptoms become a burden.

1.2 Comprehensive Assessment

Objective and comprehensive assessment of cancer treatment toxicities is paramount in their effective management. Gone are the days when clinician-reported outcomes using variable scoring systems solely dictated symptom management, often at the cost of patient quality of life. Nowadays, there are validated scoring systems used worldwide to assess and report cancer treatment-related toxicity, and it is increasingly common for patient-reported outcomes (PROs) to be considered when deciding on treatment modifications and supportive care measures. It has long been established that the severity of mucositis and its symptoms are often underreported (Bateman and Keefe 2011).

The most commonly used assessment tool to measure oral and GI mucositis is the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (NCI-CTCAE, current version 4.03; Table 1). However, it must be recognized that some Asia-Pacific regions continue to use the World Health Organization (WHO) scoring system (Table 1). For the most part, these grading tools align well; however, some disparities mean that some toxicities may be underreported or missed entirely, for example, if the WHO scale is used instead of the NCI-CTCAE for OM, where NTC-CTCAE grade 3 OM is described as severe, but grade 3 OM delineated by WHO criteria only describes mild symptoms and does not extend to downstream events (Table 1). Limitations are also evident when considering the WHO criteria in treating nausea and vomiting as a single toxicity, which may result in over- or under-reporting. These gaps may be widened further when patient-reported outcomes (PROs) are taken into account in toxicity reporting. This often renders the development of evidence-based clinical guidelines difficult; to perform best practice based on best evidence, we need to use a standardized, validated scoring system.

For toxicity reporting in targeted therapies, modified scoring systems are the most useful; for example, even though mTOR inhibitor use is associated with the development of mouth ulcers (as is the use of CT and RT), the etiology is somewhat different, with ulcers being described as aphthous; standard OM scoring systems will thus misrepresent the true manifestation of the toxicity. Thus, tools are increasingly being developed which adequately capture unique or unexpected toxicities; universal adoption and dynamic updating of these tools is crucial in order to best provide care for all patients.

1.3 Guidelines and Management

The importance and benefits of evidence-based medicine have seen progressive development of clinical practice guidelines that are based upon systematic review (Lalla et al. 2014; Rubenstein et al. 2004). It is imperative that these guidelines are continuously updated. For cancer treatment-induced mucositis, the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) has developed such guidelines. However, compared to other treatment-related toxicities (such as fatigue

Table 1 NCI-CTCAE and WHO assessment criteria for mucositis (oral and GI)

Adverse event	Scale	Grade				
		1	2	3	4	5
Oral mucositis	NTC-CTCAE, version 4.03	Asymptomatic or mild symptoms. Intervention not indicated	Moderate pain. Not interfering with oral intake, modified diet indicated	Severe pain. Interfering with oral intake	Life-threatening consequences. Urgent intervention indicated	Death
Oral mucositis	WHO	Mild erythema or ulceration $<1cm^2$	Mild erythema and ulceration $<1cm^2$	Mild erythema and ulceration 1–3 cm^2, or severe erythema and ulceration $<1cm^2$	Severe erythema and ulceration 1–3 cm^2, or mild erythema and ulceration $>3cm^2$	Severe erythema and ulceration $>3cm^2$
Nausea	NTC-CTCAE, version 4.03	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration, or malnutrition	Inadequate oral caloric or fluid intake, tube feeding, or hospitalization indicated		
Vomiting	NTC-CTCAE, version 4.03	1–2 episodes (separated by 5 min) in 24 h	3–5 episodes (separated by 5 min) in 24 h	≥6 episodes (separated by 5 min) in 24 h. Tube feeding, hospitalization	Life-threatening consequences: urgent intervention indicated	Death
Nausea and vomiting	WHO	Nausea	Transient vomiting	Vomiting requiring therapy	Intractable vomiting	–
Diarrhea	NTC-CTCAE, version 4.03	Increase of <4 stools per day over baseline Mild increase in stoma output compared to baseline	Increase of 4–6 stools per day over baseline. Moderate increase in stoma output compared to baseline	Increase of ≥7 stools per day over baseline Incontinence, hospitalization indicated, severe increase in stoma output compared to baseline	Life-threatening consequences. Bloody diarrhea, need for parenteral support. Urgent intervention indicated	Death
Diarrhea	WHO					

or febrile neutropenia), there are relatively few defined guidelines for mucositis interventions, as not only is there is a paucity of well-designed randomized controlled trials but also a lack of a universally validated and universally accepted assessment scale that would allow for a more comprehensive toxicity reporting. The best-established guidelines for mucositis treatment are targeted toward symptom management, such as controlling dehydration caused by diarrhea and vomiting and ameliorating pain caused by ulcers. The MASCC/ISOO guidelines for oral and GI mucositis are presented in Table 2.

There are no established pharmacological interventions available for mucositis, apart from palifermin for the treatment of oral mucositis (Lalla et al. 2014; Spielberger et al. 2004). There are several emerging pharmacotherapies in various stages of investigation and development; however, existing treatments for mucositis are supportive and focus on symptom management. The field of study associated with developing pharmacological interventions for mucositis is often hindered by the lack of comprehensive understanding of the underlying mechanisms; however, a shift in focus from preclinical and clinical study back to in vitro

Table 2 MASCC/ISOO clinical practice guidelines for oral and gastrointestinal mucositis (Lalla et al. 2014)

Oral mucositis	
Recommendations in favor of an intervention	1. That 30 min of oral cryotherapy be used to prevent oral mucositis in patients receiving bolus 5-fluorouracil chemotherapy (II)
	2. That recombinant human keratinocyte growth factor-1 (KGF-1/palifermin) be used to prevent oral mucositis (at a dose of 60 μg/kg per day for 3 days before conditioning treatment and for 3 days after transplant) in patients receiving high-dose chemotherapy and total body irradiation, followed by autologous stem cell transplantation, for a hematological malignancy (II)
	3. That low-level laser therapy (wavelength at 650 nm, power of 40 mW, and each square centimeter treated with the required time to a tissue energy dose of 2 J/cm^2)), be used to prevent oral mucositis in patients receiving HSCT conditioned with high-dose chemotherapy, with or without total body irradiation (II)
	4. That patient-controlled analgesia with morphine be used to treat pain due to oral mucositis in patients undergoing HSCT (II)
	5. That benzydamine mouthwash be used to prevent oral mucositis in patients with head and neck cancer receiving moderate dose radiation therapy (up to 50 Gy), without concomitant chemotherapy (I)
Suggestions in favor of an intervention	1. That oral care protocols be used to prevent oral mucositis in all age groups and across all cancer treatment modalities (III)
	2. That oral cryotherapy be used to prevent oral mucositis in patients receiving high-dose melphalan, with or without total body irradiation, as conditioning for HSCT (III)
	3. That low-level laser therapy (wavelength ~632.8 nm) be used to prevent oral mucositis in patients undergoing radiotherapy, without concomitant chemotherapy, for head and neck cancer (III)
	4. That transdermal fentanyl may be effective to treat pain due to oral mucositis in patients receiving conventional or high-dose chemotherapy, with or without total body irradiation (III)
	5. That 0.2% morphine mouthwash may be effective to treat pain due to oral mucositis in patients receiving chemoradiation therapy for head and neck cancer (III)
	6. That 0.5% doxepin mouthwash may be effective to treat pain due to oral mucositis (IV)
	7. That systemic zinc supplements administered orally may be of benefit to prevent oral mucositis in oral cancer patients receiving radiation therapy or chemoradiation (III)
Recommendations against an intervention	1. That PTA (polymyxin, tobramycin, amphotericin B) and BCoG (bacitracin, clotrimazole, gentamicin) antimicrobial lozenges and PTA paste not be used to prevent oral mucositis in patients receiving radiation therapy for head and neck cancer (II)
	2. That iseganan antimicrobial mouthwash not be used to prevent oral mucositis in patients receiving high-dose chemotherapy, with or without total body irradiation, for HSCT (II), or in patients receiving radiation therapy or concomitant chemoradiation for head and neck cancer (II)
Recommendations against an intervention	1. That sucralfate mouthwash not be used to prevent oral mucositis in patients receiving chemotherapy for cancer (I) or in patients receiving radiation therapy (I)[a] or concomitant chemoradiation (II)[b] for head and neck cancer
	2. That sucralfate mouthwash not be used to treat oral mucositis in patients receiving chemotherapy for cancer (I) or in patients receiving radiation therapy (II) for head and neck cancer
	3. That intravenous glutamine not be used to prevent oral mucositis in patients receiving high-dose chemotherapy, with or without total body irradiation, for HSCT (II)

(*continued*)

Table 2 (continued)

Suggestions against an intervention	1. That chlorhexidine mouthwash not be used to prevent oral mucositis in patients receiving radiation therapy for head and neck cancer (III)[c]
	2. That granulocyte-macrophage colony-stimulating factor mouthwash not be used to prevent oral mucositis in patients receiving high-dose chemotherapy, for autologous or allogeneic stem cell transplantation (II)
	3. That misoprostol mouthwash not be used to prevent oral mucositis in patients receiving radiation therapy for head and neck cancer (III)
	4. That systemic pentoxifylline, administered orally, not be used to prevent oral mucositis in patients undergoing bone marrow transplantation (III)
	5. That systemic pilocarpine, administered orally, not be used to prevent oral mucositis in patients receiving radiation therapy for head and neck cancer (III), or in patients receiving high-dose chemotherapy, with or without total body irradiation, for HSCT (II)
Gastrointestinal mucositis	
Recommendations in favor of an intervention	1. That intravenous amifostine be used, at a dose of $\geq$340 mg/m^2, to prevent radiation proctitis in patients receiving radiation therapy (II)
	2. That octreotide, at a dose of $\geq$100 μg subcutaneously twice daily, be used to treat diarrhea induced by standard- or high-dose chemotherapy associated with HSCT, if loperamide is ineffective (II)
Suggestions in favor of an intervention	1. That intravenous amifostine be used to prevent esophagitis induced by concomitant chemotherapy and radiation therapy in patients with non-small cell lung carcinoma (III)
	2. That sucralfate enemas be used to treat chronic radiation-induced proctitis in patients with rectal bleeding (III)
	3. That systemic sulfasalazine, at a dose of 500 mg administered orally twice a day, be used to prevent radiation-induced enteropathy in patients receiving radiation therapy to the pelvis (II)
	4. That probiotics containing *Lactobacillus* species be used to prevent diarrhea in patients receiving chemotherapy and/or radiation therapy for a pelvic malignancy (III)
	5. That hyperbaric oxygen be used to treat radiation-induced proctitis in patients receiving radiation therapy for a solid tumor (IV)[d]
Recommendations against an intervention (continued)	1. That systemic sucralfate, administered orally, not be used to treat gastrointestinal mucositis in patients receiving radiation therapy for a solid tumor (I)
	2. That 5-acetyl salicylic acid (ASA), and the related compounds mesalazine and olsalazine, administered orally, not be used to prevent acute radiation-induced diarrhea in patients receiving radiation therapy for a pelvic malignancy (I)
	3. That misoprostol suppositories not be used to prevent acute radiation-induced proctitis in patients receiving radiation therapy for prostate cancer (I)

[a]Level of evidence: level I. Evidence obtained from meta-analysis of multiple, well-designed, controlled studies; randomized trials with low false-positive and false-negative errors (high power)
[b]Level of evidence: level II. Evidence obtained from at least 1 well-designed experimental study; randomized trials with high false-positive and/or false-negative errors (low power)
[c]Level of evidence: level III. Evidence obtained from well-designed, quasi-experimental studies such as nonrandomized, controlled single-group, pretest-posttest comparison, cohort, time, or matched case-control series
[d]Level of evidence: IV. Evidence obtained from well-designed, nonexperimental studies, such as comparative and correlational descriptive and case studies

studies (incorporating newer toxicogenomic and metabolic profiling) is likely to contribute greatly to drug development.

1.4 Pharmacological/Interventional Therapies Specific to Mucositis

1.4.1 Palifermin

Palifermin is a human recombinant version of keratinocyte growth factor (KGF-1), a substance that occurs naturally in the body that is involved in growth and repair of the GI mucosa. Palifermin decreases the severity and duration of oral symptoms of mucositis and is indicated for use in patients with hematological malignancies who are undergoing high-dose chemotherapy and total body irradiation (TBI), followed by autologous stem cell or bone marrow transplant. Current MASCC/ISOO guidelines recommend administration of 60 μg/kg/day of intravenous palifermin 3 days prior to TBI conditioning and 3 days following transplant for the prevention of oral mucositis in this subset of patients (Table 2) (Raber-Durlacher et al. 2013). In patients receiving only high-dose chemotherapy (such as melphalan) as a conditioning regimen, it has been shown that palifermin has no significant impact on oral mucositis (Blijlevens et al. 2013; Goldberg et al. 2013), supporting the evidence that the underlying mechanisms of CT- and RT-induced mucositis are slightly different.

1.4.2 Other Pharmacological Agents in Preclinical Trials

GLP-2 Analogues

Glucagon-like peptides (GLPs) are regulatory peptides that are released by L cells of the ileum and colon in response to nutrient consumption. GLP-2, upon binding to GLP-2 receptors, stimulates crypt cell proliferation, aids nutrient absorption, reduces GIT mobility, and reduces epithelial permeability; however, naturally occurring GLP-2 has a very short half-life of approximately 7 minutes, making it impractical as a pharmaceutical agent. GLP-2 analogues created by changes to the N-terminus cleavage site have an increased resistance to enzymatic degradation, thus increasing the half-life to 2–3 hours. The GLP-2 analogue teduglutide has been shown to improve symptoms of a number of debilitating GI diseases (such as Crohn's disease, ulcerative colitis, and short bowel syndrome (SBS)), which have similar symptom profiles as cancer treatment-induced mucositis. Following this, a number of preclinical studies have investigated the effects of GLP-2 analogues on CT-, RT-, and TAT-induced mucositis (Boushey et al. 2001; Kissow et al. 2012, 2013; Rasmussen et al. 2010), and these studies have shown promising results, with increased body weight, decreased inflammatory response, reduced incidence of diarrhea, and improved histological parameters. Progression into phase II and phase III clinical trials has already begun in the case of teduglutide in SBS patients (Schwartz et al. 2016); further studies into mechanisms of GLP-2 analogue-induced improvement of cancer treatment-induced mucositis may precipitate similar progression into clinical trials in the near future.

R-spondin1

R-spondin1 is a protein that is involved in the modulation of the Wnt/b-catenin signaling pathway, which is involved in maintaining the homeostasis of the GI mucosa by promoting epithelial cell growth and regeneration. Several preclinical studies using mouse models have demonstrated R-Spondin1-induced increases in small intestinal length, weight, and diameter, coinciding with increased crypt hyperplasia and maintained tissue architecture and goblet and Paneth cell characteristics (Abraham and Cho 2005; Kim et al. 2005). Other preclinical studies have shown that R-Spondin1 was able to ameliorate RT-induced GI mucositis (Bhanja et al. 2009) and CT- and RT-induced oral mucositis, both oral and GI (Zhao et al. 2009). Further studies have suggested that R-Spondin1 is able to activate stem cells; in mouse models, R-Spondin1 administered to animals following a lethal dose of either 5-FU or whole body or abdominal radiation and was shown to significantly improve the rate of survival compared to controls, presumably through reduced loss of intestinal stem cells, increased

epithelial proliferation and improved intestinal architecture (Zhou et al. 2013). These findings are very encouraging and will hopefully translate into the clinical setting.

1.5 Current and Emerging Therapies

1.5.1 Basic Oral Care

The importance of basic oral care in the prevention and management of oral mucositis has been highlighted in several clinical guideline sets and is recommended for all patients receiving cancer therapy. Systematic review in 2012 resulted in the development of a MASCC/ISOO guideline recommending the use of basic oral care before and during all cancer treatment modalities in patients of all ages, to prevent the development of the symptoms of OM (Table 2) (McGuire et al. 2013). Institution and continuation of oral care protocols (such as brushing, flossing, rinsing, and moisturizing), dental care before initiation of and during cancer therapy, and the use of bland rinses such as normal saline or sodium bicarbonate are likely to play a role in achieving and maintaining a healthy oral environment that is less likely to be involved in the development of OM (Rubenstein et al. 2004).

1.5.2 Cryotherapy

Cryotherapy was first reported as a suitable intervention for oral mucositis in patients receiving 5-fluorouracil (5-FU) in 1991 (Mahood et al. 1991) and has been investigated in a number of clinical trials and meta-analyses since then (Peterson et al. 2013). The therapy is simple and cost effective and based around holding ice within the mouth for up to 30 minutes. The exact mechanisms of action have not been fully elucidated; however, the consensus is that vasoconstriction limits the delivery of cytotoxic drugs to the vulnerable tissue, therefore preventing the development of OM. The MASCC clinical guidelines regarding cryotherapy recommend use in patients receiving bolus doses of 5-FU, edatrexate, and high-dose melphalan as an HSCT conditioning agent (with or without TBI) to prevent and decrease symptoms of oral mucositis (Table 2) (Raber-Durlacher et al. 2013; Peterson et al. 2013). Time of application varies from 20 to 30 minutes; it has been shown that holding ice within the mouth for longer than 30 minutes causes discomfort and that no benefit is gleaned in extending the application period.

1.5.3 Low-Level Laser Therapy (LLLT)

The use of low-level laser therapy (LLLT) is based on the fact that low doses of radiation are beneficial to cells, rather than harmful. LLLT is a phototherapy, which is thought to work by promoting photophysical, photochemical, and photobiological changes in cells through absorption of visible light by endogenous photoreceptors, without inducing excess heat (above 37 °C) (Smith 1991). The most common sources for low-intensity lasers (LILs, representing coherent light) and light-emitting diodes (LEDs, representing incoherent light) are those that emit energy in the red or near-infrared end of the spectrum (in the wavelength range of 630–650 nm) and include the helium-neon laser (632.8 nm), the gallium-aluminum laser (630–685 nm), the helium-neon-arsenate laser (780–870 nm), the gallium-arsenate laser (904 nm), and LEDs (670–950 nm). Use of these wavelengths allows for deep penetration into tissues; additionally, hemoglobin does not absorb these wavelengths, meaning that oxygen delivery into tissues is not adversely affected. It is proposed that LLLT has a biostimulatory effect, causing increased cell proliferation (which aids in wound healing) and anti-inflammatory effects, both of which are required to decrease severity of mucositis.

In the most recent MASCC/ISOO systematic review, no difference between the use of coherent vs incoherent light was found (Migliorati et al. 2013). A recommendation was formed for the use of a LIL (wavelength 650 nm, power of 40 mW, with each square centimeter of tissue being treated for the time required to reach a tissue energy dose of 2 joules per square centimeter) for the prevention of oral mucositis in patients receiving HSCT with high-dose chemotherapy conditioning, with or without TBI (Table 2) (Lalla et al. 2014; Migliorati et al. 2013). A suggestion was

made for the use of a LIL of approximate wavelength of 632.8 nm, to prevent oral mucositis in patients undergoing radiotherapy without concomitant chemotherapy for head and neck cancer (Table 2) (Lalla et al. 2014; Migliorati et al. 2013).

1.5.4 Zinc Sulfate

Zinc is required for tissue repair processes in the body, specifically by exerting antioxidant action. Due to its essential role in epithelial proliferation, synthesis of extracellular matrix, and wound healing, zinc has become a focus as a possible intervention for mucositis. Some small RCTs have found that zinc sulfate (given either as a 0.2% mouthwash twice daily for 2 weeks or as 220 mg capsules (three per day)) results in decreased oral mucositis (decreased pain and xerostomia) as measured by the Spijkervet scale and WHO criteria (Arbabi-kalati et al. 2012; Mehdipour et al. 2011). Based on these studies, a guideline was developed, suggesting the provision of zinc supplements to prevent oral mucositis in oral cancer patients receiving radiation therapy or chemoradiation (Table 2) (Yarom et al. 2013). However, since these studies were performed in small cohorts, further investigations are required for validation.

1.5.5 Probiotics

Lactobacillus spp.-containing probiotics have been shown to be effective in preventing CT- and RT-induced diarrhea in a number of RCTs. MASCC guidelines suggest their use to reduce diarrhea in patients with pelvic malignancies, based on the best available evidence (Lalla et al. 2014; Gibson et al. 2013) (Table 2). While originally being developed to treat symptoms of GI mucositis, recent research has shown probiotics (in lozenge form) reduced the symptoms of peri-implant mucositis (Flichy-Fernandez et al. 2015); however, in another study, no improvement in mucositis was shown (Hallstrom et al. 2016). Despite these conflicting results, it may be valuable to translate the study to a cancer treatment-related oral mucositis setting.

A great deal of work has also been performed in various animal models of CT- and RT-induced GI mucositis, in order to investigate the possible mechanisms of action of probiotics. Studies by Stringer and colleagues have demonstrated that not only is the commensal bacteria within the GI tract essential for homeostasis, but can be adversely affected by cancer treatments and contribute to clinical symptoms of AT mucositis, such as diarrhea (Stringer et al. 2009a, b). A preclinical study using a tumor-bearing rat model of CT-induced mucositis showed that a probiotic mixture, VSL#3, significantly reduced clinical symptoms of mucositis, such as weight loss and diarrhea (Bowen et al. 2007). These clinical improvements correlated with improved histopathology compared to controls, including reduced apoptosis and increased proliferation of crypt epithelia. Similar observations have been reported in other preclinical studies (Prisciandaro et al. 2011); however, the mechanisms underpinning the anti-mucotoxic effects of probiotics remain poorly understood, highlighting the need for a more comprehensive in vitro investigation into the AT microbiome.

1.5.6 Honey

The use of topically applied honey is gaining evidence for effective use, with a number of recent meta-analyses and RCTs showing that honey effectively reduces the incidence, duration, and pain of CT- and RT-induced oral mucositis (Xu et al. 2016; Samdariya et al. 2015; Cho et al. 2015; Song et al. 2012). However, there are often some conflicting findings, and it is widely suggested that more robust clinical trials need to be performed to provide a higher level of evidence (Xu et al. 2016; Samdariya et al. 2015; Cho et al. 2015; Song et al. 2012). The mechanisms by which honey is able to reduce OM are not clear. However, there are a number of hypotheses to explain its effectiveness, including the fact that honey has a very high sugar content, which confers antimicrobial properties (by dehydrating microorganisms). Honey also contains glucose oxidase, which catalyzes glucose oxidation to hydrogen peroxide, a known antimicrobial agent (Xu et al. 2016). It has also been shown honey can promote wound healing through granulation formation and epithelial migration (Al-Waili et al. 2011). One of the key drawbacks is that prolonged

application of honey in the mouth is unpalatable and can give rise to a high dropout rate (e.g., >50% in an RCT investigating manuka honey) (Hawley et al. 2014). More study into this potential intervention for OM is needed for any clinical guideline to be made.

1.5.7 Complementary and Alternative Medicines (CAMs)

There are an increasing number of studies investigating the possible anti-mucositis effects of complementary and alternative medicines (CAMs) (Kuchay 2017), including (but not limited to) ginger (Rangwala et al. 2012), emu oil (Abimosleh et al. 2012; Mashtoub et al. 2016), grape-seed extract (Cheah et al. 2014), and curcumin (Yao et al. 2013); however, these studies are often preclinical models, based on small cohorts, anecdotal, and/or express conflicting data. The majority of these CAMs work by modulating the immune system, decreasing the pro-inflammatory response, and thus potentially assuaging mucositis; much of the work being done at present is in determining CAM mechanisms of action, so that these agents may be advanced into clinical trials as potential treatments of mucositis in the near future.

1.5.8 Other Non-pharmacological Therapies

Barometric Chambers

Studies have shown that the use of hyperbaric oxygen chambers may be effective in alleviating symptoms of lower GI mucositis. There exists a current MASCC/ISOO clinical guideline, suggesting the use of hyperbaric oxygen for treating proctitis in patients receiving radiation for solid tumors (Table 2) (Gibson et al. 2013). Hyperbaric oxygen is thought to work by increasing the oxygen gradient in damaged tissues to promote angiogenesis and healing (Allen et al. 2012).

Yoga, Exercise, and Acupuncture

It is suggested that symptoms of mucositis can be partly alleviated by non-pharmacological means, such as exercise (Stubbe and Valero 2013), yoga (Metri et al. 2013), and acupuncture (Pan et al. 2000). However, studies investigating these treatments are often based on small cohorts and poor study design and/or have conflicting results, making generation of clinical guidelines difficult (Lotfi-Jam et al. 2008).

2 Future Research Directions

Mucositis research has evolved greatly over the decade. It is evident that the future of treatment development for mucositis is contingent upon continuing to understand specific pathophysiologies involved, in particular, those associated with different cancer treatment modalities.

2.1 Mucositis, TLR4, and Pro-inflammatory Cytokines

Homeostasis of the gut is carefully balanced by interactions between the resident microflora, epithelial barrier function, and the mucosal immune system (Kelly et al. 2004). Recent research from our laboratory has shown that mucositis disrupts the delicate balance of these three factors (Al-Dasooqi et al. 2014; Wardill et al. 2014a, b, c). This leads to a substantial inflammatory response (Logan et al. 2008) and changes in both epithelial turnover (Gibson et al. 2002) and microflora characteristics (Stringer et al. 2009b). TLR signaling is vital for the maintenance of epithelial homeostasis (Rakoff-Nahoum et al. 2004), is an important modulator of gut bacteria (Lee et al. 2006), and is expressed on the immune cells of the gut. Recently, TLR4 has gained specific interest to mucositis (Wardill et al. 2014b, c, 2015a, b; Gibson et al. 2016). In particular, we have demonstrated TLR4 is overexpressed in the jejunum following chemotherapy during peak intestinal injury; however it is undetectable during the later time points associated with the healing phases (Gibson et al. 2016). These time points were also associated with changes in tight junctions (Wardill et al. 2014b) and changes in matrix metalloproteases (MMPs) (Al-Dasooqi et al. 2010), suggesting there may be a link between them.

Using TLR4 −/− mice, further research conducted by our laboratory demonstrated TLR4 is associated with the development of mucositis and chemotherapy-induced pain (Gibson et al. 2016; Wardill et al. 2016a). It is well established that the gut microbiome is involved in mucositis (Stringer et al. 2008; Stringer 2013), and our recent research has demonstrated that activation from increased exposure to bacterial influx is due to compromised gut barrier integrity (Wardill et al. 2014a, 2016b). Further research is essential in this area.

Activation from increased inflammatory mediators is known to have extensive roles in the pathogenesis of mucositis (Logan et al. 2007a, b, 2008). Specifically, over the time course of mucositis, there is increased production of pro-inflammatory cytokines, in particular TNF, IL-1β and IL-6, and NF-kB, a key transcriptional regulator of these pro-inflammatory cytokines in the gut mucosa (Logan et al. 2008). These are excellent markers of, and play an important role in, the pathogenesis of the chemotherapy-induced inflammatory response and treatment-induced gut toxicity. These markers offer an ideal new research direction for mucositis.

3 Conclusions and Summary

Mucositis research is a rapidly developing field. Over recent years, there has been a number of emerging areas of research that have been postulated to be involved in the pathogenesis of the condition. We have made huge leaps in our understanding of the disease, and new research directions have been undertaken. However, despite these emerging areas, very little has been able to be translated to clinical practice to assist clinicians in treating cancer patients with mucositis. It is hoped that with our continued understanding and new research directions, this will change in the future.

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Mouth Care

20

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_37

Abstract

Mouth care is very commonly neglected in people with life-limiting illness and in the elderly and frail. However, people with life-limiting illnesses, the treatments required to manage them and the medications used for symptom management, have significant effects on the mouth. The focus of this chapter will be on good oral assessment and care of the mouth in order to maximize quality of life, maintain self-esteem, feelings of well-being and comfort at the end-of-life. The compartmentalization involved in viewing the mouth separately from the rest of the body must cease because oral health affects general health by causing considerable pain and suffering and by changing what people eat, their speech, and their quality of life and well-being (Sheiham 2005).

1 Introduction

Palliative care is an interdisciplinary medical specialty that focuses on prevention and relief of suffering, and yet mouth care is often seen by health professionals as of minor importance despite the high incidence of oral discomfort and infection. People, therefore, do not perceive these symptoms as clinically important and will not always report them and subsequently suffer significant discomfort (Oneschuk et al. 2000). Mouth problems can make a person miserable and prevent them enjoying a healthy diet.

The intraoral structures: the tongue, palate, and teeth serve a number of important functions such as defense, mastication, incision, and signaling with facial expressions. Good oral health is vital for carrying out activities of daily living such as speaking, eating, swallowing, and socializing. It maintains self-esteem, dignity, and respect, providing quality of life. People at the end-of-life are susceptible to a range of oral complications including pain, salivary gland dysfunction, dysphagia, and oral mucosal infections (Wilberg et al. 2012).

The aim of this chapter is to raise awareness of the importance of mouth care for all health professionals involved in the care of people with life-limiting illness and in the older person and those with dementia as oral care is often a neglected area of care. It has distressing implications for quality of life for these people if poorly managed and must therefore become part of individualized care plans. Mouth care is an important indicator as to the quality of care a person is receiving.

2 Anatomy and Function of the Mouth

The oral cavity includes the lips, cheeks, palate (roof of the mouth), floor of the mouth, and the part of the tongue in the mouth, and ducts of the salivary glands. A mucous membrane lines and protects the inside of the mouth. All these organs work together to aid in the ingestion and digestion of food. The structures in the mouth also play an important role in speech, taste, and the first steps of digestion.

Saliva from the salivary glands enters the mouth through ducts. There are four pairs of salivary glands. The submandibular glands are under the jaw, the sublingual glands are under the tongue on the floor of the mouth, the parotid glands are between the ear and the jaw, and the buccal glands are in the mucous membrane in the cheeks and mouth, but they only produce a small amount of saliva. Saliva plays an important role in digestion and is made up of electrolytes, mucus, antibacterial compounds, enzymes, and the main component is water, which forms 98% of the saliva. The saliva moistens the mouth and helps a person chew and swallow food.

Saliva is important for maintaining a healthy mouth by cleansing and lubricating it. It is antimicrobial so reduces the risk of oral infection. It is important for taste and the enzymes it contains helps with the breakdown of food and digestion. Saliva helps maintain mucosal integrity. Saliva maintains oral hygiene.

Taste is another major function of the mouth as the tongue, a strong muscle which moves food around, also has around 10,000 sensory structures (taste buds) located at the sides and base of the tongue. This helps us distinguish four main

flavors: sweet, sour, salty, and bitter. It lets us distinguish flavors and warns us when food should not be eaten.

The gingiva (gums) is the pink soft tissue that surrounds the teeth and covers the jaw bone. Gums are a delicate tissue that can easily get irritated, inflamed, and start to bleed if infected by the bacteria.

3 Why Worry About Mouth Care?

1. People at the end-of-life are vulnerable to oral problems.
2. The impact of oral discomfort impacts on many aspects of the lives of people – the ability to communicate, socialize, and enjoy food and drinks.
3. People at the end-of-life are frequently exposed to compromising factors – the disease process, medications, and the inability to maintain oral fluids.
4. Research has ranked xerostomia in people with advanced disease as the third most distressing symptom (Sweeney and Bagg 2000).

3.1 Risk Factors for Mouth Problems

Preventive mouth care is essential for people receiving palliative care. In a study looking at nursing knowledge and attitudes concerning preventive mouth care, 1 in 20 nurses did not think that mouth care was his/her duty. This care was considered unpleasant and difficult (Bellior and Riou 2014). As disease advances, people become frailer and more debilitated and so the oral mucosa becomes more vulnerable. Medications for symptom management, for example, opioids and anticholenergics, and treatments such as irradiation or chemotherapy can lead to dryness of the mouth allowing the entry of infection through damaged mucosa. The person may be less able to maintain oral intake leading to dehydration and dryness of the mouth. Regular dental appointments may not be a priority, and damaged teeth and dental caries are an added risk for mouth problems.

3.2 Physical Effects of Poor Oral Care

- The person's comfort is compromised.
- Loss of enjoyment of food.
- Loss of appetite and inability to maintain nutrition.
- Swallowing difficulties.
- Poor protection from infection.
- Communication difficulties.

3.3 Psychological Effects of Poor Oral Care

- Frustration.
- Loss of taste means lack of enjoyment of food and fluids.
- Prolonged periods of eating pureed foods.
- Unbearable at times.
- Frustration gives way to annoyance and anger.
- Being misunderstood because of slurred speech.

3.4 Social Effects of Poor Oral Care

- Difficulties in communication leading to embarrassment.
- Social impact of not being able to enjoy and share meals with family and friends.
- Limits social outings and participants at special occasions.
- People avoid close physical contact.

4 Assessment of the Mouth

4.1 Individualized Care

As with all palliative care, planning must be holistic and individualized to be effective. Timely oral care assessment and an individualized regime are required to establish the frequency and type of care required in order to limit the occurrence of oral complications (McGuire 2003).

The key questions to assess oral care are: Is there infection present? Is the mouth dry? Is the mouth dirty? Is the mouth painful? Inspect the mouth carefully and gently using a torch or

light source and a spatula to depress the tongue. Listen carefully to what the person has to say about their mouth and the issues they are experiencing physically, psychologically, and socially.

The use of an oral assessment tool is recommended, and there are many available. When deciding on an oral assessment tool, ensure that it assesses the lips, tongue, mucosa, gingiva, saliva, and teeth or dentures. It should also assess the four phases of oral health: when the mouth is healthy, any early warning signs of problems developing, problems that are present, and any serious problems that need urgent and more intensive treatment. Ensure it is appropriate to the setting where it will be used. (Links to some examples are in the appendix at the end of the chapter). This will ensure better planning of an individualized care regimen.

4.2 Oral Assessment Guide

- Listen to the person's voice – Has it changed?
- Are they able to swallow or are they experiencing any difficulties?
- What is the texture of their lips? (dry, cracked, bleeding?)
- Look at the tongue – Is it coated, blistered, red, dry or sore?
- Do they have saliva? What is the consistency?
- Look at the mucous membrane – Is it coated? Are there any ulcers?
- What does the gingiva look like? (edematous, red, bleeding?)
- Check the teeth/dentures (plaque or debris, broken or cracked?)

4.3 Dry Mouth (Xerostomia)

This is a common symptom causing significant morbidity and distress as a result of a lack of saliva. There are multiple causes and each needs careful consideration (Figs. 1 and 2).

- Dehydration
- Psychological such as fear and anxiety

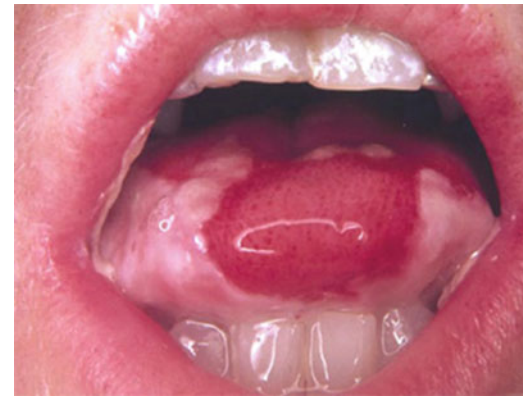

Fig. 1 Severe mucositis caused by radiation

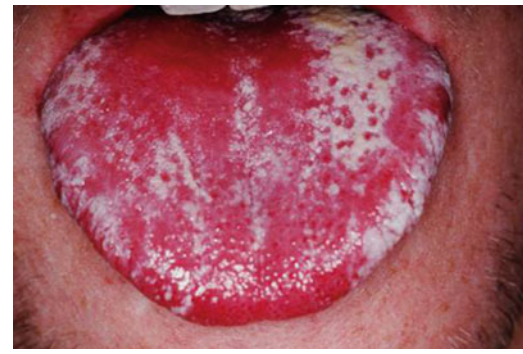

Fig. 2 Candidiasis (oral thrush) in a dehydrated person

- Medications such as antidepressants, anticholinergics, morphine
- Radiation to head and neck
- Diabetes mellitus
- Liver cirrhosis
- Infections
- Sjogren syndrome
- Oral candida must be excluded or if present treated

To manage a dry mouth, it is necessary to keep it moist and to replicate or stimulate saliva production. The oral cavity, including the lips, requires moisture for its integrity.

Several options may need to be tried to gain relief.

- Treat any causes that are treatable such as candida
- Have frequent sips of water and/or artificial saliva spray/drops

- Sucking on sugar-free candy or chewing sugarless gum
- Drinking diet drinks which have a low pH
- Reducing caffeine and alcohol
- A cool mist humidifier at night may provide some relief
- Eat soft, moist foods that are cool or at room temperature
- Moisten dry foods with broth, sauces, butter, or milk
- Semifrozen fruit juice or pieces of fruit
- Moisten lips or apply lip balm
- Clean teeth after each meal with a soft tooth brush
- Dental referral as necessary
- Medications such as pilocarpine **(check drug information before using)**
- Avoid dry, coarse, or hard foods
- Avoid acidic or spicy foods that can burn the mouth
- Avoid glycerine and thymol mouthwash as this is hygroscopic

Oral pain needs to be treated with both systemic and topical treatments. Opioids may be necessary especially when there is severe mucositis or candida infections. Local anesthetics can be used topically.

4.4 Care Plan Summary

Meticulous documentation of the assessment and plan of care for managing any identified problems is important to ensure continuity of oral care. Mouth care should be offered at least four times a day: after each meal and at night. The oral assessment should be repeated daily and management changed as needed.

5 Oral Care for People with Dementia

The number of people with dementia is increasing as the population ages. Dementia is a life-limiting illness, and these people need a palliative approach to care from diagnosis. Special attention to oral hygiene is therefore important as they may be neglecting it themselves or no longer able to attend to their own oral care. "Poor dental health can affect the person's comfort, appearance, eating, nutrition, behaviour and general health. Every person with dementia needs an individualised preventive approach to dental care." (Boyle et al. 2014).

When a person is diagnosed with dementia, an oral hygiene plan should be established. Family and/or carers will need to be part of the planning and ongoing explanations of the importance of good oral hygiene are given to the person with dementia. The use of an assessment tool will be useful as the information provided by the person with dementia may be unreliable.

Dementia is under recognized and therefore oral problems can occur and become problematic. Challenging behaviors may occur in these people as they may have significant pain, infection, and broken teeth or ill-fitting dentures that have not been addressed.

As dementia progresses, communication may also be impaired, and it is vital that an individualized preventive oral hygiene plan is in place and must involve the family, carers, and person's dentist. Prevention of issues is preferable to the person needing dental procedures as they may cause unnecessary anxiety and pain.

Oral hygiene prevention must be part of care planning for all people with dementia and there needs to be resources, policies, and procedures in place to ensure that this is done.

6 Care of the Mouth as Death Is Imminent

The desire to eat or drink at the end-of-life usually decreases. This is a natural response of the body as the organs are slowing down, and it becomes difficult to manage the intake of food and/or fluids and the person can feel quite dry. This is a normal part of having advanced disease – it is not that "they are starving to death." They are dying from their advanced disease and trying to force them to eat or giving artificial fluids through artificial

means will not alter the dry feeling they have. Communicating this to the family is an important part of palliative care.

The best way to make the person feel better is to provide frequent fluids while they are able to drink and when that is no longer possible to keep moistening their mouth as will be discussed below. Good mouth care is as important as death approaches as at any other time when living with a life-limiting illness.

People at the end-of-life are vulnerable to oral problems, such as candida, no matter how well their mouth is cared for so it is important to assess the mouth regularly as discussed earlier in this chapter.

Xerostomia (the subjective sensation of dryness of the mouth) is the most common oral issue experienced as a person is dying. The options suggested previously can be used but first assess the person's ability to swallow.

6.1 Dry Mouth Alternatives That May Be Tolerated at the End-of-Life

- Semifrozen tonic water and gin
- Semifrozen fruit juice or pieces of frozen pineapple
- Frequent sips of cold water or water sprays
- Warm tea or coffee
- Warm miso soup or other familiar tastes
- Frozen popsicles made from fluids the person likes
- Lip balm on the lips

6.2 Mouthwashes

There is little conclusive evidence to support the use of many of the proprietary mouth washes, but some people have used them daily for much of their life and may wish to continue to do so, but often towards the end-of-life the taste can be too strong. Outlined are some mouthwashes that may be tried and may need to be used for short periods if there is oral candida or coating in the mouth.

In end-of-life care, it is more important that fluids used are acceptable and palatable to the person.

- Water – is usually acceptable, it is inexpensive, but it will not remove coating.
- Normal saline (salt and water – 1 tsp to 500mls) – is inexpensive, mildly antiseptic but may not be acceptable if a person has altered taste or feels sick.
- Sodium bicarbonate – can clean coated tongue, **BUT** it has an unpleasant taste and can be irritant. Sodium bicarbonate is sometimes on sponge swabs – these can be used for **short** periods for a coated tongue but not as the regular mouth swab.
- Cider and soda water 1:1 – pleasant tasting and the effervescence may help in loosening debris.
- Over the counter mouthwashes – often too astringent and painful in sore mouths.
- Glycerine and lemon mouthwashes or mouth swabs **should be avoided.**
  - **INCREASE** dryness as they are hygroscopic
  - Exhaust the salivary glands from the effects of lemon
  - Citric acid damages tooth enamel
  - Accelerates decalcification
  - Increases the likelihood of painful tooth sensitivity
  - No evidence of cleaning properties (Milligan et al. 2001)

6.3 Oral Care for the Person Who Is Dying and Can No Longer Drink

This is an important aspect of end-of-life care and is something that family, friends, and carers can be taught to do very easily, if they wish, and this can allow them special time with the person. As food has significant cultural connection to caring for a person, inviting the family to do the oral care can help reduce the feeling that their loved one is being "starved to death." People with advanced disease at some point, lose their appetite, stop eating, and drinking and mouth care is a very

special way to care and maintain comfort and dignity until death.

- Find out from the person and the family what fluids they like.
- Mouth care should be done two hourly or more frequently if required to keep the mouth moist.
- Use large plain swabs not swabs that are impregnated with sodium bicarbonate or other substances.
- Teeth can be gently cleaned with a soft toothbrush.
- Use any fluids familiar to the person to swab the mouth – cooled tea or coffee, fruit juice, carbonated drinks, alcohol, cooled clear soups, ice cream, or yogurt. This will allow family to provide special things for their loved one. The familiar fluids and touch of family or friends will lessen the shock for the person, of having something placed in their mouth, particularly if they are not fully awake.
- Avoid iced water – this can be a shock for a person especially if they have sensitive teeth.
- It is the act of moistening the mouth and **NOT** the fluid you use that is important in the last days of life.
- Take care if the mouth is painful or ulcerated and bonjela may be useful to relieve the pain – just put a little on a swab and very gently coat any sore areas. Bonjela is contraindicated if there are bleeding mouth ulcers.
- If a person has a history of high alcohol intake, swabbing their mouth with alcohol may keep them more settled.
- Clean dentures and soak in antiseptic solution overnight.
- Take care not to put a toothbrush or swab near the back of the mouth or it may cause gagging.
- Use gentle pressure with swabs or toothbrush.
- Lip balms are useful to keep lips moist.

7 Changing Practice

Stress the importance of mouth care to all health professionals and provide ongoing education to begin the process of change. Creating guidelines and implementing protocols and procedures for oral assessment and care planning will be imperative and will also provide a way to audit oral care practice.

Ensure resources and products are available. Providing information leaflets for health care professionals and for people and their families about the importance of oral care and how to assess the mouth will give understanding of the significance of oral symptoms by all concerned.

8 Conclusion

Oral problems especially dryness are a significant problem for people at the end-of-life and impact on people's feelings and affect their quality of life. Oral care must therefore be raised to a clinical priority in hospice, hospital, and community settings to improve standards of holistic palliative care (Rohr et al. 2011). Oral care documentation must be implemented in all settings and audit used to ensure oral care is seen as a priority in order that people are not subjected to unnecessary discomfort and die with dignity and comfort.

Appendix: Oral Health Assessment Tools

Oral Assessment Guide (OAG): For use in acute care settings and rehabilitation settings. Anderson P, et al. Oral health problems in elderly rehabilitation patients. *Int J Dent Hyg*. 2004;2(2):70–7.

Brief Oral Health Status Examination (BOHSE): Has been validated in long-term care, residential aged care, and can be used with people with cognitive impairment. Kayser-Jones J, et al. An instrument to assess the oral health status of nursing home residents. *Gerentologist*. 1995;35(6):814–24.

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Skin Symptoms

21

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Contents

Abstract

The skin is the largest organ of the body. In life-limiting illnesses, there are a number of important skin manifestations that may cause considerable suffering to patients and, indirectly, to their family and carers. They include pruritus, pathological sweating, skin failure, and malignant cutaneous wounds. This chapter will review the pathophysiological mechanisms, epidemiology, assessment, and management

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https://doi.org/10.1007/978-3-319-77740-5_18

of these manifestations. Each section will be accompanied by a set of evidence-based management recommendations for clinicians.

1 Introduction

This chapter will review the symptomatology of the skin. The skin is our largest organ. It provides a protective border between the internal and external environment. Life-limiting illnesses can often manifest with skin problems. Those manifestations include troubling symptoms (pruritus, sweating), skin failure, and malignant cutaneous wounds. All are vexatious. All may add grievously to the suffering of the patient. Historically, management of these skin manifestations has largely been empirical, hampered by an inadequate understanding of their pathophysiological bases. Greater understanding is leading to a more strategic approach to management.

This chapter will examine, as they relate to life-limiting illnesses:

1. Pruritus
2. Sweats
3. Skin failure
4. Malignant cutaneous wounds

2 Pruritus

Itch or pruritus is defined as "an unpleasant sensation associated with the desire to scratch" (Haffenreffer 1660). The symptom of pruritus has a physical and psychosocial dimension and can cause great suffering to patients. Until recent years it was a poorly understood symptom. Pruritus can manifest in several life-limiting illnesses including:

1. Cholestatic pruritus in disorders of the liver and biliary tract
2. Uremic pruritus in chronic renal disease
3. Paraneoplastic pruritus

Prior to reviewing the current understanding of these discrete pruritus syndromes, it is useful to summarize the current knowledge of the pathophysiology of pruritus generally. Hopefully, that knowledge illuminates the etiology and management of each syndrome and guides future treatment strategies. Management of these pruritus syndromes disconnected from an understanding of underlying pathophysiology means that treatment remains empirical. For pruritus, "management divorced from mechanism reveals only part of a complex story. An alliance between mechanism and management will, ultimately yield greater dividends for basic scientists, clinicians and patients alike" (Brennan 2016).

The Pathophysiology of Pruritus: A Brief Summary

As with other somatosensory modalities, the initial signaling of pruritus occurs in the skin and is transmitted by sensory fibers to the dorsal horn of the spinal cord and via spinothalamic fibers centrally to the thalamus and brain. Modern research reveals:

1. The signal of itch is transmitted from the skin by C and A delta fibers. A small cohort (approximately 5%) of C fibers are itch-dedicated fibers.
2. Of those itch-dedicated C fibers, 10% are histamine dependent, and 90% are histamine independent. Those cohorts of neurons are mutually exclusive.
3. Histamine activates histamine-dependent itch fibers.
4. Multiple other pruritogens activate non-histaminergic itch fibers.
5. The activation of nerve endings transmitting the signal of itch results from a complex interaction or "cross talking" between skin cells in the epidermis and dermis.

For a more detailed overview of the pathophysiology of pruritus, readers are advised to consult a recent review (Brennan 2016). The above summary reveals that several widely held conceptions of pruritus are false. The first is that itch, of whatever etiology, is the result of peripheral histamine released by dermal mast cells triggering histamine itch receptors on nerve afferents. Certainly, that mechanism reflects histaminergic

itch, but 90% of itch is transmitted via a non-histaminergic pathway. The second myth, a corollary of the first, is the first-line therapy for all forms of pruritus is antihistamines. For itch that has a non-histaminergic etiology, antihistamines have little if any efficacy.

Itch Assessment

There are various instruments used to measure the severity of pruritus. In research, the most widely used has been the visual analogue scale (VAS). In recent years there has been an increasing focus on developing multidimensional itch instruments to better reflect the full experience of itch by a patient, including the effect of itch on sleep quality, quality of life, and anxiety and depression. One of these instruments is the 5-D itch scale. It comprises five questions that address the duration, degree (severity using a 5-point numerical rating scale), direction of severity (change of symptom in the past 2 weeks), disability, and distribution of pruritus on the skin. It has been validated in patients with chronic pruritus.

Main Pruritus Syndromes Encountered in Patients with Life-Limiting Illnesses

The following section examines in detail the epidemiology, etiology, and management of the main pruritus syndromes encountered in the practice of palliative care. It is a fundamental truth that clinicians will not be aware of a symptom experienced by a patient unless the patient complains of the symptom or the clinician enquires. Given the prevalence of pruritus, it is imperative that clinicians enquire regularly, respond competently, and, where they cannot relieve a symptom such as pruritus, refer wisely to clinicians with an expertise in symptom management such as palliative care.

2.1 Cholestatic Pruritus

Cholestatic pruritus is pruritus that results from cholestasis. Cholestasis, in turn, is defined as an impaired secretion of bile. Normally, bile is produced by hepatocytes, is secreted into the biliary system, and ultimately flows into the small intestine. Accordingly, any interruption to this enterohepatic system leads to an accumulation of substances that are normally excreted into bile. That accumulation causes pruritus, directly or indirectly. The interruption of this enterohepatic circulation has three main causes:

1. *Hepatocellular cholestasis* – failure of hepatocellular secretion of bile. Causes include chronic viral hepatitis or significant hepatic metastases.
2. *Cholangiocellular cholestasis*. This is pathology of the intrahepatic bile ducts. Examples here are primary biliary cirrhosis, primary sclerosing cholangitis, and hepatic metastases.
3. *Obstruction of the intrahepatic and extrahepatic bile duct system*. Examples here are cholangiocarcinoma and carcinoma of the head of the pancreas.

Cholestatic pruritus may be mild to excruciating in severity. It is circadian in presentation with the highest intensity typically occurring in the evening and early night (Kremer et al. 2008). As a result, it may be associated with sleep deprivation and daytime somnolence. The pruritus may be localized or generalized. While there are no primary skin lesions, scratching results in excoriations and if persistent, prurigo nodularis, a pathological response to repeated scratching manifested by skin thickening with nodules (Swain 1999).

Historically, elucidating the precise mechanism of cholestatic pruritus has been elusive. Many theories have been proposed including bile salts, bile acids, endogenous opioids, histamines, serotonins, or steroids. None of these theories have satisfactorily explained the cause of cholestatic pruritus, and for each, no correlation between serum and tissue concentrations and itch intensity has been demonstrated (Kremer et al. 2014). A significant breakthrough in our understanding of the pathogenesis of cholestatic pruritus came recently with the discovery of elevated levels of autotaxin in cholestatic patients with pruritus and, crucially, that the levels correlate with the intensity of pruritus

(Kremer et al. 2012). Autotaxin is an enzyme that converts lysophosphatidylcholine (LPC) to lysophosphatidic acid (LPA):

$$\text{LPC} \xrightarrow{\textit{Autotaxin}} \text{LPA}$$

LPA is a phospholipid. There are several facts that suggest LPA may be critical in the pathogenesis of cholestatic pruritus:

(a) LPA is an active compound and signaling lipid.
(b) LPA injected intradermally causes pruritus. That pruritus is dose dependent (Kremer et al. 2010).
(c) LPA signals LPA receptors that lie on afferent nerve endings in the skin.
(d) LPA activates TRPV1, a known itch channel on afferent nerve endings (Nieto-Posadas et al. 2012).
(e) LPA induces substance P (SP) released from afferent nerve endings.

Substance P is an important signaling neurotransmitter in pruritus and appears to be an important part of the mechanism of cholestatic pruritus. The concentration of serum SP is increased 12-fold in patients with liver diseases experiencing cholestatic pruritus compared to those liver patients without cholestatic pruritus (Trivedi and Bergasa 2010). Substance P stimulates dermal mast cells to release pruritogens. SP is an agonist of the NK-1 receptor, an itch receptor on primary afferent itch nerve fibers in the skin and at the dorsal horn. Substance P acts locally in the skin to increase the production of nerve growth factor (NGF) by keratinocytes. NGF, in turn, causes fresh sprouting of afferent nerve endings in the epidermis.

Another theory of the pathogenesis of cholestatic pruritus that is regularly cited is the so-called opioid hypothesis (Bergasa 2014). This hypothesis states that cholestatic pruritus is mediated by an increase in central opioidergic tone. The evidence for this is that endogenous opioids accumulate in the liver and bile of patients with liver disease (Bergasa et al. 2002), that there is an opioid withdrawal-like reaction triggered by opioid antagonism (Thornton and Losowsky 1988), and that opioid antagonists relieve cholestatic pruritus (Tandon et al. 2007).

Table 1 A clinical approach to the management of cholestatic pruritus

1. Establish the diagnosis. Exclude other causes of pruritus
2. If there is a reversible extrahepatic obstruction, consider a biliary drainage procedure such as a biliary stent or transcutaneous drainage. This involves a careful balancing of the potential benefits and burdens of the procedure and the patient's prognosis, performance status, and wishes
3. Consider one of the following medications:
(a) Cholestyramine 4 g 1 h before and 1 h after breakfast
(b) Rifampicin 300–600 mg/day either 30 min prior to or 1 h after a meal
(c) Ursodeoxycholic acid 15 mg/kg in two to three divided doses per day
4. Other medications with evidence – sertraline, SNRIs, naltrexone, lignocaine, UVB therapy

2.1.1 Management

Cholestatic pruritus is notoriously difficult to treat. Necessarily, that difficulty has been compounded by the mystery of its mechanism. The interventions with the highest level of evidence are listed below. Table 1 summarizes the recommended management.

Surgical Interventions

The objective of a surgical intervention is biliary drainage. That drainage may take various forms – the insertion of a biliary stent, transcutaneous drainage, nasobiliary drainage, or an extrabiliary diversion. As with any surgical intervention in patients with life-limiting illnesses, a careful evaluation is needed of the benefits and burdens of the intervention including the anesthetic risk, performance status, prognosis, and wishes of the patient.

Medical Interventions

The current treatment recommendations for cholestatic pruritus are based on a modest body of literature and clinical experience.

Cholestyramine

Cholestyramine is an anion-exchange resin. It is not absorbed, binds to anions in the small intestine, and is fecally excreted. The level of evidence for its use in cholestatic pruritus is modest. Its efficacy has been shown in small, uncontrolled case series (Datna and Sherlock 1966). Cholestyramine should be avoided in primary biliary cirrhosis (Weisshaar et al. 2012). The dose is 4 g 1 h before and 1 h after breakfast. The most common side effect is constipation.

Rifampicin

Rifampicin is a pregnane X receptor (PXR) agonist. The activation of this receptor inhibits the expression of autotaxin. There are several randomized controlled trials showing significant efficacy in the management of cholestatic pruritus (Ghent and Carruthers 1988). Approximately 10–15% of treated patients develop hepatotoxicity if the treatment extends for weeks to months (Heathcote 2007). The recommended dose is 150 mg bd-tds, either 30 min before or 2 h after a meal.

Ursodeoxycholic Acid

Ursodeoxycholic acid reduces cholestasis by stimulating the secretory capacity of hepatocytes and cholangiocytes. There is limited evidence in cholestatic pruritus. It is not recommended in patients with a significant biliary stenosis. The recommended dose is 10–15 mg/kg/day in two to three divided doses. It is generally well tolerated with few side effects.

Naltrexone

Naltrexone is a mu-opioid receptor antagonist. Several small placebo-controlled trials showed a moderate antipruritic effect (Bergasa et al. 1992; Terg et al. 2002; Wolfhagen et al. 1997). The recommended dose is 25 mg bd on Day 1 and then 50 mg daily.

Sertraline

Sertraline is a selective serotonin reuptake inhibitor (SSRI). In a small pilot, randomized placebo-controlled study, sertraline was reported to be associated with a significant reduction in cholestatic pruritus (Mayo et al. 2007). The recommended dose is 100 mg/day.

Cannabinoids

The endocannabinoid receptors CB1 and CB2 have an antipruritic effect (Gingold and Bergasa 2003). Dronabinol relieved intractable cholestatic pruritus in three patients with chronic liver disease (Neff et al. 2002).

Metronidazole

Refractory cholestatic pruritus in a group of patients with primary biliary cirrhosis was relieved by metronidazole (Berg and Gollan 1992). Metronidazole has not been studied in cholestatic pruritus secondary to malignancy.

Thalidomide

In a small double-blind, placebo-controlled pilot study to assess the efficacy of thalidomide in primary biliary cirrhosis, an improvement in pruritus was felt by five out of seven patients with pruritus in the treatment arm compared to three out of six patients in the placebo group (McCormick et al. 1994). The overall change in itching score did not reach statistical significance.

Ultraviolet Therapy

In an observational case series, Decock and colleagues reported a reduction in pruritus scores in a heterogeneous group of patients with cholestatic pruritus treated with UVB therapy for 8 weeks (Decock et al. 2012).

Lignocaine

Lignocaine has been reported to relieve cholestatic pruritus (Villamil et al. 2005).

Antihistamines

There is no correlation between histamine concentrations and pruritus. In an authoritative review, the authors concluded that histamine is “highly unlikely to play a causative role in cholestatic pruritus” (Beuers et al. 2014). Antihistamines are mostly ineffective in management.

Gabapentin

In a double-blind, randomized, placebo-controlled trial in the management of cholestatic pruritus, gabapentin did not provide significant benefit over placebo (Bergasa et al. 2006).

Ondansetron

In a systematic review of the role of ondansetron in the management of cholestatic and uremic pruritus, To et al. found that ondansetron had negligible effect in both forms of pruritus on the basis of a limited number of studies (To et al. 2012).

2.1.2 Future Therapies

Undoubtedly, the growing level of understanding of the mechanism of cholestatic pruritus will lead to an exploration of new therapeutic agents. Examples include autotaxin inhibitors and LPA receptor antagonists. Examples of a promising class of medications that is currently available are NK-1 receptor antagonists. Aprepitant is a NK-1 receptor antagonist. Substance P triggers the NK-1 receptor located in multiple skin cells and at the dorsal horn. Logically, given the role of substance P in cholestatic pruritus outlined above, and the efficacy shown by NK-1 receptor antagonists in other pruritic conditions in which SP plays a critical role (Stander and Luger 2015), this medication has a promising role. At time of writing, there are no studies on the efficacy of aprepitant in cholestatic pruritus.

2.2 Uremic Pruritus

Uremic pruritus (UP) is itch secondary to chronic kidney disease. It is also named chronic kidney disease-associated pruritus (CKD-aP). It is a common symptom of patients with end-stage kidney disease (ESKD) being managed with dialysis or conservatively. The most comprehensive epidemiologic data is from DOPPS (Pisoni et al. 2006), a large study of dialysis patients which found that 41.7% of patients reported moderate to extreme pruritus. Uremic pruritus is also common in patients with end-stage renal disease being managed conservatively, with a prevalence in studies ranging from 47% (Noble et al. 2010) to 74% (Murtagh et al. 2007).

Uremic pruritus is associated with a decreased quality of life (QOL). Mathur et al. showed a statistically significant relationship between the intensity of UP and health-related quality of life (HR-QOL), particularly with regard to mood, social relations, and sleep. Conversely, they noted that a decrease in intensity of UP of 20% was sufficient to produce a significant improvement in HR-QOL (Mathur et al. 2010). UP is associated with depression, is an independent predictor of mortality, and amplifies other symptoms, especially poor sleep, that impairs QOL and can lead to other poor patient outcomes.

The precise mechanism of UP remains opaque. Multiple theories abound including inadequacy of dialysis, xerosis (dry skin), hyperphosphatemia, hypercalcemia, or hyperparathyroidism. None of these theories are consistently convincing. Indeed, "despite this vast array of possible explanations, none consistently have been demonstrated to be the underlying cause of pruritus associated with CKD. Large epidemiological studies ultimately may facilitate our understanding of the elusive pathophysiological process of this distressing symptom" (Patel et al. 2007). Future basic research has several challenges – to determine the precise precipitant (s) of UP, the immunochemical cascade in the skin in UP that results in the signaling of itch along afferent itch fibers, and the precise neurotransmitters and itch receptors at the dorsal horn and more centrally.

2.2.1 Clinical Presentation

A prospective observational study of 103 HD patients followed over 12 weeks found that 84% of patients with UP experienced itching daily or nearly daily and had itching that affected large, discontinuous but bilateral and symmetric skin areas, which was worse at night and was likely to persist for months to years (Mathur et al. 2010).

It is important to note at the outset that not all patients with ESKD who have itch have uremic pruritus. A differential diagnoses for the cause of pruritus should always be considered in these patients. Diagnoses such as scabies, fungal rashes, psoriasis, allergic reactions to medications, and atopic dermatitis are among the many possible

etiologies. Therefore, the etiology of pruritus in a patient with ESKD is likely, but not invariably, to be uremic pruritus.

2.2.2 Management

As with other pruritic conditions, the management of uremic pruritus has struggled with an inadequate understanding of its mechanism. Over time, multiple therapies have been suggested. Management, if commenced, may be largely empirical. What does the evidence state? Table 2 contains a recommended therapeutic approach.

The management of uremic pruritus may be usefully categorized as:

1. Topical therapies
2. Systemic therapies
3. Ultraviolet therapies
4. Acupuncture

Table 2 Current clinical practice in the management of uremic pruritus

1. Take a careful history. Not every patient with end-stage kidney disease with pruritus has UP. There are a wide number of other dermatological or systemic diseases that may present with pruritus
2. Physical examination with a particular focus on checking for rashes consistent with other dermatological conditions
3. If a diagnosis of uremic pruritus is made:
(a) Check biochemistry, especially calcium, phosphate, and parathyroid hormone (PTH) levels
(b) Check the efficiency of the dialysis. If poor, consider a trial of an increased dialysis dose
(c) If xerosis (dry skin), apply moisturizers bd-tds, especially after bathing. Use gentle soap
(d) Gabapentin. This is a good choice if the patient with UP also reports uremic restless legs syndrome and/or painful diabetic peripheral neuropathy. There is evidence for the efficacy of gabapentin in both. Dosing for dialysis patients – 100 mg post dialysis. For patients with eGFR <15–100 mg, every second night. If eGFR >15–100 mg nocte. Titrate all doses by 100 mg increments according to response and side effects
(e) Other medications to consider: pregabalin, gamma-linolenic acid (GLA) (an active constituent of evening primrose oil), capsaicin cream, sericin cream, pramoxine cream, sertraline, montelukast, kappa-opioid agonists, thalidomide, and UVB phototherapy

Topical Therapies

Emollients

Xerosis is not a cause of UP. Nevertheless its presence exacerbates the symptom. Skin hydration with aqueous skin emollient (Morton et al. 1996) and baby oil (Lin et al. 2012; Karadag et al. 2014) reduces skin dryness and the severity of UP. It is recommended that treatment should therefore begin with moisturizers and cleansers with a low pH (Yosipovitch and Bernhard 2013).

Capsaicin Ointment

Several small placebo-controlled trials have shown a significant benefit in UP with capsaicin cream 0.025–0.03% ointment applied two to four times per day to affected areas (Breneman et al. 1992; Markhlough et al. 2010; Tarng et al. 1996). Unfortunately capsaicin is not well tolerated due to a transient burning feeling on the skin.

Sericin Cream

Aramwit et al. conducted a randomized, double-blind, placebo-controlled experimental study on the use of sericin cream in UP. The mean itching score decreased significantly from moderate to severe at the time of enrollment to mild pruritus after 6 weeks of treatment (Aramwit et al. 2012).

Pramoxine Lotion

Pramoxine hydrochloride 1% lotion was shown to be effective in a randomized controlled double-blind study on 28 hemodialysis patients when applied twice daily for 4 weeks (Young et al. 2009).

Tacrolimus Ointment

There are conflicting results in studies of the efficacy of tacrolimus for UP. Kuypers et al. conducted an uncontrolled prospective study on the effect of 6-week treatment with sequential concentrations of tacrolimus ointment (0.1% and 0.3%) on the severity of UP in 21 hemodialysis patients and again after 2-week washout. The study showed tacrolimus ointment significantly reduced the severity of UP and was well tolerated) (Kuypers et al. 2004). Subsequently, however, in a randomized, double-blind, vehicle-controlled

study of hemodialysis patients, Duque et al. did not demonstrate a significant improvement of tacrolimus 0.1% over a vehicle ointment in relieving UP (Duque et al. 2005).

It is important to note that the US FDA, in response to case reports and animal studies reporting rare associations with malignancies such as lymphoma and skin cancer, issued a black box warning for tacrolimus ointment and recommended that its use be limited to those who have failed other therapies and to treatment periods of less than 6 weeks.

Gamma-Linolenic Acid

In a crossover, placebo-controlled trial of 17 patients with severe refractory uremic pruritus, Chen et al. showed significant efficacy with gamma-linolenic acid, a constituent of evening primrose oil (Chen et al. 2006).

Systemic Therapies

Gabapentin

Gabapentin effect on UP has been studied in 11 studies (8 randomized and 3 observational). In the randomized trials, gabapentin was compared to placebo in five studies. A qualitative systematic review examined this data and recommended gabapentin use for patients not responding to emollients, but that the "results should be interpreted cautiously due to the lower quality of included studies." The authors recommended starting at a dose of 100 mg orally after hemodialysis three times weekly (Lau et al. 2016). In practice, the recommended commencement dose for patients having peritoneal dialysis is 100 mg post dialysis. For those patients on a conservative, non-dialysis pathway, we recommend commencing gabapentin 100 mg every second night if eGFR is <15 mls/min and 100 mg nocte if eGFR is >15 mls/min.

Pregabalin

There is one study that compares pregabalin with placebo in a randomized, double-blind methodology. This was contained in a three-way study conducted by Yue and colleagues (Yue et al. 2015). The trial was a 12-week prospective, randomized, double-blind study of UP in dialysis patients comparing pregabalin 75 mg twice weekly, ondansetron 8 mg daily, and placebo. Over the 12-week period, only pregabalin improved UP significantly. Several prospective cohort studies of pregabalin in UP have shown efficacy (Aperis et al. 2010; Shavit et al. 2013).

Gabapentin and Pregabalin in Sequence

Rayner et al. conducted a trial in a mixed cohort of hemodialysis patients, peritoneal dialysis patients, and patients with chronic kidney disease (CKD) Stage 4 or 5 who were not on dialysis (Rayner et al. 2012). All had UP (median itch severity on VAS was 8 (range 6–10)) with a median duration of pruritus of 6 months. Patients were commenced on gabapentin 100 mg after dialysis or daily. If intolerant to gabapentin, patients were offered pregabalin 25 mg after dialysis or daily. Gabapentin or pregabalin relieved itching in 85% of the 71 patients.

Gabapentin Versus Pregabalin

Solak et al. examined a cohort of hemodialysis patients with *both* UP and neuropathic pain (Solak et al. 2012). Strictly speaking, therefore, then it may be difficult to draw broader conclusions from this study. Looking specifically at the symptom of pruritus, both gabapentin and pregabalin improved the symptom significantly. Indeed, there was no difference between the two medications.

Gamma-Linolenic Acid (an Active Constituent of Evening Primrose Oil)

The efficacy of gamma-linolenic acid has been studied in the management of uremic pruritus in both topical and systemic forms. In the oral form, Yoshimoto-Furuie et al. found that oral gamma-linolenic acid-rich evening primrose oil improved overall skin symptom scores (pruritus, erythema, and dryness) significantly compared to those who received linolenic acid alone (Yoshimoto-Furuie et al. 1999). The pruritus scores obtained from the evening primrose oil group showed a trend toward a greater improvement ($0.05 < p < 0.1$). The mechanism of action is unknown although almost

certainly involves the supplementation of early parts of the n-6 essential fatty acid cascade in the epithelium, thereby increasing the balance of anti-inflammatory cytokines over pro-inflammatory and pruritogenic substances.

Sertraline

Shakiba et al. conducted a before-and-after trial of 19 HD patients with uremic pruritus. Each was given 50 mg daily for 4 months. The itch instrument was an itch questionnaire. The difference in the level of pruritus before and after sertraline was significant (Shakiba et al. 2012).

Thalidomide

There is a single randomized, double-blind placebo-controlled crossover trial of thalidomide showing significant efficacy in the management of UP (Silva et al. 1994). The dose of thalidomide was 100 mg daily.

Kappa-Opioid Agonists

Recent neuroscience literature reveals that activating kappa-opioid receptors has an antipruritic effect. Nalfurafine, a kappa-opioid agonist, has been tested in oral and intravenous form in UP (Kumagai et al. 2010, 2012). The oral form was studied in a randomized, double-blind, placebo-controlled trial and an open-label single-arm prospective trial. In both studies there was a significant response. In the intravenous form, Wikstrom et al. reported a statistically significant effect in two randomized, double-blind placebo-controlled trials of 144 patients on HD with UP who received 5 mcg nalfurafine intravenously three times per week after hemodialysis for 4 weeks. The authors did a meta-analysis of these two studies and showed a moderate, although significant, benefit in pruritus (Wikstrom et al. 2005).

Montelukast

Montelukast is a leukotriene receptor antagonist. Leukotriene B4 is a potent pruritogen. Nasrollahi et al. conducted a randomized, single-blind, placebo-controlled crossover study of the efficacy of montelukast in the treatment of refractory UP in 16 hemodialysis patients in 5 dialysis centers (Nasrollahi et al. 2007). The patients were divided into two groups to receive, firstly, montelukast and then placebo or vice versa. The dose of montelukast was 10 mg daily for 20 days with a washout period of 14 days. With montelukast, the severity of pruritus was reduced by 35% (95% CI, 9.5–6.2%), while it was reduced 7% (95% CI, 0.5–15.9%) with placebo ($p = 0.002$).

Antihistamines

Antihistamines have not been shown to be effective in UP (Weisshaar et al. 2004). They are not recommended in recent reviews of UP (Mettang 2014; Combs et al. 2015). Crucially, fMRI reveals that the central transmission of itch in UP is through a non-histaminergic pruritus pathway and not a histaminergic pathway (Papiou et al. 2014).

Naltrexone

The rationale behind the use of naloxone is the so-called opioid theory of pruritus. It has been noted that mu-receptor agonists can precipitate itch, especially the use of morphine in spinal anesthesia. Does naloxone have an antipruritic effect in UP? There are three randomized controlled trials examining the antipruritic effect of oral naltrexone in UP. Two were placebo-controlled, double-blind crossover trials. In the third study, the comparator was antihistamine. The studies have conflicting results. One of the placebo-controlled trials of 15 hemodialysis patients showed a statistically significant benefit (Peer et al. 1996). The second placebo-controlled study of 16 dialysis patients showed no statistically significant benefit (Pauli-Magnus et al. 2000). In the study comparing naltrexone to antihistamine, there was no significant difference in the VAS scores of pruritus after treatment with oral naltrexone (Legroux-Crespel et al. 2004).

Ondansetron

A randomized, placebo-controlled, double-blind trial of ondansetron in UP showed that ondansetron was no better than placebo (Murphy et al. 2003). In a systematic review, To et al. found that ondansetron has a negligible effect on UP on the basis of a limited number of trials (To et al. 2012).

Ultraviolet Therapy

The results of the studies on the efficacy of ultraviolet light for uremic pruritus are inconsistent. That inconsistency may, with time, be explicable on the basis of the specific bandwidth of the ultraviolet therapy employed. In the 1970s Gilchrest et al. published two small studies showing efficacy for broadband UVB (BB-UVB) therapy for UP (Gilchrest et al. 1977; Gilchrest et al. 1979). In 1991, Tan et al. published a meta-analysis of randomized controlled trials of UP and concluded that UVB therapy successfully fulfilled the criteria for clinical significance of a reduction in pruritus scores of at least 50% (Tan et al. 1991). More recently, a single-blind, randomized controlled trial of narrowband UVB (NB-UVB) therapy by Ko et al. did not show a significant benefit compared to a control group for refractory UP (Ko et al. 2011).

Acupuncture

Kim et al. published a meta-analysis of six studies (three RCTS and three uncontrolled observational studies) of needle acupuncture for UP (Kim et al. 2010). The authors concluded that, despite all trials reporting efficacy, most of the trials showed a high risk of bias, and therefore current evidence is insufficient to support its efficacy.

Future Therapies

Various agents have been mooted as possible future therapies. They include cannabinoids and NK-1 receptor antagonists.

A summary of current clinical practice based on this literature appears in Table 2.

2.3 Paraneoplastic Itch

Pruritus may be a paraneoplastic manifestation of malignancy. It is defined as "the sensation of itch as a systemic (not local) reaction to the presence of a tumor or a haematological malignancy neither induced by the local presence of cancer cells nor tumor therapy" (Weisshaar et al. 2015).

There is limited data on the epidemiology of paraneoplastic pruritus. One retrospective study of 700 patients with solid tumors and hematologic malignancy reported a 5.85% prevalence of pruritus (Kilic et al. 2007). The most common malignancy associated with generalized pruritus is Hodgkin's lymphoma with a prevalence of 25% of presentations (Rubenstein and Duvic 2006). Other malignancies associated with pruritus are cutaneous T-cell lymphomas (CTCL), multiple myeloma, breast cancer, carcinoid syndrome, and gastrointestinal and hepatocellular carcinomas.

Cutaneous T-cell lymphomas are characterized by a clonal accumulation of T lymphocytes in the skin. There are multiple subtypes. The most common variant is mycosis fungoides; the most aggressive variant is Sezary syndrome. Pruritus is common in both variants. It occurs more commonly in Sezary syndrome than mycosis fungoides. In both conditions, pruritus is significantly more severe in the later rather than earlier part of the disease trajectory.

2.3.1 Pathogenesis

The pathogenesis of pruritus in malignancy is unknown. Almost certainly, malignant cells release substances that, directly or indirectly, precipitate the triggering of itch. To date, evidence for the precise details of this process is circumstantial. For instance, Hodgkin's lymphoma is a B-cell lymphoproliferative syndrome characterized by the presence of Reed-Sternberg cells. Between 25% and 50% of patients suffer various B-cell symptoms including weight loss, fever, sweats, and pruritus. Sezary syndrome is characterized by an increased production of Th2 lymphocytes. This leads to an imbalanced production of Th2 cytokines (IL-4, IL-5, IL-10, IL-31) and IgE and an infiltration of eosinophils. The level of serum IL-31, a key pruritogen produced by Th2 lymphocytes, correlates with the level of pruritus in CTCL, and resolution of pruritus correlates with a decreased serum IL-31. There is a circumstantial evidence for the pruritogenic role of substance P in Hodgkin's lymphoma and CTCL as there is a positive role for aprepitant, a NK-1 receptor antagonist, in the management of intractable pruritus in these conditions.

2.3.2 Management

Paraneoplastic pruritus is often refractory to conventional medications such as antihistamines or corticosteroids. In Hodgkin's lymphoma, case studies have shown a significant improvement with thalidomide (Gonclaves 2010) and aprepitant (Villafranca et al. 2014). The pruritus of Hodgkin's lymphoma may be enhanced by concurrent *Staphylococcus aureus* colonization of the skin and may settle with antimicrobial treatment (Rubenstein and Duvic 2006). In non--Hodgkin's lymphoma, kappa-opioid receptor agonists have been shown to rapidly reduce pruritus (Dawn and Yosipovitch 2006). For the management of pruritus in CTCL, there is a modest body of evidence. Antihistamines have no or negligible response. High-dose topical steroids have shown efficacy in early-stage CTCL. Gabapentin and mirtazapine have been reported to show efficacy (Demierre and Taverna 2006). In Sezary syndrome, aprepitant is a promising intervention. Several case series have shown a significant improvement (Duval and Dubertret 2009). A similar benefit for aprepitant was shown in a small case series of patients with mycosis fungoides (Booken et al. 2011). Histone decarboxylase inhibitors, such as vorinostat and romidepsin, inhibit the replication of T lymphocytes and, as a result, their release of pruritogens including IL-31. This class of medications could be considered, therefore, in patients with CTCL suffering from pruritus to treat both the underlying malignancy and the pruritus (Rowe and Yosipovitch 2016).

3 Sweating

3.1 Introduction

Sweating is a normal physiological response to hyperthermia or physical exertion. If sweating is pathological, it may be highly distressing and debilitating. Like pruritus, this symptom is often overlooked, underdiagnosed, and poorly managed. The underlying mechanism of normal sweating is poorly understood by most clinicians, and its pathological manifestation beyond sepsis is mysterious and inexplicable. Inevitably, this inexplicability leads to faltering management and therapeutic nihilism. The objective of this section is to review the normal physiology of sweating, the etiology of pathological sweating with a particular focus on sweating as a symptom of life-limiting illnesses, and its management.

3.2 Physiology of Normal Sweating

In a resting condition, humans dissipate body heat at a rate approximately equal to heat production. The body is sensitive to changes in temperature and adapts to higher or lower temperatures. The human body has central and peripheral thermoreceptors. The central receptors are in the brain stem, spinal cord, and viscera. The peripheral thermoreceptors lie in the skin. Of the two sets of receptors, the central thermoreceptors have the most influence on the body's response to temperature change.

An elevated or reduced temperature activates these thermoreceptors. That information is communicated to the central thermoregulatory center, located in the anterior hypothalamus. In this center, warm-sensitive and cold-sensitive neurons respond to variations in body temperature. The center integrates this information. Efferent nerves pass from the hypothalamus to effect both an autonomic and peripheral thermoregulatory responses. If the body temperature is high, the autonomic thermoregulation takes the form of heat dissipation by two methods: vasodilation of the blood vessels in the skin and sweating. Sweating reduces the body temperature by evaporation. Classically, sweating "is the greatest avenue of heat loss in hyperthermia" (Smith and Johnson 2016).

Impulses originating from the central thermoregulatory center are transmitted via the spinal cord, exit the spinal cord at the ventral horn, and synapse with sympathetic ganglia. Postganglionic fibers combine with the peripheral nerves and travel to and entwine around the sweat glands. The sympathetic nerves consist principally of cholinergic terminals (M3 receptors) and, to a lesser extent, adrenergic terminals (alpha and

beta receptors). The sympathetic nerve fibers that release acetylcholine (ACh) stimulate M3 receptors on sweat glands. While ACh is the major neurotransmitter responsible for sweating, there is also an activation of alpha- and beta-adrenergic receptors. In addition to a central drive for sweating, a local enhancement occurs. ACh stimulates an axonal reflex which travels back up the nerve to other nerve terminals culminating in the further release of ACh.

In the practice of palliative care, sweating may be a pathological and disabling symptom of a life-limiting illness or its management. Such pathological sweating may be the source of significant suffering. For a list of causes of pathological sweating, see Table 3.

Paraneoplastic fevers and sweating are difficult to diagnose with certainty. These symptoms are identical to a presentation with sepsis as a complication of the malignancy itself or the cancer treatment. There are three indications that the symptoms may be paraneoplastic in origin. The first is that the results of blood cultures are consistently negative. The second is that antibiotics have no effect on the symptoms. The third is a diurnal rhythm to the pyrexia or sweats. It is usually at this juncture that the possibility of cancer-related pyrexia and sweats is considered.

Table 3 Causes of pathological sweating

Localized pathological sweating
1. *Disruption of sympathetic chain or white rami*
An example here is the Pancoast's tumor involving the apical lung causing localized loss of sweating (anhidrosis). Another example occurs in neurogenic tumors at the level of the hypothalamus or spinal cord.
2. *Irritation of sympathetic chain*
The sympathetic chain may be irritated by an encroaching tumor. Examples are lung cancer, lymphomas, or mesothelioma. This cause sweating on one side (unilateral hyperhidrosis).
Generalized pathological sweating
Systemic diseases
Endocrine conditions
Diabetes mellitus
Diabetes insipidus
Acromegaly
Pheochromocytoma
Thyrotoxicosis
Carcinoid syndrome
Infections – tuberculosis, HIV/AIDS
Endocarditis
Malignancy
Drugs (opioids), antidepressants (fluoxetine, naproxen)
Drug withdrawal
Malignancy

Malignancy can cause a local or generalized disruption to sweating. A Pancoast's tumor involving the apical lung may cause a localized loss of sweating (anhidrosis). Another example occurs in neurogenic tumors at the level of the hypothalamus or spinal cord. The opposite may occur (excessive sweating) if the sympathetic chain is irritated by an encroaching tumor. Examples are lung cancer, lymphomas, or mesothelioma. This causes sweating on one side (unilateral hyperhidrosis). Unilateral sweating in mesothelioma usually signifies advanced disease and has a poor prognosis (Waran 2016).

Classic causes of generalized excessive sweating (hyperhidrosis) are Hodgkin's and non-Hodgkin's lymphoma. Hodgkin's lymphoma is a B-cell lymphoproliferative syndrome, and in addition to lymphadenopathy, patients may present with a constellation of fever, pruritus, excessive sweating, and weight loss. The excessive production of IL-1 by activated macrophages may be involved. IL-1 increases the synthesis of PGE-2 in the hypothalamic central thermoregulatory center causing an elevation of the body's temperature. In addition, an excessive production of IL-6 by Hodgkin's lymphoma cells may also be implicated in fever and sweating. Apart from lymphomas, advanced solid tumors may also cause sweating via an immunologic mechanism related to TNF-alpha and interleukins on central thermoregulation.

3.3 Management

A critical threshold in the management of paraneoplastic sweating is making the diagnosis or at least considering the possibility of its presence. As stated above, it is often a diagnosis of

exclusion. This can cause significant delays in commencing management. A localized absence or excess of sweating should alert the clinician to think of a local mechanism. In terms of generalized sweating, an attempt should be made to identify the timing, duration, and severity of the sweats and whether they are associated with pyrexia. Non-pharmacological approaches include a tepid sponge, a cooling fan, or a cooling bath or shower. There is limited evidence for a pharmacological approach to sweating and/or pyrexia. Nevertheless, it is important to try a series of medications to determine which one or combination has efficacy and relieves the suffering of the patient. The first approach is to commence antipyretics such as paracetamol and, if considered safe, nonsteroidal anti-inflammatories. If there is no response, consider antimuscarinic medications such as oxybutynin, amitriptyline, Pro-Banthine, or glycopyrrolate (Twycross et al. 2014). Other medications that may be used include olanzapine (Zylicz and Krajnik 2003), cimetidine, propranolol, nabilone (a cannabinoid) (Maida 2008), and thalidomide (Calder and Bruera 2000). Table 4 summarizes this information with the recommended doses of each medication.

Table 4 The clinical approach to pathological sweating

1. Is the sweating localized or generalized?
2. For localized dysfunction (absence or excess of sweating), think of the mechanism. If the cause is cancer mass, is it amenable to radiotherapy?
3. For generalized sweats:
(i) Non-pharmacological approaches – tepid sponge, fan, cool bath/shower
(ii) Pharmacologic management. Stepwise approach:
(a) Commence with simple antipyretics – paracetamol, NSAIDS (if safe to use)
(b) If insufficient, consider antimuscarinics:
Oxybutynin 5 mg bd (2.5 mg bd if older patient)
Amitriptyline 10 mg nocte and titrate to efficacy
Pro-Banthine 15 mg bd – tds
Glycopyrrolate up to 2 mg tds po
(c) If insufficient, consider: olanzapine 5 mg bd, propranolol 10–20 mg bd-tds, cimetidine 400–800 mg bd, thalidomide 100 mg nocte, and nabilone

4 Skin Failure

The skin itself is the largest organ of the body, and as is the case with any other organ of the body, it too can fail. Multiple papers since 1989 have used the term "skin failure," though this is often poorly defined and is often defined within the parameters of multiple organ failure (MOF) (Brown 2003; Goode and Allman 1989; Hobbs et al. 1993; Irvine 2016; La Puma 1991; Witkowski and Parrish 2000; Worley 2007). In MOF, damaged tissue loses its ability to resist pressure and trauma, and as the body shunts its blood supply to the core organs in order to preserve life, the skin is deprived (Worley 2007). Skin failure has therefore been defined as when the skin and its underlying structures die due to hypoperfusion that occurs concurrently with severe dysfunction or failure of other organ systems (Langemo and Brown 2006).

Skin failure has further been subcategorized into acute, chronic, and end-of-life skin failure (Langemo and Brown 2006; Worley 2007). Acute skin failure is an event in which skin failure occurs concurrently with a critical illness and is related to hypoperfusion. Such events can include, but are not limited to, trauma, stroke, sepsis, cardiac events, or complications from surgery. Mortality rates range from 33% within 30 days of the detection of skin failure up to 73.3% at 12 months in the intensive care setting (Brown 2003). Chronic skin failure is represented by hypoperfusion which occurs during a chronic or multiple chronic disease states. For example, a patient may have multiple comorbidities, such as end-organ failure, diabetes, ischemic heart disease, stroke, or any innumerable combinations of comorbid conditions. This type of skin failure occurs progressively over time as opposed to the quicker presentation of acute skin failure. End-of-life skin failure occurs when the skin and its underlying structures die due to hypoperfusion concurrent with the end of life (Langemo and Brown 2006). Mortality rates range from 20.8% within 30 days of the detection of skin failure up to 73.3% at 12 months in the long-term care setting (Brown 2003).

The result of skin failure ultimately ends in skin compromise through localized hypoperfusion and hypoxia which may occur at the tissue cellular and molecular levels (Sibbald et al. 2009). In 2009 a consensus group gathered to discuss and describe these phenomena and coined the mnemonic Skin Changes at Life's End (SCALE) (Sibbald et al. 2009). The Kennedy Terminal Ulcer (KTU), often described as a subcategory of pressure injury, is associated with skin failure, particularly skin compromise at life's end. The KTU is described as an ulcer that occurs and deteriorates rapidly, despite preventative measures, often accompanying an impending death (Schank 2009). A KTU is usually shaped like a pear, butterfly, or horseshoe and is primarily located, but not limited to, the skin overlying the coccyx or sacrum. Hanson et al. (1991) reported that 62.5% of hospice patients with a pressure injury had their pressure injury develop in the 2 weeks prior to their death.

Unfortunately, the majority of the literature surrounding skin failure is observational in nature. There are currently no diagnostic criteria for skin failure to aid in a clinician's diagnosis. Therefore, currently a diagnosis is made by the clinician's knowledge of the phenomena and diagnosing its presence in an individual patient. This is not an ideal situation. Skin failure is a phenomena that needs and deserves further research, especially surrounding diagnostic criteria.

4.1 Pressure Injuries

Previously known as decubitus ulcers, pressure injuries include pressure sores, bed sores, and pressure necrosis or pressure ulcers. A pressure injury is damage to the skin with or without concurrent injury to the underlying tissue as a result of pressure or a combination of shear and/or friction with pressure (Australian Wound Management Association 2012).

As defined by the National Pressure Ulcer Advisory Panel (2016), pressure injury can be categorized into the following stages:

Stage 1 pressure injury: non-blanchable erythema of intact skin
Stage 2 pressure injury: partial-thickness skin loss with exposed dermis
Stage 3 pressure injury: full-thickness skin loss
Stage 4 pressure injury: full-thickness skin and tissue loss

Unstageable pressure injury: obscured full-thickness skin and tissue loss, i.e., unable to visualize the wound bed due to necrosis or slough.

Deep tissue pressure injury: persistent non-blanchable deep red, maroon, or purple discoloration.

Risk assessment for pressure injury should be attended on all patients and should include a clinical history, pressure injury risk scale, skin assessment, mobility and activity assessment, nutritional assessment, continence assessment, cognitive assessment, and an assessment of extrinsic risk factors (Australian Wound Management Association 2012). If a patient is found to be at risk, the appropriate prevention regime should be instituted including appropriate positioning, the use of an appropriate support surface, reducing shear and friction, and making the appropriate referrals to any allied health teams (such as dieticians for nutritional support).

5 Malignant Cutaneous Wounds

Malignant cutaneous wounds are caused by the infiltration of skin and its blood and lymph vessels by tumor (Alexander 2009). These wounds can occur anywhere on the body. Unless the patient is having anticancer therapy such as chemotherapy, radiotherapy, or targeted therapies, malignant cell division will continue to occur and therefore cause the malignant wound to progress/enlarge. These wounds most commonly occur in breast and head and neck cancers, although are often seen in patients with skin cancers and vulva and bladder cancers (Seaman 2006). See Figs. 1 and 2.

Malignant cutaneous wounds can be described as either ulcerative or proliferative in nature.

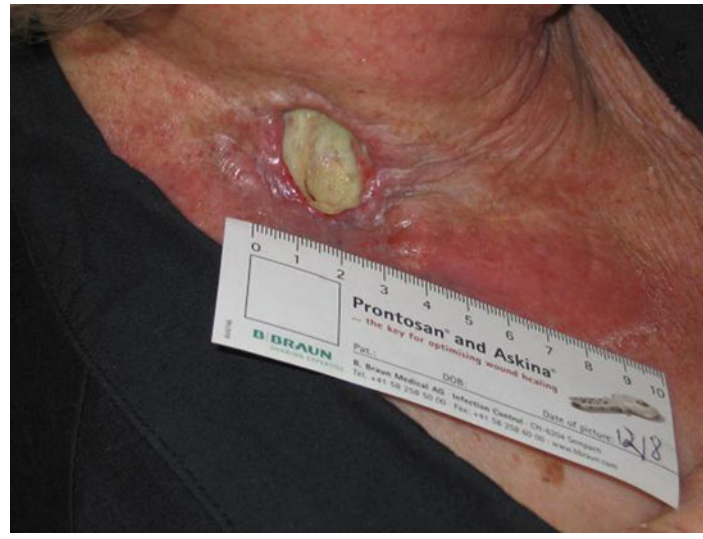

Fig. 1 Ulcerative malignant cutaneous wound

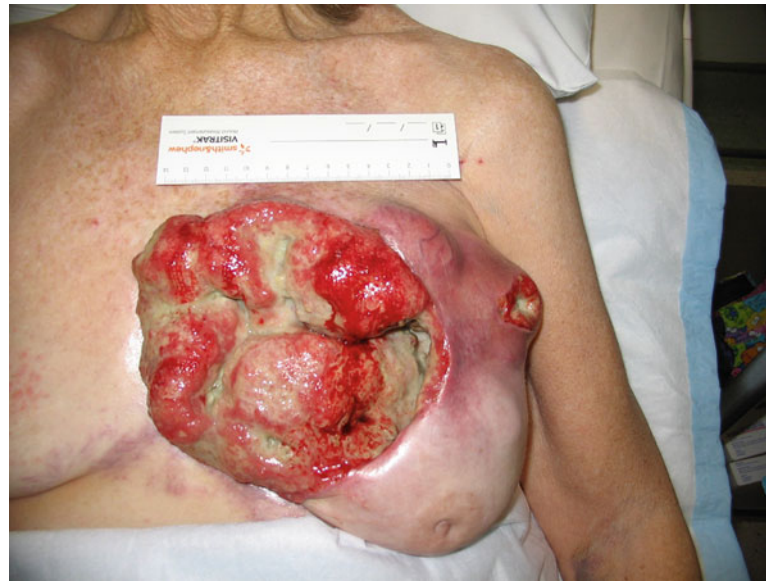

Fig. 2 Fungating malignant cutaneous wound

Fungating wounds rarely heal, so palliation through effective pain and symptom management as well as psychological support is essential. Although most fungating wounds occur in more advanced disease, it is possible for people to live many years with such a wound if the disease is localized. Incorporating the key principles of palliative care to managing these difficult wounds is, therefore, essential to reduce the impact of the wound on the patient's quality of life. A multidisciplinary approach to these wounds is also essential with input often required from wound care specialists, stomal therapy, social work, psychology, as well as palliative care teams (Maida et al. 2009).

The management of malignant cutaneous wounds is very often challenging for health-care professionals, and the symptoms can be vastly different between patients. Priorities for care involve good management of pain, exudate, odor, and bleeding and the provision of psychological support for patients and their loved ones.

Body image and self-esteem are also often adversely affected requiring ongoing emotional and psychological supports.

5.1 Patient Assessment

A comprehensive patient and wound assessment is essential to the development of a patient-centered plan of care and should include:

- A good understanding of the patient's disease process and plans for further anticancer treatments versus comfort measures.
- Review of the patient comorbidities such as peripheral vascular disease and diabetes.
- History of the wound – how long it has been there, and how has it changed?
- Assessment of the wound location and appearance.
- Pain and symptom assessment.
- Signs of infection/odor noted.
- Amount of exudate.
- What has the patient tried and what has worked for pain and symptoms or dressing requirements?
- What medications are prescribed for pain or symptoms associated with the wound?
- Assessment of the psychological impact of the wound on the patient and on their carers.
- Assessment of the risk of bleeding or airway obstruction needs to be taken into consideration as part of assessment depending on the location of the wound (Dowsett 2002; Wilson 2005).

5.2 Pain Management

Causes of pain in patients with malignant fungating wounds can be many, and it is important to take into account the emotional factors associated with these wounds. Pain may be caused by the infiltration or pressing of nerves and blood vessels, or there may be exposure of the dermis (Seaman 2006).

Providing optimal pain management is essential, and careful titration of systemic opioids may be necessary. Adding an antineuropathic agent into the pain regimen is also an important consideration following a thorough pain assessment. Using breakthrough opioid analgesia 20 min prior to dressings or the use of immediate acting sublingual fentanyl or fentanyl lozenges may prove very effective for the incident pain associated with movement or dressings.

Topical opioids such as morphine gel may also be useful for management of painful malignant wounds. The use of topical opioids remains controversial, and there are still few high-quality studies to support it. Nevertheless, it is worth consideration especially in patients who are experiencing side effects with systemic opioids.

Radiotherapy is often an effective treatment for the management of painful or bleeding tumors. The aim of radiotherapy is not to cure the cancer but rather to improve symptom burden and improve quality of life.

5.3 Bleeding

If a patient's wound is situated near major vessels, the risk of bleeding or hemorrhage may be significant. For most fungating tumors, bleeding is often characterized by slow capillary ooze. Medications which may be useful to slow or stop bleeding include oral tranexamic acid, sucralfate paste applied to the wound, topical adrenaline as a vasoconstrictor, as well as the use of non-adherent dressings.

For tumors which have the capacity to erode major vessels causing catastrophic bleeding, the prescribing of medications for such a crisis is important. An opioid for pain and benzodiazepine for anxiety are recommended. In the hospital setting, however, evidence is growing that the most reassuring thing a health professional can do for a patient with catastrophic bleeding is remain with and reassure the bleeding patient rather than leave the patient to retrieve medications to administer. Providing red or green drapes or towels to disguise the sight of blood can also reassure the patient (Grocott 1995; Seaman 2006; Naylor 2001).

5.4 Exudate

Malignant fungating wounds can produce exudate which can be quite challenging to control. Inflammation and edema are commonly present in malignant fungating wounds and can contribute to the exudate. Exudate is often increased if there is infection. Excessive exudate may cause leakage through dressings, staining of clothes, and further embarrassment for the patient.

Most fungating wounds produce moderate to high amounts of exudate, and when choosing an appropriate dressing, it is important to choose a dressing that will be absorptive but still able to maintain a moist environment. These may include alginate or hydrofiber dressings, foam dressings, soft silicone dressings, or knitted viscose with an absorptive pad. In cases of high exudate and where able to site, a stoma bag may be an appropriate way of managing the excessive exudate for the patient (Grocott 1995; Seaman 2006; Naylor 2001).

5.5 Odor

Management of odor is of particular importance for patients with malignant fungating wounds. An offensive smelling wound can lead to feelings of embarrassment, shame, and guilt and to social isolation and even depression. Uncontrolled malodor can lead to nausea and vomiting, decreased sense of taste, and decreased appetite.

Malodor is often due to a number of factors:

- Bacteria – aerobic and anaerobic
- Necrotic tissue
- Poor vascularization
- Exudate

Debridement of the necrotic tissue causing the malodor may be an appropriate treatment for a patient depending on the patient's condition and their wishes. Caution needs to be taken with debridement due to the increased risk of bleeding.

To combat the bacteria contributing to the malodor, antibiotic therapy is often useful, in particular metronidazole. This can be given systemically but also topically as gel. Metronidazole gel is often not as effective if the wound has excessive exudate. Caution should be used with the use of systemic metronidazole as it may cause nausea, neuropathy, and alcohol intolerance. Impaired blood supply to the tumor may also limit systemic metronidazole's effectiveness.

Topical antiseptic dressings may also be useful here such as silver-impregnated dressings which have a broad antimicrobial cover and exist in a variety in dressings that may aid in exudate management. Polyhexamethylene biguanide (PHMB) is another commonly used antiseptic that comes in a variety of applications including as a cleansing solutions which, as a result, can be used with a combination of other dressing types to aid in more versatile dressing choices.

Cleansing the wound is important as it reduces odor by removing debris and reducing bacteria counts, and it is also important as it makes the patient feel clean. Patients often feel self-conscious and distressed by the unpleasant odors so air fresheners, air filters, aromatherapy, and odor neutralizers can be helpful to disguise the smell. However, please take into consideration that the sense of smell is an extremely potent memory stimulator and that the patients' carers and loved ones may associate any aromatherapy scents with their loved ones' wound or death for the rest of their life (Grocott 1995; Naylor 2001; McMurray 2003; Seaman 2006).

5.6 Psychological Supports

Psychological care of patients with malignant cutaneous wounds is as vital as the care of their physical symptoms. Patients may experience many emotions including shame, guilt, embarrassment, anxiety, and anger. Some patients may withdraw from family and friends, and carers may be left with feelings of anxiety and helplessness (Lo et al. 2008). Fungating wounds may also lead to a degree of social isolation especially if there is malodor or exudate which is difficult to control. Impact on relationships and sexuality can also be significant (Probst et al. 2013).

A wound such as this is a constant reminder to both patient and those they love that they are living with a life-limiting illness. The many physical symptoms experienced by patients can significantly impact patient's physical, emotional, and spiritual well-being which is why a holistic approach to care is paramount (Probst et al. 2013).

Clear and honest communication to patient and family is important in building trust and rapport. Exploring therapeutic strategies and goals of care can reassure patients and families and decrease feelings of anxiety and fear (Seaman 2006).

6 Conclusion

The direct and indirect effects of malignancy and end-organ failure on the skin are protean. Each may cause significant suffering to the patient and carers. Our understanding of the pathophysiology, diagnostic criteria, assessment, and management of these manifestations is limited but growing. This chapter has sought to synthesize the current knowledge of those skin syndromes that have the most impact on the practice of palliative care – pruritus, paraneoplastic sweating, skin failure, and malignant cutaneous wounds. Rather than greeting these manifestations with therapeutic nihilism, we should be confident that basic interventions can provide significant comfort, relief, and support to our patients.

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Dealing with a Wound in Palliative Care

22

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Contents

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_115

Abstract

Wounds are a significant issue in palliative care, and to deliver the best wound management, it is essential to understand the principles of wound management and how the body heals. The pathophysiology of wound cause is an essential part of wound assessment as treatment is based on a clear diagnosis of the underlying etiology. The management of a wound in palliative care will be impacted by specific issues such as pain, odor, exudate, and infection. Although it may not be possible to prevent all wounds, good skin care is important. The principles of wound assessment and wound management including the specific problems are explained.

1 Overview of the Principles of Wound Management

Wounds either acute, postsurgical, or chronic are a growing area of palliative care practice and it is important to review the current methods of management and developments in diagnosis, assessment, and treatment. The aim of this chapter is to explain how wounds heal, what impacts on healing and how to deal with the specific issues in palliative wound care.

Wound management is now defined as "The provision of the appropriate environment for healing by both direct and indirect methods together with the prevention of skin breakdown" (Sussman 1998) and thus on wound management is not merely the application of a dressing to an acute or chronic wound but must be part of an holistic approach to the patient to ensure the best practice is applied in treatment – we should "treat the whole patient and not just the hole in the patient."

1.1 The Basic Principles of Wound Management

1.1.1 Etiology of Wounds

Wounds are either acute or chronic in nature and the approach to each type can be different.

Acute wounds	Chronic wounds
Higher risk of infection	Lower risk of infection
Due to debris contaminating wound	Symptom of underlying condition
Inflammation occurs	Heal by secondary intention
May heal by primary intention	Not sterile
May require antiseptic use and antibiotics	May be sloughy and exudative

Wounds heal either by:

- Primary intention

  Involves the apposition of the wound edges and the reunion of tissue structures and should result in minimal scaring.
- Secondary intention

  Open, gaping wounds where there is loss of tissue, or infected, closed wounds heal by the formation of granulation tissue (vascular and fibroblast proliferation) which fills the defect and by contraction of the wound edges. Healing by secondary intention is slow and can result in a large distorted scar.

1.1.2 Physiology of Wound Healing

Healing should be considered as a continuum of the three phases of wound healing: inflammatory (destructive), proliferative (regenerative), and maturation (reparative). Each phase continues on in a steady process merging with the next phase and one wound may be in more than one phase at one time. During all of these phases, there are a number of cells that are essential to the process of the healing including platelets, neutrophils, macrophages, and fibroblasts.

1.1.3 Phases of Healing

Inflammatory Phase

The inflammatory phase is normally the shortest, and is manifest at the beginning of the wound itself where a wound is either surgically created, caused by trauma, or some other reason. There will be bleeding, and a clot will develop to induce hemostasis. The tissue around the wound may often be red, hot, sore and swollen. This does

not indicate infection, it is merely the inflammatory process itself; consequently, it is not always necessary to apply topical antiseptics or topical antibiotics. Wound exudate is often seen during the inflammatory phase. It is not a passive component of the healing process, but serves to nourish the tissues and to flush out necrotic tissue and foreign debris from the wound. The continued presence of foreign material, necrotic tissue, or even excessive antimicrobial use or other continued disruption of the wound can result in prolonged inflammation thereby preventing the onset of proliferation and maturation; this may lead to fibrosed tissue. At this stage, one of the most important cells are the platelets whose task is not only hemostasis, but also the production of a growth factor. Neutrophils, are also involved, in the phagocytosis of bacteria as well as aiding in the extracellular release of protease – an enzyme used by the body for the destruction of necrotic tissue (Sussman 2001, 2014).

Proliferative Phase

During the proliferative phase, the new vascular bed is formed by angiogenesis. Capillary buds are formed which link up with the existing capillary network and allow oxygenated blood to provide a lush bed of capillary vessels. During the proliferative phase, collagen is deposited by the fibroblasts and forms the essential framework for the connective tissue which will eventually fill the wound. Fibroblasts also synthesize proteoglycans or ground substance, and it is collagen and ground substance which form the scaffolding for wound repair. The collagen then realigns itself by cross-linking, resulting in an increase in the tensile strength in the wound. There are a number of elements essential for collagen production and deposition including vitamin C, oxygen, iron and zinc. A deficiency in these nutrients could lead to the development of a weakly bonded matrix, and ultimately to dehiscence of the wound.

During the proliferative phase, wound contraction occurs. This is an action of the myofibroblasts, contractile cells which pull the wound margins together. Contraction and granulation are the processes by which the wound becomes smaller. During the latter stage of the proliferative phase epithelialization occurs, involving the growth of the epidermal cells over the surface of the granulation tissue, a process which is completed most efficiently in a moist, clean environment.

Maturation Phase

The maturation phase is the final stage of healing. During this stage, the fibroblasts decrease in number, vacuolization decreases, and the tensile of strength of the wound increases. Maturation is the most misunderstood phase of healing. It is assumed that a wound is healing once the epithelium has closed the surface of the wound but the tensile of strength of the wound may in fact may take quite a considerable time, and in some patients it can take up to 12 months. A re-ephithelialized wound may not be fully healed but the wound may not be totally healed beneath the surface and the lack of tensile strength in a wound will increase the risk of breakdown that may be related to tension the tissue below the surface (Sussman 2001, 2014)

1.1.4 General Principles of Management

The major objective is to facilitate optimal healing (that is, with as little scar tissue as possible, with a good cosmetic appearance). Therefore, to treat an acute wound, you should first ensure it is clean and then, if necessary, the wound edges should be held together by sutures or tape, and finally an appropriate dressing applied. Medical intervention may be necessary if there is a possibility of tetanus spores or other foreign bodies being trapped in the wound.

For contaminated wounds, closure is not recommended since the risks of infection and breakdown are considerable treat as a delayed primary closure – cover with sterile dressing for approximately 4 days, then treat as a primary wound.

The management of the wound environment is now based on the concept of wound bed preparation (WBP) interventions, which address

debridement, bacterial balance, exudate management, and the local tissue in the wound environment. These important assessment elements have led to the development of the concept of the TIME principles (**T**issue, **I**nflammation/**I**nfection, **M**oisture, **E**dge/**E**pithelialization). This simple principle enables a wound to be assessed for most of the important aspects of the wound; this enables the health professional to consider the factors for healing or delayed healing and what must be considered in the choice of treatment (Leaper et al. 2014; Schultz et al. 2003).

1.1.5 Moist Wound Management

Knowledge and understanding of wounds, tissue, and healing have grown rapidly over the past 30 years, resulting in a major change in the method of wound management. There has been a growing awareness that traditional wound-care products do little to aid healing, and in many cases actually delay it.

Traditional theory has always been that wounds should be kept clean and dry so that a scab may form over the wound, the wounds should be exposed to the air and sunlight as much as possible, and where tissue loss is present, the wound should be packed to prevent surface closure before the cavity is filled, and then the wound should be covered with dry dressing.

The clear disadvantages of these principles are that the scab, which is made up of the dehydrated exudate and dying dermis, is a physical barrier to healing, which is then delayed because the epidermal cells cannot move through the scab formed and this may ultimately result in a poor cosmetic results even scarring. Exposure to the air reduces the surface temperature of the wound and further delays healing causing peripheral vasoconstriction affecting the flow of blood to the wound. This lower blood flow will also effect the supply of oxygen, nutrition, and other factors to the wound. Air exposure will also cause the wound to desiccate and forma scab.

Where a wound is packed with dry gauze, the quality of healing is impaired due to adhesion of the material to the surface of the wound causing it to dry out. Equally covering the wound with a dry dressing that adheres to the wound surface may traumatize the wound surface on removal. Wounds covered by an occlusive dressing do not form a scab, so epidermal cells are able to move rapidly over the surface of the dermis through the exudate which collects at the wound/dressing interface. The application of a totally occlusive or semipermeable dressing to wound can also prevent secondary damage as a result of dehydration.

Dr. George D. Winter was able to demonstrate scientifically the difference between wounds of a similar nature when healing was open to the air, and when healing was under occlusive dressing (Winter 1962). The experiment showed that the wounds healing under moist conditions healed 50% faster than the wounds healing under dry conditions, open to the air. Winters work has since formed the basis of the principles of modem moist wound management. Many subsequent studies have confirmed the theory that wound heal faster in a moist compared to a dry environment (Hinman and Maibach 1963; Winter 1962).

Moist wound healing also simplifies debridement by assisting in the autolytic debridement of wounds. It facilitates wound cleansing, since the wound exudate is part of the healing cascade. It also protects granulation and encourages epithelialization. It has now been shown to carry a number of growth factors essential to the healing of wounds (Sussman 2014).

2 Wound Assessment

Wound Assessment is the most important function to enable the clinician to identify both the patient and the wound-specific issues.

To help differentiate the basic etiology of a wound, such as a leg ulcer, information is needed:

- History
- Medical/surgical
- Health status, e.g., cardiorespiratory function
- Concurrent illness such as diabetes, autoimmune diseases
- Diet and smoking
- Medications

- Psychosocial issues
- Examination
- Wound (color, depth, and exudate)
- Surrounding skin
- General condition
- Investigation
- FBE – anemias, ESR
- Blood glucose, HbA1c
- Serum albumin and liver function
- Renal function
- ABI
- Bacteriology to identify infection
- Histology to diagnose a carcinoma/metastasis or for atypical wounds

Disruption of circulation and perfusion impairs delivery of cell nutrients and immune cells (leukocytes, macrophages), which delays wound healing. Note any concurrent illnesses that might have an effect on healing, i.e., diabetes mellitus or atherosclerosis, autoimmune diseases, e.g., SLE (Grey et al. 2006; Sussman 2001, 2014).

All these areas should be checked and particular attention paid to the following.

2.1 Medication

A number of medications may impair wound healing, in particular corticosteroids and other immunosuppressive drugs, some over the counter medication, such as NSAID. . . and complementary medication, including Ginko, may also impact healing. However, this may not be a major consideration in palliative care as the aim is often not wound healing. With patients living longer and having earlier palliative care, healing may be an aim/possibility (Graves and Sun 2013; Sussman 2007).

2.2 Nutritional Status

Nutrition plays a very important role in tissue repair and wound healing, and patients who are malnourished do not heal well and are at a greater initial risk of developing pressure injuries. It is essential to perform a nutritional assessment examining issues such as weight loss or gain, caloric intake, macronutrients, and hydration. The estimation of albumin level may be helpful – a serum albumin less than 3.5 gm/dl indicates the need for further assessment and action, and a level below 3.0 gm/dl is correlated with poor patient outcomes (Harris 2004; Wild et al. 2010).

2.3 Ageing Issues

Wounds in general and leg ulcers, pressure sores, and skin tears in particular are common problems in an ageing population. To fully understand the nature and causes of these chronic wounds, it is essential to consider the main physiological effects of ageing on tissue and the factors that influence healing. The ageing process will impact on most of the structures of skin. Ageing skin loses hair follicles, sebaceous glands that supply natural moisture to the skin, receptors, blood supply, and sweat glands. The result of these tissue changes is that the skin becomes thinner, brittle, avascular, and more prone to injury. Thus, the elderly have thinner and more fragile skin will often present with skin dryness, thinning, laxity, uneven skin pigmentation, and hair thinning, the skin is often tissue paper thin at risk of skin tears (Gosain and DiPietro 2004; Sussman and Golding 2011; Sussman 2016). Although healing may be slower and may be more complex in older patients, it is still important to aim for healing. Patients receiving palliative care are often elderly and have multiple morbidities and wound management should be for comfort, and, if possible, for healing. It is important to continue, to manage and not to just give up small gains can have a significant impact on the patient.

2.4 Patient/Family Awareness

As the patient and the family will be caring for the wound at home the support and psychosocial aspects of the patient, within their family, is important. Assessment of their abilities and willingness to be involved is important as coping with a deteriorating family member with a wound is often very stressful (Probst et al. 2013).

2.5 Wound Assessment

After patient assessment, the next step is to carefully assess the wound. Wound assessment includes the wound's etiology, its location and its size and depth. A thorough wound assessment also includes evaluation of the wound bed in terms of type of tissue present; observation of the quality and amount of exudate; and determination of the presence or absence of infection. It also involves assessment of the condition of the peri-wound area and evaluation of any past and current treatments (Grey et al. 2006; Sussman 2001, 2014).

2.6 Determination of the Presence or Absence of Infection

It is important to determine if a wound is infected before treatment is initiated. Most chronic wounds with tissue loss are contaminated, but this contamination only becomes significant when local defenses can no longer contain the bacterial growth (10^5 organisms per gram of tissue). Therefore, culturing is of little use unless true signs of infection are present for although many strains of bacteria will be found this may not be an indication of true infection, only contamination. The classic signs of infection include advancing erythema, fever, warmth, edema/swelling, pain, and purulence (pus). However, these are not always observed and more commonly the signs may be of delayed healing, change in color of wound bed including friable granulation tissue, increased or abnormal odor, increased serous drainage, and increased pain at wound site, these are the secondary signs of infection (International Wound Infection Institute 2016).

3 Different Wound Types

A large proportion of wounds seen in clinical practice are chronic in nature. The difficulty in the management of any chronic wound is that there is always an underlying physiological cause of the wound which must be treated, but many patients have multifactorial issue and comorbidities. For best results, the basic cause of the problem must be managed, and the negative factors altered.

It should be understood that some patients may never heal due to the basic pathophysiology of the disease process and our inability to alter some or all of the major factors influencing the nonhealing of the wound. However, even in the most extreme cases, good wound care can be a great help in minimizing the worst effects of such chronic wounds.

3.1 Leg Ulcers

Leg ulcers have a number of different causes, including venous insufficiency, arterial disease, diabetes mellitus, vascular complication of autoimmune disease (such as rheumatoid arthritis), malignant disease, trauma, and deliberate self-injury.

Part of the diagnosis of a leg ulcer to differentiate the cause is to obtain an Ankle/Brachial Index (ABI) – this compare ankle systolic pressure with brachial systolic pressure with a normally ratio should $= 1$ ABI < 0.8 implies arterial insufficiency. If ABI < 0.7 no compression should be applied. The result can be > 1.2; this is due to pain at site, incompressible (calcified) vessels.

3.2 Venous Ulcers

Venous ulcers result from the breakdown of the venous circulation of the leg and are an association of the inability of the leg to force the passage of blood through the various connecting veins via the bicuspid valves by muscular contraction. They are most often found in the lower one-third of leg, in the gaiter area, are usually irregular in shape, not painful, and edema is often present. The skin is often stained and also has changes, e.g., eczema, atrophy blanche (white stippled scars on the skin), and there is a history of varicose veins, obesity, past DVT, poor mobility resulting in venous stasis. Venous leg ulcers are usually

often painless, irregular shape, and there may be copious exudate.

As venous incompetence is often the main cause of the ulcer treatment is the application of compression therapy toe to knee 30–40 mmHg at ankle. It is, however, essential to exclude arterial involvement before commencing compression.. It is important to encourage exercise and address occupational factors such as long periods standing that lead to venous stasis.

Leg ulcers may also result in patients with lymphedema, caused by a reduction in the function of the lymph vessels to drain extracellular fluid. The resultant edema will place the patient at risk of ulcer development as a result of minor trauma and by the hyperkeratotic nature of the skin (Alexander House Group 1992; Sussman 2014).

The management of venous and lymphatic ulcers will depend on the depth, exudate level, and if infected.

Table 1 list the appropriate products depending on the wound. If the wound is infected, then Table 3 lists appropriate management.

3.3 Ischemia or Arterial Ulcers

The death of skin automatically follows occlusion of its arterial blood supplies unless this is gradual enough to allow a collateral blood supply to be established. Atheroma (thickening) is the most common cause of arterial ulcers of an ischemic nature. The loss of arterial circulation may be also due to extramural strangulation, with scar tissue or other factors causing strangulation of the arterioles, or fibrosis resulting from longstanding, chronic edema, or chronic infection may also obstruct arterial flow. Mural changes (to vessel wall), Atherosclerosis (deposits on the wall surface) caused by plaque formation reducing blood flow until thrombosis, embolism, or infection cause complete closure.

Intramural occlusion of small vessels by changes in blood viscosity, platelet adhesiveness, and fibrinogenesis (especially in small painful ulcers of the feet and ankles).

Arterial ulcers are very painful, especially at night. This pain is observed in both small and larger arterial ulcers. Their edges are sharply defined and the ulcer is "punched out." The base is often covered with slough. This may deepen to bare the tendons. There is usually a history of intermittent claudication (pain on exercise), dependent foot (dusky foot) white on elevation, a history of peripheral vascular disease, lower ABI, weak/absent pulses, sluggish/poor capillary refill. The ulcer site is usually below ankles to toes, the skin is often shiny and friable. Uncontrolled diabetes and smoking are significant factors causing arterial insufficiency. Healing is often slow and may depend on control of the underlying cause.

Treatment of arterial ulcer may involve a surgical opinion – angioplasty, stenting, bypass grafting, and ultimately amputation. Pain control is an important aspect of the management of arterial ulcers (Hopf et al. 2006; Sussman 2014). In addition, for the wound itself Tables 1 and 2 lists products for management.

It is important to note that between 10% and 15% of leg ulcers are of mixed etiology. These ulcers are often hard to heal due to associated edema, cellulitis, thrombophlebitis, diabetes, or underlying vascular disease, rheumatoid diseases especially in bedridden patients, general conditions of the skin in elderly patients which is often associated with malnourishment (Humphreys et al. 2007).

3.4 Other Causes of Ulcers

In addition to the more common forms of ulceration, there are a number of less familiar causes. Vasculitic ulcers may develop as a result of other medical conditions, such as rheumatoid arthritis and polyarthritis. Infections of the skin can produce ulcers especially if necrotizing bacteria are involved and skin conditions like pyoderma gangrenosum and epidermolysis bullosa (Sussman 2001, 2014). These autoimmune and inflammatory wounds are managed by immunosuppression and topically with hydrogels and secondary dressings.

Table 1 Management of the exudate (This will depend on the volume of exudate)

Exudate volume	Wound type	Dressing type
None (Dry)	All	Simple NA dressings Hydrogels IntraSite®, Purilon®, Flaminal®
Scant	All	Simple NA dressings Hydrogels IntraSite®, Purilon®, Flaminal®
Small	All	Hydrocolloids DuoDerm®, Comfeel®, Hydrocoll®
Moderate	Surface	Foam Allevyn®, Lyofoam Max®, Permafoam® Silicone Foam Mepilex®, Allevyn Life®, Foam-like Biatane®, Tielle®, Super absorbents ExuDry®, Mesorb®, Zetuvit®, Mextra®
Moderate	Cavity	Foam Allevyn®, Foam-like Biatane®, Fiber dressing (Alginate, CMC) Kaltostat®, Algisite M®, Aquacel®,
Large	Surface	Foam Allevyn®, Lyofoam Max®, Permafoam® Silicone Foam Mepilex®, Allevyn Life® Foam-like Biatane®, Tielle®, Super absorbents ExuDry®, Mesorb®, Zetuvit®, Mextra®
Large	Cavity	Foam Allevyn®, Foam-like Biatane®, Fiber dressing (Alginate, CMC) Kaltostat®, Algisite M®, Aquacel®

Sussman (2017)

Table 2 Modern Tulle dressings

Tulle type	Product
Standard	Adaptic®, Cuticerin®, Atrauman®
Silicone	Mepitlel®, Adaptic Touch®, Atrauman Silicone®

Sussman (2017)

3.5 Mechanical Etiologies

Pressure injury is the most preventable of all of the chronic wounds – see ▶ Chap. 23, "Pressure Injury Prevention and Management in Palliative Care." Pressure injury may be as simple as the blister which occur from footwear to the extensive pressure sores experienced by bedridden patients suffering from stroke, spinal injury, multiple sclerosis, dementia, and receiving palliative care.

The capillary pressure in the arterial blood system is some 32 mm of mercury. It therefore requires a pressure of only about 30 mm of mercury to restrict the arterial blood flow. The consequence of this restricted blood supply is a reduction in oxygen supply and nutrition to the tissue, accompanied by the problem of waste products not being removed from the site of the wound. The result of this is hypoxia, tissue acidosis, increased capillary permeability, which allows intravascular fluid to escape causing edema and cell death.

The main causes of pressure wounds are (Leigh and Bennett 1994) the following:

3.5.1 Pressure

Direct pressure on tissue over a bony prominence in excess of 30 mm of mercury will cause ischemia in the surrounding tissue. This will occur not only from a patient being in bed but also on a trolley or sitting in a chair. The extent of tissue damage will depend on the intensity of the pressure and the length of time the pressure remains unrelieved. The tissue can tolerate pressure for short periods of time. However, even low pressure over a long period of time will have some detrimental effect.

3.5.2 Friction

Friction occurs when the top layers of skin are worn away by continued rubbing against an external surface. This can manifest itself in a simple blister or tissue edema, or an open pressure wound. This can be caused by ill-fitting footwear, or even bed linen.

3.5.3 Shearing Forces

Shear is when the skin remains in place, usually unable to move against the surface it is in contact with, while the underlying bone and tissue are forced to move. This force will contribute to the destruction of microvasculature in a manner similar to direct pressure. This type of pressure injury

Table 3 Management of infected, odorous, bleeding wounds, and fungating

Wound issue	Surface	Cavity
Infection	Silver dressings Acticoat®, Atrauman Ag® Aquacel Ag®, Silvercel® If exudating use a silver foam Mepilex Ag® or silver CMC foam Aquacel Ag Foam® Iodine complex dressings Iodosorb®, Inadine® Metronidazole gel Medicinal honey dressings	Silver ribbon dressings Acticoat Absorbent®, Aquacel Ag®, Silvercel® Acticoat Flex®
Odor	Metronidazole gel Activated charcoal dressings Carboflex® Actisorb Plus® Medicinal honey dressings	Metronidazole gel plus packing gauze plus Activated charcoal as a secondary dressing
Bleeding	Calcium alginate dressing Kaltostat®, Algisite M® Silver nitrate	Calcium alginate ribbon dressing Kaltostat®, Algisite M®
Fungating These wounds are the most difficult as they often combine all of the above issues	A combination of products may be needed. There is a product that combines calcium alginate, absorbent CMC, and activated charcoal CarboFlex®	

Sussman (2017)

is seen in patients left sitting up in bed or on a chair, while gravity causes the patient to slide down with the skin adhering to the bed linen or the surface of the chair.

The prevention and management of pressure injury requires that the patient has pressure relieving surfaces on which to lay. The management of the wound itself will depend again on size, depth, tissue type, exudate, and presence of infection. Tables 1, 2, 3 indicate the products for management.

4 Management of Wounds in Palliative Care

The most common wounds found in palliative care include pressure injury, arterial/Ischemic wounds, neoplastic wounds, and surgical wound breakdown (Brink et al. 2006; Langemo and Black 2010). The main issues in palliative care are the management of the following factors.

4.1 Pain

It is important to consider pain control as all wounds are painful and over time wounds may become more painful, the skin surrounding the wound can become sensitive and painful and for some patients, the lightest touch can be intensively painful.

Analgesic medications are used to provide symptomatic pain relief; they do not modify the underlying cause of pain. Combining pharmacological and nonpharmacological approaches may allow lower drug doses to be employed. Selection of medication should be based on the highest likelihood of gaining pain relief with the lowest likelihood of side effects.

The WHO analgesic ladder recommends simple analgesia for minor pain adding NSAID or codeine for more severe pain and opioids for major pain. The choice of analgesic will also depend on the pain type, nociceptive pain is managed with the standard analgesia as per the WHO pain ladder. Neuropathic pain, when there is associated nerve damage, is managed with specific medication including tricyclics and Gabapentin, Pregabalin and GTN patches, or ointment. Nonpharmacological methods include the use of relaxation methods, coping strategies, distraction, warm socks, legs down, and raising the bed head.

The goal of analgesic therapy needs to be established as complete pain relief is rarely achievable when dealing with pain of neuropathic

origin and the aim may only be to reduce it to tolerable levels. Pain management requires a balance between pain relief and the maintenance of function.

Where wound pain is an issue then it must be established is the pain constant, intermittent, or only as dressing changes. Where dressing pain is the issue, then consider the careful selection of dressings for pain reduction, such as soft silicone dressings. Where the pain is more general, then in addition to any oral or systemic medication, topical treatment can be added. Topical analgesia includes opioids as patches or gels, capsaicin, local anesthetics (such as lignocaine). Topical morphine has been successfully used in the palliative setting the usual strength is 1 mg of morphine to 1 gm of sterile hydrogel, e.g., IntraSite gel. There is evidence for the use of topical Lignocaine from 3% to 5% (Braschi et al. 2017; Desai et al. 2014; Graham et al. 2013; LeBon et al. 2009; Peppin et al. 2015; Steele 2017; Woo et al. 2008).

In addition to analgesia for pain management use a pain assessment form/scale and minimize procedural pain. If necessary, medication may be given prior to a wound care procedure and all involved should be aware of pain at dressing changes. It is also important to select appropriate dressings that are atraumatic on removal. It is helpful to develop guidelines to prevent tissue damage and to educate staff about pain/trauma with dressing.

4.2 Odor

According to Gethin "Malodour is cited as one of the most distressing symptoms of these wounds, is a complex phenomenon with multiple potential causes, and may signify infection or necrosis. Malodor can cause depression, social isolation, nausea, anorexia and, in some individuals, a gagging or vomiting reflex." (Probst et al. 2013, p. 48). The cause of malodor includes the presence of both anaerobic/aerobic bacteria but this does not always indicate infection The issue is that odor is a major problem often caused by bacteria often on the surface of the wound and not infecting tissue. Odor removal is very important as it impacts not only the patient but family and staff. The management of odor will depend on the cause. The most commonly used treatments are topical metronidazole gel that will kill anaerobic bacteria, topical antiseptics including silver and iodine dressings, and honey. The secondary method of odor removal is the use of absorption activated charcoal dressings as some come combined with silver and some with hemostats and absorbent fibers, see Tables 1, 2 (Akhmetova et al. 2016; Finlay et al. 1996; Haycocks and Chadwick 2014; Kuge et al. 1996).

4.3 Exudate

Exudate management is very critical, both to remove excess exudate and to prevent primary damage to the wound and secondary damage to the peri-skin. This is the skin around the wound that has an important function to aid in wound contraction it needs to be in good condition.. The type and level of exudate will impact on the choice of product to manage the exudate, see Table 1.

Exudate is generated as part of the inflammatory response (Cutting and White 2006). It is essential to the healing process and, together with inflammation, should not be considered as a necessary evil but as a vital component of the reparative process. Exudate may be regarded as a transport mechanism, as plasma, from which exudate is derived, delivers all the necessary ingredients, oxygen, and nutrients to the tissues and organs of the body. Similarly, exudate on its way to the surface delivers these components to the wound bed. Traditionally, wound fluid has been considered a reflection of the internal wound environment and it has been used to monitor and reflect on the chronic status of a wound or to measure the efficacy of wound treatment. However, on closer inspection of chronic wound fluid, certain components of the fluid, particularly matrix metalloproteinases (MMPs) and their subcomponents (MMP-9) have been found to exist at higher levels in wound fluid than in the corresponding wound, and there is mounting

evidence that much of the destructive effects observed in chronic wounds may be compounded by these components of the wound exudate which are corrosive in nature resulting in a continuum of extra cellular matrix (ECM) breakdown, the ECM is the combined fiber structure providing tensile strength to the tissue. Additionally, an association has been made between high bacterial levels and elevated MMP9 in chronic wounds.

It is also important to clearly identify both the volume and the type of exudate. The volume may be none, scant, small, moderate, or large and exudate appearance will vary including serous (clear, watery consistency), fibrinous (cloudy, contains fibrin protein strands), purulent (contains pyogenic organisms and other inflammatory cells), Hemo-purulent (contains neutrophils, dead/dying bacteria, and inflammatory cells damage to dermal capillaries leads to blood leakage), and Hemorrhagic (blood is the major component of this type of exudate) (Chadwick and McCardle 2015; Cutting and White 2006; Tickle 2015; Vowden et al. 2015).

Where the exudate is very large and there is a need to change the dressings multiple times a day to keep the cost in check then the use of continence pads can be used. It is, however, essential to apply a contact material over the wound such as modern tulle or silicone tulle dressing first so that the pad does not come into direct contact with the wound. See Tables 1, 2, 3 (Sussman 2014; Weller and Sussman 2006).

4.4 Hemostasis

Where bleeding is present in the wound, the simplest method is to apply firm pressure over the area. The use of hemostatic agents, such as a calcium alginate, will help speedup the process of clot formation. The use of topical adrenaline for vasoconstriction in severe/terminal bleeding has been found to be helpful. It is essential to establish if there is any blood vessel damage, and if there is, prompt medical intervention is mandatary. It is also helpful to ascertain whether the patient is taking any anticoagulation medication. See Table 3 (Terrill et al. 2003).

4.5 Cleansing (*Decontamination I Cleansing*)

If the wound is basically clean, then water or saline are most suitable. If there is any level of contamination, a surfactant solution such as QV Wash™ or some similar product is the most satisfactory, due to the ability of the product to remove material by a soap-like action without altering the acid pH of the skin.

The use of topical antiseptics have a place in acute wounds, it is entirely different from that used in chronic wounds. In a traumatic wound, the risk of infection from contamination at the time of wounding is very high. In general, chronic wounds do not require the use of topical antiseptics unless they are heavily colonized or infected then the use of the less toxic antiseptics, e.g., Polyhexamine methyl biguanide (PHMB) are indicated (Cutting 2010; International Wound Infection Institute 2016).

5 Wound Management Principles

The management of a wound must start with appropriate cleansing with minimal trauma palliative wounds often have fragile tissue. If there is slough present, if possible gentle debridement is helpful. The choice of product will depend on the wound itself in particular the level and type of exudate. It is essential to prevent wound contamination and infection. The role of wound products is to control the wound environment and to protect damaged and healing tissue and the peri-skin. In palliative care, it is pivotal to ensure patient comfort. Dressing selection is important for management of the wound environment and the dressings choices overwhelming will take a function-based approach for selection. In general, avoid adhesive dressings other than those with a soft silicone adhesive due to the fragile nature of the skin.

The secondary considerations are the specific wound properties. A deep cavity wound needs to be gently packed to fill the dead space and absorb exudate if dry then packing with a

hydrogel is appropriate. Wounds that are locally infected or heavily contaminated need a topical antiseptic. Wound related pain and other patient comfort issue must be addressed. Care must be taken at dressing changes to minimize wound trauma and pain.

6 General Rules for Dressings Use

When applying a dressing allow 2–3 cm of dressing greater than wounds, this will enhance the product wear time. Place one-third above and two-third below the wound, this will allow the greatest surface area for exudate absorption. The dressing should remain in place for as long as possible, only remove when strike through occurs. With older patient or those with fragile skin, remove the dressings with great care; if necessary remove under the shower. The choice of management product may change as the condition of the wound changes.

7 Neoplasia and Complex Wounds with Infection

Neoplasia both directly and indirectly play a major role in palliative care. Many patients with terminal cancer of various types are referred to palliative care services. Some specific neoplastic wounds such as fungating breast cancer are a challenge to manage. They are painful, exudating, malodorous, and tend to bleed and may hypergranulate. Squamous Cell Carcinoma (SCC) can develop in nonhealing wounds and these are called Marjolin Ulcers SWCC's and some will metastasize. There are many forms of treatment for skin cancer but surgery is the most successful treatment, radiotherapy and intralesional interferon are also used, however, surgery is the only suitable treatment for SCCs and melanoma. Management of these wounds is complex specific issues such as management odor and bacteria are addressed in Table 3 (Addison and Richard 2014; Merz et al. 2011).

8 Skin Care

Skin integrity reduces with age and disease, dermal thickness is reduced, there is a weakened dermal-epidermal junction. The level of vitamin D, collagen, and moisture is reduced. Migration of capillary epithelial cells, epidermal turnover is reduced, and fragility of capillaries is increased. There is also a compromised inflammatory response and concomitant illnesses and many medications impact on both skin integrity and on healing.

It is important to ensure that all patients receive good skin care and their skin integrity is assessed regularly; the greater the emphasis on skin protection and integrity, the significant reduction in the risk of skin breakdown. Good skin care can have a significant impact and reduce skin damage. Adequately hydrating dry skin with effective moisturizing agents, ointments, lotions are better than creams and should be used twice a day on dry skin areas and extremities (Peppin et al. 2015; Sussman 1998). The essential aspect of the use of skin moisturizers is to ensure that the moisturiser used is ones that will not cause a greater loss of moisture through the skin or damage skin cells. Aqueous creams are known to increase transepidermal water loss and dry the skin; some aqueous creams have also been shown to be cytotoxic (Carville et al. 2014; Greive 2015; Kempf et al. 2011; Mohammed et al. 2011; Tsang and Guy 2010).

9 Conclusion

The management of palliative wounds should be the first and foremost patient comfort and symptom reduction. The patient and the absolute requirement for quality of life is to ensure the symptoms which impact not only on the

patient's but on the patient family, and the treating staff are managed to ensure the lowest impact (Graves and Sun 2013).

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Pressure Injury Prevention and Management in Palliative Care

23

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Contents

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_116

Abstract

Pressure injury, pressure ulcer, decubitus ulcer, bed sore are synonymous terms that define a wound that is deemed by many to be preventable. However, palliative care patients who are close to death may have compromised skin perfusion and ischemic skin changes as physiological responses divert blood flow from the integument to other major organs. Tissue tolerance to pressure, shear, and friction is further compromised by malnutrition, cachexia, immobility, and inactivity and comorbidities, which are frequently associated with end of life. Palliative care patients are considered to be at high risk of pressure injuries because of these challenges and an informed and collaborative approach to prevention and management is of paramount importance. The chapter provides an overview of the etiology of pressure injuries and the evidence presented in the National Pressure Injury Advisory Panel, European Pressure Injury Advisory Panel, and Pan Pacific Pressure Injury Alliance (NPUAP, EPUAP, and PPPIA) *Prevention and Treatment of Pressure Ulcers: Clinical Practice Guideline* (Prevention and treatment of pressure ulcers: clinical practice guideline. Cambridge Media, Perth, 2014) and the dedicated chapter on palliative care.

1 Introduction

Pressure injury, pressure ulcer, decubitus ulcer, bed sore are synonymous terms that define "a localized injury to the skin and/or underlying tissue, usually over a bony prominence, resulting from sustained pressure (including pressure associated with shear)" (NPUAP et al. 2014, p. 18). Pressure injury prevalence among palliative populations has been reported to range between 10.5% and 26.0%, although these findings appear to be limited to small palliative care units or home care cohorts (Artico et al. 2017; Brink et al. 2006; Galvin 2002; Hendrichova et al. 2010; Queiroz et al. 2014). Pressure injuries pose significant health issues for susceptible individuals regardless of age or care setting. They result in increased morbidity and mortality and increase demands on clinical resources and health expenditure (Carville 2017). Furthermore, they contribute to a significant decline in quality of life, increased pain and discomfort, carer and family stress, and potentially lead to an earlier than anticipated demise. The chapter aims to provide an overview of the etiology, risk factors, and prevention and management options for pressure injuries among palliative care patients.

2 Pressure Injury Etiology

The development of a pressure injury is subject to factors that affect the "mechanical boundary" conditions which describe: the magnitude of mechanical load, the type of loading (pressure, shear and friction) and the duration of the load applied to the tissues (Coleman et al. 2013; NPUAP et al. 2014; Oomens 1985; Takahashi et al. 2010). Secondly, the susceptibility and tolerance of the individual's tissues is influenced by the: mechanical and morphological properties of their tissues, physiology and repair properties, and transport and thermal properties of tissues (Coleman et al. 2013; NPUAP et al. 2014; Oomens 1985; Takahashi et al. 2010).

Pressure is defined as perpendicular force (or force applied at right angles) applied to an anatomical surface per unit area of application (Takahashi et al. 2010). Capillary-closing pressure or the pressure required to collapse capillaries and inhibit blood flow was cited by Landis (1930) as 32 mm Hg. However, capillary-closing pressure will vary between individuals, depending on vessel structure, adipose tissue deposition overlying bony prominences, tissue turgor, blood pressure, and general health status (Burman 1994). When compression exceeds the perfusion pressure and structural resistance of capillaries, oxygen and nutrient supply to the skin and underlying tissue is impaired.

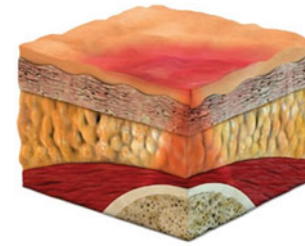
Shear stress is defined as parallel or tangential force and produces distortion of the tissues, causing two adjacent internal tissues to deform in the transverse plane (Reger et al. 2010; Takahashi et al. 2010). Shear results from sliding or dragging the skin across a support surface. Shearing injuries commonly occur in the cachexia or dehydrated palliative care patient when skin turgor and elasticity is impaired and the skin and underlying tissues are flaccid. Shear stress more readily distorts flaccid tissues, resulting in compression of capillaries or larger blood vessels in subdermal tissues. Shear is a common problem when an individual is positioned in a high or semi-Fowler's position on a resistant surface and they slide down the bed or chair.

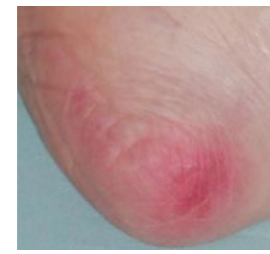
Friction defines the parallel force or load applied to the skin surface (NPUAP et al. 2014). Friction is commonly referred to as rubbing or sliding of one surface against another or the force that resists the relative motion of two objects that are touching (Reger et al. 2010). The coefficient of friction is the measurement of the amount of friction existing between two surfaces and is dependent upon the contact surface material, the skin or support surface moisture, and the ambient humidity (Reger et al. 2010). The coefficient of friction is higher in the presence of macerated skin or contact with wet support surfaces or rough or wrinkled textiles or bedding (Carville 2017). Injuries that result from friction alone or friction and pressure combined are commonly seen on the heels or elbows and may present as intact or open blisters (NPUAP et al. 2014). Sustained mechanical loading results in the following sequelae: vessel occlusion, tissue hypoxia, pallor, ischemia, increased capillary permeability, alterations in skin pH due to accumulation of metabolic waste products in the interstitial space; edema, and necrosis (Pieper 2007; Takahashi et al. 2010). Pressure injuries are generally categorized or staged according to the NPUAP and EPUAP (2009) terminology (Australian Wound Management Association (AWMA) 2012; NPUAP 2014).

3 Staging Pressure Injuries

3.1 Stage I

Intact skin with non-blanchable redness of a localized area usually over a bony prominence. Darkly pigmented skin may not have visible blanching; its color may differ from the surrounding area. The area may be painful, firm, soft, warmer, or cooler as compared to adjacent tissue. May be difficult to detect in individuals with dark skin tones. May indicate "at risk" persons (a heralding sign of risk) (NPUAP et al. 2014).

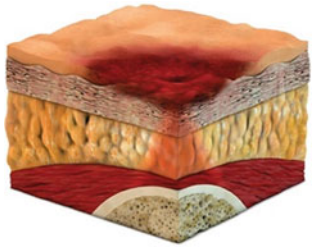


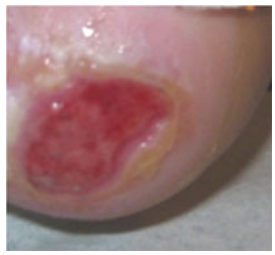


3.2 Stage II

Partial thickness loss of dermis presenting as a shallow, open wound with a red pink wound bed, without slough. May also present as an intact or open ruptured serum-filled blister. Presents as a shiny or dry shallow ulcer without slough or bruising (bruising indicates suspected deep tissue injury).

Stage II should not be used to describe skin tears, tape burns, perineal dermatitis, maceration, or excoriation (NPUAP et al. 2014).



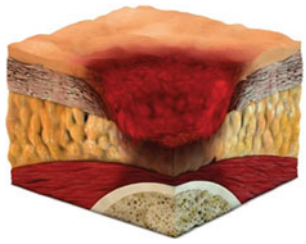


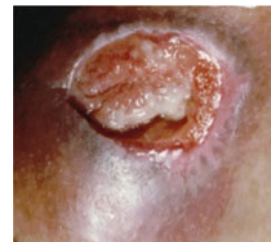
3.3 Stage III

Full thickness tissue loss. Subcutaneous fat may be visible but bone, tendon, or muscle are not exposed. Slough may be present but does not obscure the depth of tissue loss. May include undermining and tunneling.

The depth of a stage III pressure injury varies by anatomical location. The bridge of the nose, ear, occiput, and malleolus do not have subcutaneous tissue and stage.

Stage III pressure injuries can be shallow. In contrast, areas of significant adiposity can develop extremely deep stage III pressure injuries. Bone/tendon is not visible or directly palpable (NPUAP et al. 2014).

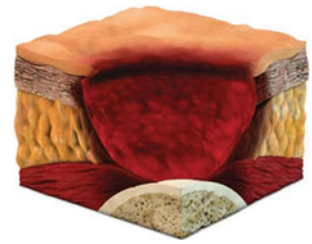


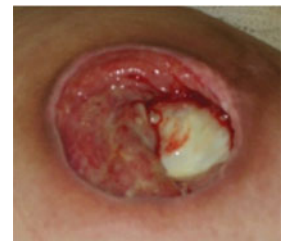


3.4 Stage IV

Full thickness tissue loss with exposed bone, tendon, or muscle. Slough or eschar may be present on some parts of the wound bed. The depth of a stage IV pressure injury varies by anatomical location.

The bridge of the nose, ear, occiput, and malleolus do not have subcutaneous tissue and these pressure injuries can be shallow. Stage IV injuries can extend into muscle and/or supporting structures (e.g., fascia, tendon, or joint capsule) making osteomyelitis possible. Exposed bone or tendon is visible or directly palpable (NPUAP et al. 2014).

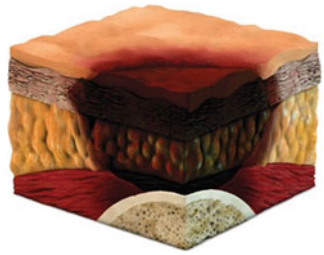


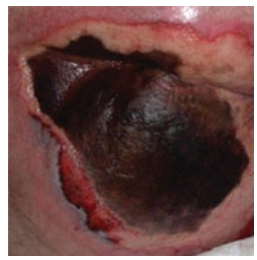


3.5 Unstageable Pressure Injury

Full thickness tissue loss in which the base of the pressure injury is covered by slough (yellow, tan, grey, green, or brown) and/or eschar (tan, brown, or black) in the pressure injury bed. Until enough slough/eschar is removed to expose the base of the pressure injury, the true depth, and therefore the stage, cannot be determined.

Stable (dry, adherent, intact without erythema or fluctuance) eschar on the heels serves as the body's natural biological cover and should not be removed (NPUAP et al. 2014).

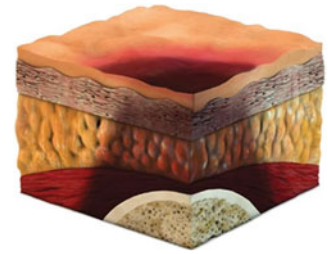


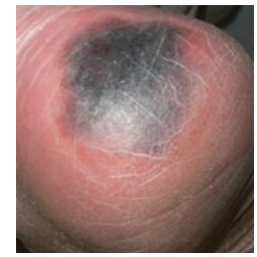


3.6 Suspected Deep Tissue Injury

Purple or maroon localized area of discolored intact skin or blood-filled blister due to damage of underlying soft tissue from pressure and/or shear. The area may be preceded by tissue that is painful, firm, mushy, boggy, warmer, or cooler as compared to adjacent tissue.

Deep tissue injury may be difficult to detect in individuals with dark skin tones.





Evolution may include a thin blister over a dark wound bed. The pressure injury may further evolve and become covered by thin eschar. Evolution may be rapid exposing additional layers of tissue even with optimal treatment (NPUAP et al. 2014); Images and graphics "Reproduced with permission of Wounds Australia. All rights reserved."

4 When Is a Pressure Injury Not a Pressure Injury?

Palliative care patients can have coexisting wounds such as skin tears, leg ulcers, dehisced or draining wounds, and pressure injuries. A comprehensive health history and clinical assessment will assist in identifying the etiology of these wounds and direct appropriate care decisions. Nevertheless, the skin is the largest body organ and like other body organs, it is subject to pathophysiological and morphological changes when confronted with ageing, injury, critical illness, active dying, or the effects of vasopressor medications that induce vasoconstriction. In critically ill and end-of-life patients, acute "skin failure" is an emerging concept, albeit one that is based on anecdotal clinical observation rather than

quantifiable diagnostic markers. Skin failure has been described as a pressure-related injury reported to occur simultaneously with circulatory or organ failure, acute hypoperfusion, hemodynamic instability, and sepsis (Nowicki et al. 2017). However, some authors deem end-of-life skin failure to be a distinctly different pathological disorder as compared to pressure injuries (Curry et al. 2012; Delmore et al. 2015; Levine 2016).

Attempts to describe pathological skin alterations at end of life have resulted in palliative care practitioners reference to the term "Kennedy Terminal Ulcer" (KTU), which was first described in 1989 as a red, yellow, black, or purple pear, butterfly- or horseshoe-shaped lesion occurring primarily over the sacrococcygeal region within days to weeks of death (Kennedy 1989; Kennedy-Evans 2009). It is proposed that the KTU forms as a quick onset blister or abrasion, which deteriorates rapidly to a deeper stage III or IV pressure injury (Kennedy 1989; Kennedy-Evans 2009). The Trombley-Brennan Terminal Tissue Injury (TB-TTI) is a more recent addition to palliative care terminology and is defined as a pink, purple, or maroon ulcer that can occur over bony or non-bony tissues, including the extremities and trunk (Trombley et al. 2012). The lesions appear as non-blanchable, potentially white-centered, butterfly- or linear-shaped lesions, which do not progress to erosion or ulceration. They are reported to occur within hours to days of death (Carlsson and Gunningberg 2017).

Some authors describe these ambiguous lesions as unavoidable pressure injuries, while others propose that they are a distinctly different pathology and warrant a different nomenclature (Black et al. 2011; Steinberg 2016; Yastrub 2010). Regardless, the lack of consensus on what constitutes skin failure, a KTU, a TB-TTI, and unavoidable pressure injury, indicates a need for further research and quantifiable physiological and pathological criteria for assessment and diagnosis. In the meantime, comprehensive assessment of the patient and their wound should differentiate pressure injuries from wounds of other etiologies and guide the implementation of preventative strategies for those at risk.

5 Risk Factors for Pressure Injury

Predisposing risk factors for pressure injuries can be both intrinsic and extrinsic. Intrinsic factors (those that pertain to the person) alter the ability of the skin and underlying tissues to resist pressure, shear, and friction and they compromise recovery. Extrinsic factors (those that pertain to the external environment) increase the susceptibility of the tissues to damage. Palliative care patients especially in the terminal stage of disease are considered to be at high risk of pressure injury (Delmore et al. 2015; Langemo and Black 2010).

A structured approach to risk assessment of palliative care patients is a recommendation to be found in the International *Prevention and Treatment of Pressure Ulcers: Clinical Practice Guideline* (referred to hereon as the International Guideline), which was published in 2014 following a rigorous review of the evidence in the literature (NPUAP et al. 2014). The International Guideline ranks the strength of evidence presented as level A, B, and C as outlined in Table 1. In addition, the guideline provides strength of recommendations which are determined by the strength of internal or external evidence, clinical importance, potential to improve patient outcomes, feasibility, and cost-effectiveness of the recommendation.

Table 1 International Guideline strength of evidence (NPUAP et al. 2014)

Strength of evidence (SOE)	Recommendation
Level A	Recommendation supported by direct scientific evidence from properly designed and implemented controlled trials on PU in humans (level 1 studies)
Level B	Recommendation was supported by direct scientific evidence from properly designed and implemented clinical series on PU in humans (level 2, 3, 4, 5 studies)
Level C	Recommendation was supported by indirect evidence and/or expert opinion

A dedicated chapter for individuals receiving palliative care is to be found in the guideline, and the focus of this chapter is to build on the evidence for pressure injury prevention and management generally, with special consideration to optimizing comfort and patient preferences during active dying. A comprehensive health history and clinical assessment should be performed on admission and in accordance with changes in the patient's condition (NPUAP et al. 2014). Assessment of the palliative care patient should include: comorbid health problems, medications, nutritional status, risk factors, diagnostic test results, psychosocial implications, environmental resources, and the wishes and concerns of the individual and their significant others (NPUAP et al. 2014).

A structured approach to risk assessment can be directed by a number of pressure injury risk assessment tools such as the Braden Scale (Braden and Bergstrom 1992), Waterlow Score (Waterlow 1985), and Norton Score (Norton et al. 1962), which have been validated in different health settings and employed in palliative care. However, their validity and reliability in the palliative care setting lacks consensus. The Marie Curie Centre in Hunters Hill, Glasgow, devised and validated a risk tool specific to the needs of palliative patients and it is this tool that is proposed to have more utility in palliative care (Chaplin 2000). Comparative analysis was conducted between the numerical scores achieved with the use of the tool and the clinical judgment of experienced palliative care nurses. The seven risk parameters incorporated in the Marie Curie Centre Hunters Hill Risk Assessment Tool focus on the clinical changes evident in the tissues and activities of deteriorating palliative care patients and included: altered sensation, reduced mobility, excessive moisture, inactivity in bed, malnutrition, alterations in skin condition, and impacts of friction and shear on loose or cachectic tissues. Each risk factor is scored on an increasing four-point numerical scale and a minimum score of seven determines minimal risk and a maximum score of 28 determines very high risk (Chaplin 2000).

5.1 Altered Sensation

Altered sensation inhibits physiological responses to pain. Alterations in sensation are generally associated with loss of consciousness, analgesia, and neuropathy associated with malignant infiltration, surgical trauma, diabetes, or spinal cord injury (Chaplin 2000). Alterations in sensation impact significantly on patient mobility and activity.

5.2 Mobility and Activity

Immobility and inactivity results from neurological, cognitive, or physical dysfunction and impacts on the individual's ability to independently reposition and off-load mechanical forces (Carville 2017). Individuals who require assistance to reposition are susceptible to shear and friction due to dragging or sliding activities against support surfaces. Immobility impairs the blood flow to compressed tissues and retards the venous and lymphatic function, leading to edema which further compromises tissue oxygenation (Carville 2017).

The International Guideline discusses the need to reposition and turn the palliative patient at periodic intervals in accordance with their wishes, comfort, and tolerance (NPUAP et al. 2014). It is also recommended that premedication be offered 20 to 30 min prior to repositioning and that the patient be repositioned at least 4 h if on a reactive pressure redistributing mattress such as viscoelastic foam or 2 h on a regular mattress (NPUAP et al. 2014).

5.3 Nutrition and Hydration

Adequate hydration and a balanced diet containing essential nutrients is necessary for optimizing: tissue status, immune responses, a stable body mass index, and healing potential. Morbid obesity or cachexia will increase the individual's predisposition to pressure injuries. Individuals with morbid obesity have large amounts of poorly vascularized adipose tissue, and the capillaries in

adipose tissue are vulnerable to shear stress (Reger et al. 2010). Furthermore, morbid obesity compromises movement and activity and thus increases the risk of prolonged interface pressure. Alternatively, cachexia individuals have reduced adipose and muscle tissue, which reduces the tissues tolerance to pressure. Anorexia and nausea are common symptoms among palliative patients and nutritional protein and multivitamin supplements should be offered, especially when wound healing is the aim (NPUAP et al. 2014).

5.4 Alterations in Skin Condition

Skin assessment should be a component of the health agency's risk assessment screening policy (NPUAP et al. 2014). Alterations to skin perfusion, moisture, temperature, and pH can alter skin tolerance to pressure, shear, and friction (Carville 2017). Skin perfusion and oxygenation is compromised when blood vessels are compressed under pressure or damaged by shear or friction. Conditions such as ischemic heart disease, diabetes, peripheral arterial disease, cyanosis, hypotension, and smoking, as well as vasopressor medications can impair skin perfusion. In days or hours prior to death, skin failure as discussed earlier in this chapter may be demonstrated and the skin takes on a mottled, bluish appearance, which indicates hypoxia and ischemia (Curry et al. 2012; Kennedy-Evans 2009). Therefore, it is important to inform the patient or their significant others of potential skin changes at end of life (NPUAP et al. 2014).

5.5 Moisture

The tensile strength of the skin is impaired when there is frequent or excessive contact with moisture and the skin becomes macerated (Carville 2017). Moisture may result from incontinence of urine or faces, diaphoresis, uncontained wound exudate, dribbling of saliva and spilled food, drinks, or failure to maintain a stable microclimate. The latter term relates to the skin surface temperature and humidity or skin surface moisture when in contact with a support surface (Reger et al. 2010). The aim is to keep the skin clean and dry (NPUAP et al. 2014). Gentle skin cleansing practices and the use of tepid water will assist in preventing skin trauma, and the use of skin barrier creams, emollients, and protective barrier films can protect the skin from excessive moisture (NPUAP et al. 2014).

5.6 Temperature

An increase in body or skin temperature and ambient humidity increases the amount of skin moisture. Increases in skin temperature are closely aligned to changes in core body temperature (Carville 2017). However, local increases in skin temperature can occur due to contact with plastic or vinyl covered support surfaces or the use of excessive amounts of bed linen, clothing, or plastic-covered incontinence pads. An increased body temperature of 1 °C raises the metabolic demands of tissues by approximately 10% (Fisher et al. 1978). It has been proposed that individuals with pyrexia and associated increased tissue metabolic demands may be even more susceptible to pressure injuries when lesser amounts of pressure are applied or for shorter duration (Sae-Sia et al. 2005). Therefore, skin assessment should include assessment of skin temperature, edema, and change in surrounding tissue consistency (NPUAP et al. 2014).

5.7 Skin and Tissue pH

The skin pH averages 5.5 and is referred to as the acid mantle, which discourages bacterial colonization and reduces the risk of opportunistic infection (Carville 2017). Skin pH can best be maintained by avoidance of alkaline soaps and cleansers in favor of those that are perfume free and pH neutral. The use a pH balanced skin cleanser to maintain the normal acidic skin pH is highly recommended (NPUAP et al. 2014).

The pH of chronic wounds has been demonstrated to be alkaline with a pH range from 7.15 to 8.9 (Romanelli et al. 2002). Tsukada et al. (1992)

demonstrated increased alkalinity in deeper pressure injuries and wound healing to be associated with neutral or acidic pH. Stage I pressure injuries with intact skin were found to have an acidic pH of 5.4–5.6 which is aligned with normal skin pH, however, stage II injuries were found to have a pH of 6.9, and stage III injuries 7.6 (Tsukada et al. 1992). An acidic pH in the wound improves oxygen release and angiogenesis, impairs protease activity, and reduces toxicity and detrimental effects of bacterial end products such as ammonia and proteases (Geltin 2007).

6 Support Surfaces

The ability to off-load pressure and reduce shear impact is greatly aided by using appropriate support surfaces, which comprise: replacement mattresses, mattress overlays, or cushion support surfaces. The selection of these devices for prevention and management of pressure injuries is very much determined by the capability of the device to improve pressure redistribution and comfort (NPUAP et al. 2014). Support surfaces are broadly categorized as reactive and active devices, hybrid surfaces, or specialty beds. Reactive devices promote a constant low pressure principle that facilitates immersion and envelopment of the body (NPUAP et al. 2014). The devices can be powered or non-powered support surfaces and are comprised of high density, low resistance foams, polyester fiber, air or gel mediums that are covered with a two- or three-way stretch cover. These devices conform to the body contours on emersion which increases the load-bearing surface area.

Active support surfaces are powered air-filled devices that provide either constant low pressure or alternate pressure loading in cycles from one body part to another (NPUAP et al. 2014). Some alternating devices provide a one-in-two cycle (50% of the body is off-loaded at any time, others provide a one-in-three cycle (33% of the body is off-loaded at any time). Some active devices automatically adjust off-loading to support pressure on demand or movement. Active support surfaces can reduce the frequency of repositioning; however, extremely cachexia patients may find these devices afford less comfort than reactive mattresses or overlays that rely on emersion principles.

Hybrid support surfaces combine both reactive constant low-pressure foam support surface properties with active alternating air features when a pump is connected. Other hybrid support surfaces combine both reactive non-powered constant low-pressure foam and air cells that automatically respond to patient weight distribution and movement. Hybrid devices accommodate the need to "step-up" or "step-down" off-loading as pressure injury risk changes, without changing the support surface (Carville 2017).

Specialty beds combine a mattress and bed unit and incorporate low air loss systems, air fluidized systems, or pulsating or kinetic (continuous oscillation or rotation movement) therapies. These advanced technologies may convert from a bed to a chair position or combine repositioning capabilities, which makes repositioning easier for bariatric, cachexia, or immobile patients (Carville 2017).

7 Management of Pressure Injuries

Optimal management of a pressure injury involves comprehensive assessment and evidence-based interventions. See also ► Chap. 22, "Dealing with a Wound in Palliative Care." A comprehensive health assessment of the individual precedes a wound assessment which should include the following parameters:

- Pressure injury location and effectiveness of off-loading strategies and devices
- Clinical appearance of the wound bed or type and amount of tissue characteristics such as slough, necrosis, granulation, epithelium or exposed muscle, tendon, or bone
- Two- and three-dimensional measurement of depth, width, length, and circumference
- Amount, type, color, consistency, and odor of exudate

- Raised, rolled, undermined, colored, or macerated wound edges
- Surrounding skin characteristics identified on inspection and palpation which may include: blanching or non-blanching erythema, warmth, coolness, hemosiderin staining, edema, and induration
- Clinical signs of local or spreading infection
- Pain associated with wound or dressing procedure or removal (Carville 2017)

Assessment outcomes will guide evidence-based care plan decisions for the pressure injury and peri-wound, and these decisions should be consistent with the patient's wishes (NPUAP et al. 2014). However, wound healing may not be a realistic or achievable goal in the management of palliative care patients in the terminal stages of dying. This is especially so when the patient or family have made an informed decision to minimize repositioning or decline to use recommended support surfaces due to pain or patient decisions. However, this does not mean that the management of wound symptoms such as exudate, odor, infection, and wound pain are less deserving of the most diligent and informed assessment and best practice management. A collaborative and informed approach to care can do much to improve symptom management, quality of life, optimize comfort, and reduce patient and carer stress.

7.1 Exudate

Exudate is defined as the fluid that is produced and seeps from a wound (World Union Wound Healing Societies 2007).

Exudate is comprised of water, filtered red cells and platelets, electrolytes (sodium, potassium, chloride, bicarbonate), increased white cells (immune response), glucose (levels lower than those in blood), albumin, macrophages, cellular debris, proteolytic enzymes (elastase, collagenase, matrix metalloproteinases), high levels of lysosomes (antimicrobial agents), and growth factors (GF) (platelet-derived GF, basic fibroblast GF, epidermal GF) (Cutting 2003; Romanelli et al. 2010).

Exudate in acute wounds is usually initially sanguineous because of surgery or trauma, but in chronic wounds it tends to be produced in response to physiological changes in tissue pressures, inflammation, infection, and autolysis of necrotic tissue and can differ in type. Exudate has many purposes including wound cleansing, acts as a transport medium for white cells, proteases and growth factors, provides nutrients to cells, and promotes a moist wound healing environment (Cutting 2003; Winter 1962).

The amount of wound exudate depends on the wound etiology, the size of wound, the stage of wound healing (inflammatory or reconstruction phases), autolysis of necrotic tissue, and the presence of infection. A breach in the skin reduces the tissues' ability to maintain interstitial osmotic and hydrostatic pressures necessary to control normal fluid inflow from blood and outflow via lymph and the increased interstitial fluid leaks from the wound. Inflammatory responses and increased temperature results in capillary dilation and increased capillary permeability which in turn produces edema or increased interstitial fluid. Granulation deposition is an important aspect of the reconstruction phase of healing and granulation tissue has a high component of water-absorbing connective tissue components. Extensive granulation tissue or hypergranulation therefore influences the amount of exudate (Cutting 2003; Romanelli et al. 2010).

Autolysis is a physiological response to the presence of devitalized tissue and cellular debris which are denatured by phagocytic cells and endogenous proteolytic enzymes in the wound or wound fluid, which in turn adds to the moisture burden. Extremes in exudate volume can impact on the wound healing environment. Desiccation of the wound bed inhibits tissue reconstruction and epithelization, and an overly wet wound leads to maceration and impaired tensile strength in the tissues and subsequently can lead to peri-wound breakdown (Carville 2017). Excessive exudate can also increase the risk of infection.

Management of exudate in the management of palliative care patients with pressure injuries is determined by the short-term goal of care. Should

the goal of care be removal of eschar by promoting autolytic debridement, then this can be expedited if moisture donating hydrogels (for example: IntraSite®, SoloSite®, Flaminal®,) or moisture retention hydrocolloids (for example: Comfeel®, Duoderm®, Suprasorb H®), semipermeable films (for example: OpSite®, Tegaderm™, Hydrofilm®), or interactive wet dressings (HydroClean Plus®) dressings are used.

If exudate containment is the goal, then dressings are selected according to their moisture absorption and retention properties. Calcium alginate (for example: Kaltostat®, Biatain®, Urgosorb®), gelling fiber (for example: Aquacel®, Durafibre®, Exufibre®), foam (for example: Allevyn®, Biatain®, Tielle™) dressings are appropriate for low to moderate amounts of exudate while the super absorbent dressings (for example: Zetuvit Plus®, Relevo®, Vliwasorb®) are suitable for heavy exudate.

7.2 Odor

Odor can be a most distressing wound symptom and may be due to wound infection (especially anaerobic organisms), autolysis of necrotic tissue, or enteric or colonic fistula erosion into a pressure injury. Odor control is of paramount importance and involves regular wound cleansing, assessment, and management of infection and debridement of devitalized tissues with consideration to the individual's wishes and goals of care (NPUAP et al. 2014). Local wound infection usually responds to more frequent wound cleansing and the application of tissue-friendly antimicrobial cleansing solutions such as polyhexamethylene biguanide (Prontosan®), octenidine dihydrochloride (Octenilin®), or super-oxidized solution (Microdacyn®), and antimicrobial dressings (for example: silver, cadexomer iodine, wound honey). Spreading or systemic infection will require microbiological diagnostic investigations for appropriate antibiotic treatment. While fistula effluent within a pressure injury warrants containment in a wound or ostomy appliance. A variety of odor-absorbing dressings such as carbon-backed or impregnated dressings (for example: Carboflex®, Actisorb™, or Carbonet®) exist and should be considered if malodor is problematic.

Odor associated with autolysis of devitalized tissue may be curtailed with the assistance of faster debridement methods such as sharp or low-frequency ultrasound. However, noninfected dry eschar is nature's dressing, and it is usually considered prudent and more comfortable to leave it intact should the patient be close to death (Carville 2017).

7.3 Infection

Infection occurs when microorganisms multiply and host resistance is overcome. Host resistance is lowered when autoimmune status is impaired, immunosuppressant medications are prescribed, or chemotherapy and radiation therapy is involved. Infection adversely affects wound healing and can lead to life-threatening systemic infections. Assessment of the individual and their wound for clinical signs of infection should substantiate the need for microbiological assessment.

The classical signs of wound infection include: pain, heat, erythema, swelling, and purulence or increased exudate. Lymphangitis, crepitus, and wound deterioration or new breakdown may be indicative of spreading infection. However, signs and symptoms of local infection in chronic pressure injuries may be more subtle and involve:

- No signs of healing for 2 weeks
- Friable, bright red hypergranulation tissue
- New, increased, or altered pain
- Increased or altered exudate
- Malodor
- Increased necrosis
- Pocketing or bridging in the wound bed (International Wound Infection Institute (IWII) 2016).

These signs and symptoms of local infection are indicative of biofilm within the wound (IWII 2016). Biofilms are polymicrobial communities, which proliferate and are encased in a protective glycocalyx matrix also referred to as an extracellular polymeric substance (EPS). Microorganisms secrete the glycocalyx, which forms a biofilm that

protects the organisms from immune responses by phagocytes and from many topical and systemic antimicrobials (Phillips et al. 2010).

Biofilms evolve in the following sequence:

1. Planktonic attachment as free floating, single organisms attach to the surface of the wound (IWII 2016).
2. Irreversible attachment that is aided by the production of an extracellular polymeric substance (EPS), which protects against the host immune response. The EPS is comprised of polysaccharides, proteins, glycolipids, and bacterial DNA (Phillips et al. 2010).
3. Cell proliferation occurs as sessile (firmly attached) organisms communicate between microorganisms of same or different species via a process referred to as quorum sensing. Quorum sensing is responsible for phenotypic diversity and some of the genotypic diversity seen in wound biofilms, which enhances the community's nutrient-gathering capacity, defense, and reproductive abilities (IWII 2016).
4. Growth and maturation into a mature biofilm, which is immune to host defenses and many topical and systemic antimicrobials. Biofilms stimulate chronic inflammatory responses to dislodge biofilms, and there is a significant increase in neutrophils, pro-inflammatory cytokines, and proteases. Inflammatory cells secrete reactive oxygen species and proteases (matrix metalloproteases, elastase) to denature the biofilm; however, proteases can impair healing. Increased capillary permeability and tissue breakdown that occurs because of these host attempts to eradicate the biofilm produce nourishment for the biofilm (IWII 2016; Phillips et al. 2010).
5. Biofilm dispersal as the mature biofilm releases planktonic bacteria which attach to other parts of the wound and the cycle is repeated (IWII 2016; Phillips et al. 2010).

The International Guideline proposes that clinicians should suspect biofilm when:

- A pressure injury has been present for more than 4 weeks.
- Lack of healing progress in the previous 2 weeks.
- Clinical signs and symptoms of inflammation present.
- No response to antimicrobial therapy (NPUAP et al. 2014).

The management of biofilms replicates the principles of wound bed preparation, which involves: thorough cleansing, debridement, and the use of topical antiseptics to inhibit planktonic bacteria and the reformation of new biofilms. Some antimicrobial solutions and dressings such as polyhexamethylene biguanide (PHMB) with a surfactant (betaine) (Prontosan®) and cadexomer iodine (Iodosorb®), octenidine dihydrochloride (Octenilin®) and super-oxidized solution (Microdacyn®) have demonstrated ability to denature biofilms (IWII 2016; Phillips et al. 2010). While other antimicrobial dressings such as silver and medical-grade honey contribute bacteriostatic or bactericidal effects against planktonic microorganisms (Carville 2017; Phillips et al. 2010).

7.4 Wound Pain

Pain management is an important tenet of palliative care, whether the pain be associated with malignant infiltration or dressing procedure. Allodynia or pain at light touch may be experienced during wound cleansing or dressing removal and can be a significant issue for some. It is important to ascertain the pain etiology and patient preferences for management. Allodynia may be best managed by premedication and supporting the patient to undertake their own dressings if possible. The provision of simple directions for dressing removal and wound cleansing may prove beneficial. As is the use of silicone dressings that promote atraumatic removal or the use of highly absorbent dressings that require less frequent changing (NPUAP et al. 2014).

8 Conclusion

Pressure injury prevention and management is optimized when a collaborative approach, which involves the patient, their family, carers, and

health professionals is utilized. First and foremost, there is an utmost need to validate that the patient, their family, and care providers understand the goals and plan of care, and the palliative care patient's choices are acknowledged and accommodated if possible. At the end-of-life prevention of pressure injuries may not in every instance be a realistic goal due to the alterations in skin and tissues associated with active dying or conscious decisions made by the patient or their family to avoid regular repositioning or the use of recommended support surfaces. Should a pressure injury occur, palliative care principles for optimizing symptom management and patient comfort are employed.

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Sleep Difficulties

24

Doris Howell

Contents

Abstract

Sleep disturbance is a prevalent and debilitating problem in palliative care that contributes to worse quality of life and adds to patient and caregiver suffering. Screening for this symptom in routine practice followed by a focused assessment and evaluation is essential given its consequences on daytime functioning and distress. The causes of disrupted sleep in palliative care populations are multifactorial and include disease physiology, uncontrolled physical symptoms, adverse effects of medications, and emotional distress or psychiatric disorders. Attention to reversible causative factors where possible, detection of specific sleep disorders

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_20

to ensure appropriate treatment, and development of a treatment plan individualized to the patient that takes into consideration prognosis are essential. Simple approaches such as sleep hygiene education may be helpful, but usually a combination of psychological and pharmacological agents is necessary for effective management. Cognitive behavioral therapy for insomnia (CBT-I) is considered first-line treatment for insomnia that targets the cognitive and behavioral factors that perpetuate this symptom but may require adaptation in the context of palliative care. Common medications used to manage insomnia include the benzodiazepine receptor agonists, benzodiazepines, and sedating antidepressants, but there is a lack of information about adverse effects of these drugs. High-quality research is needed to establish efficacy of psychological therapies and pharmacological agents for management of insomnia and other sleep disorders in palliative care. This chapter provides an overview of sleep disturbance, causative factors, and management of common sleep disorders of insomnia, sleep-wake cycle reversal, hypersomnia, and nightmares in palliative care.

1 Introduction

Sleep is a basic human need that is essential to physical and mental health. Sleep disturbance is a widespread and debilitating problem in the general population with rates of 20–41% reported in epidemiologic studies, whereas the prevalence of insomnia disorder defined by stringent diagnostic criteria ranges from 12 to 20% (Ohayon 2011; Buysse 2013). Sleep disturbance has profound consequences on physical and mental health including daytime fatigue, cognitive impairment, traffic and work site accidents, and work absences; increases the risk for cardiovascular disease, diabetes, obesity, and psychiatric disorders; and is associated with an increase in inflammatory processes, higher mortality, and healthcare costs (Garbarino et al. 2016).

Sleep disturbance is highly prevalent in patients with chronic diseases such as cancer and in advanced stages of disease but is often underrecognized and undertreated in clinical care. Patients and clinicians may both assume that little can be done to improve disruptions in sleep in the context of life-threatening or chronic disease. The estimated prevalence of sleep disturbance varies across studies due to differences in definitions of sleep disturbance and measurement, but rates of greater than 70% and as high as 95% have been noted in small and large observational studies in palliative care populations and in hospice and palliative care settings (Hugel et al. 2004; Renom-Guiteras et al. 2014; Mercadante et al. 2017).

A large body of research on insomnia has been conducted in the general population and cancer populations but less in advanced disease. Sleep disturbance is also a prevalent and serious symptom in cancer and other advanced disease populations. A systematic review across diverse advanced disease populations found sleep disturbance to be common in cancer, chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), end-stage renal disease (ESRD), dementia (DD), acquired immunodeficiency syndrome (AIDS), Parkinson disease (PD), motor neuron disease (MND), and multiple sclerosis (MS) (Moens et al. 2014). The highest rates of insomnia were reported for ESRD (1–83%), followed by PD (40–74%), COPD (15–77%) and cancer (3–67%). Like sleep disturbance in the general population, insomnia as a comorbid problem with advanced disease has profound consequences on daytime functioning including cognitive impairment and interference with daily life activities and exacerbates severity of other physical symptoms such as pain, stress, psychological distress, and psychiatric disorders such as depression (Davidson 2002; Davis et al. 2014). Sleep disturbance may also be a problem for caregivers of palliative care patients with rates equivalent to those with the disease and contributes to caregiver burden, poor health, and hospitalization at the end-of-life (Maltby et al. 2017).

The causes of sleep disturbance in advanced disease are multifactorial and include biological, behavioral, and psychological factors and other contributors such as medications to manage other symptoms, adverse effects of medical treatments,

and environmental factors (Mystakidou et al. 2009; Berger 2009; Davis and Goforth 2014). Thus, sleep is a complex symptom that is challenging to manage in palliative care. Early identification and comprehensive evaluation of sleep disturbance are essential to determine the nature of the problem, causative factors, and impact on patients and caregivers and to detect the presence of specific sleep disorders that require appropriate treatment. The aim of treatment is to address reversible causes and enable restorative sleep through appropriate use of non-pharmacological and pharmacological interventions. Early intervention is extremely important in palliative care as this symptom can exacerbate symptom and psychological distress and has a negative impact on daily living, overall quality of life, and compounds suffering for patients and their caregivers. Poor sleep quality is a strong predictor of suicide in chronic disease and is associated with a desire to hasten death in palliative care (Rosenfeld et al. 2014).

The aim of this chapter is to provide an overview of normal sleep architecture and physiology, identify the factors associated with sleep disturbance, and discuss the comprehensive evaluation and management of this symptom and applicability of intervention approaches to palliative care. Specific sleep disorders in palliative care and management strategies will also be discussed in this chapter and include insomnia, hypersomnia, sleep-wake cycle reversal, and nightmares.

2 Definitions of Sleep Disturbance

A glossary of terms is shown in Table 1. Sleep health is defined as a multidimensional pattern of sleep-wakefulness, adapted to individual, social, and environmental demands, that promotes physical and mental well-being (Buysse 2014). Buysse defines good sleep health as subjective satisfaction, appropriate timing, adequate duration, high efficiency, and sustained alertness during waking hours.

The terms sleep disturbance (SD), sleep disorders, and insomnia or insomnia syndrome are often used interchangeably in the literature; however, there are distinctions between these problems. Sleep disturbance (also called sleep-wake disturbance) is an overarching term defined as perceived or actual alterations in nighttime sleep in terms of the quantity and quality of sleep with daytime impairment in the absence of a diagnostic label (Roscoe et al. 2007). Whereas, sleep disorders encompass diagnostic entities that are defined by the American Academy of Sleep Medicine (AASM) in the International Classification of Sleep Disorders manual third edition (ICSD-3, 2014) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5, 2013). As shown in Table 2, common sleep disorders include the insomnias (initiating and maintaining sleep with daytime impairment), central disorders such as hypersomnolence (hypersomnia or excessive sleepiness), sleep-disordered breathing (e.g., obstructive sleep apnea), circadian rhythm disorders (e.g., sleep-wake reversal), sleep-related movement disorders (e.g., restless leg syndrome), and other dysfunctions associated with sleep stages or partial arousals or parasomnias, e.g., night terrors (Morin et al. 2015).

The sleep and arousal disorders most frequently encountered by the clinician are disorders of initiating and maintaining sleep, the insomnias. Insomnia is characterized as difficulty falling asleep (prolonged sleep latency) and maintaining asleep (waking up often with difficulty returning to sleep and/or early morning awakening), despite having the opportunity to sleep that is associated with a feeling of non-restorative sleep, daytime sleepiness, and impairment in daily functioning and activities. A clinical diagnosis of insomnia also called insomnia syndrome is confirmed on the presence of these subjective symptoms occurring on three nights or more per week for at least 1 month (ICSD-3 2014).

Insomnia can occur over a few days in response to stressful life events termed acute or adjustment insomnia or may be chronic (occurs three nights/week or more for 3 months). The diagnostic criteria for insomnia syndrome derived from the ICSD-3 and the DSM-5 are as follows:

- Difficulty initiating and/or maintaining sleep, whereby sleep onset latency is greater than

Table 1 Glossary of sleep disturbance terms

Term	Definition
Sleep disturbance	Termed sleep-wake disturbance and includes perceived or actual alterations in the quantity and quality of nighttime sleep with daytime impairment in the absence of a diagnostic label
Insomnia	Disruption in sleep, characterized by difficulty falling asleep (prolonged sleep latency), staying asleep (sleep maintenance), or a feeling of non-restorative sleep, associated with impairment in daytime functioning
Insomnia syndrome	Presence of insomnia symptoms on three nights or more per week for at least 1 month, accompanied by distress and impairment in daytime functioning
Acute insomnia	Termed adjustment or situational insomnia with insomnia symptoms experienced acutely in response to situational stressors; usually resolves when the stressful trigger has been resolved
Chronic insomnia	Presence of insomnia and insomnia syndrome symptoms on three nights or more per week for more than 3 months with daytime impairment in functioning and distress
Rapid eye movement (REM) sleep	Initial short phase of sleep characterized by random/rapid movement of the eyes, accompanied with low muscle tone throughout the body, and the propensity of the sleeper to dream vividly
Non-rapid eye movement (NREM) sleep	Four stages of NREM sleep (stages 1, 2, 3, and 4). Stage 1, lightest stage of sleep, characterized by slow eye movements. Stage 3 and 4 sleep is the deepest stage of sleep shown as slow-wave patterns on electroencephalography
Sleep disorders	Sleep disorders are a group of syndromes characterized by disturbance in the patient's amount of sleep, quality or timing of sleep, or behaviors or physiological conditions associated with sleep and a diagnostic entity identified by criteria in the International Classification of Sleep Disorders (ICSD-3) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5)
Sleep hygiene	Behavioral or environmental practices that positively or negatively affect sleep including avoiding stimulants such as caffeine or alcohol several hours before bedtime and other behaviors to enhance learned association of going to bed with sleep and includes attention to sleep environment (dark environment, quiet, and comfortable)

References: Ohayon (2011), Buysse (2013), Carskadon and Dement (2005), ICSD-3, DSM-5

30 minutes or frequent or prolonged nocturnal awakenings lasting greater than 30 minutes that is non-restorative.

- Sleep difficulty occurs despite adequate opportunity to sleep.
- Sleep efficiency (ratio of total sleep to time spent in bed) is lower than 85%.
- Difficulties occur at least three times per week.
- Difficulties occur for at least 1 month.
- Difficulties cause distress or daytime impairment in at least one of the following forms of daytime impairment:
  - Fatigue or malaise
  - Attention, concentration, or memory impairment
  - Social or vocational dysfunction or poor school performance
  - Mood disturbance or irritability
  - Daytime sleepiness
  - Motivation, energy, or initiative reduction
  - Proneness for errors/accidents at work or while driving
  - Tension, headaches, or gastrointestinal symptoms in response to sleep loss
  - Concerns or worries about sleep

Daytime impairment is a key feature of clinically relevant insomnia and can include fatigue, cognitive and memory impairment (changes in executive functioning, learning, and recall), and mood disturbances. Symptoms of insomnia can differ between older adults (>65) and younger populations. Older adults are more likely to report problems with waking after sleep onset (difficulty maintaining sleep) than problems with sleep onset latency (time to fall asleep) (Bloom et al. 2009).

Insomnia is differentiated into primary insomnia without comorbid illness or secondary insomnia

Table 2 Sleep disorders and characteristics

Disorder	Definition and characteristics
Insomnia disorder	Disorders of initiating and maintaining sleep with symptoms of difficulty initiating or maintaining sleep (early morning awakening and unable to resume sleep) occurring three nights/week for a month that is associated with distress and impairment in daytime functioning
Breathing-related sleep disorders	Conditions during which respiration pauses occur during sleep due to either complete or partial collapse of the person's airways lasting up to 10 seconds. Includes obstructive sleep apnea (OSA, in which no ventilation occurs) and hypopneas (reduced ventilation due to partial airway obstruction) with intermittent and abrupt reduction in blood oxygen levels. Symptoms include snorting, snoring, gasping, choking in one's sleep, and excessive daytime sleepiness. Includes OSA central sleep apnea, sleep-related hyperventilation
Restless legs syndrome (RLS)	A neurological disorder that causes achy, uncomfortable (and sometimes painful) tingling, tugging, or creepy crawly sensations in the legs associated with a need to move. Symptoms are worse in the evening and improve with walking or stretching
Narcolepsy	A hypersomnia characterized by profound sleep onset paralysis and vivid hallucinations that occur as a person is falling asleep. Excessive daytime sleepiness, cataplexy, hallucinations upon falling asleep or awakening. Narcolepsy with cataplexy also involves sudden loss of muscle control
Circadian rhythm sleep disorders	Disorders that involve an abnormal sleep-wake rhythm caused by a circadian clock that is not in phase with, and cannot be entrained to, the 24-hour light-dark cycle. Symptoms of habitually early sleep onset and wake times, compared with societal or preferred norms. Those with irregular sleep-wake disorder typically have three or more sleep episodes during a 24-hour period
Nightmare disorder	Disturbing mental experiences that generally occur during rapid eye movement (REM) sleep in the later portion of the night and often result in the person waking up. Occasional nightmares are normal; a nightmare disorder is diagnosed only if nightmares become more frequent and significantly affect daytime functioning and mood
Hypersomnolence disorder	Disorders of excessive daytime sleepiness (EDS) that interferes with functioning; can manifest itself as a tendency to fall asleep during normal waking hours when unstimulated. EDS and "hypersomnia" are currently used interchangeably. Although persons with hypersomnia chronically fall asleep when unstimulated, they do not necessarily require longer than average hours of sleep
Parasomnias	Parasomnias are a group of sleep disorders that involve unwanted events or experiences that occur, while you are falling asleep, sleeping, or waking up; may include abnormal movements, behaviors, emotions, perceptions, or dreams including sleep sex and night terrors

References: Gillette and Abbott (2005), Morin and Benca (2012), Morin et al. (2015), ICSD-3 and DSM-5

that is comorbid with a pre-existing medical condition. Primary insomnia can be divided into psychophysiologic and physiologic insomnia. Psychophysiologic primary insomnia is related to heightened arousal and learned sleep preventing behaviors. Physiologic primary insomnia is a confirmed sleep abnormality associated with abnormal polysomnography (PSG) indicating disruptions in non-rapid eye movement (NREM) sleep or rapid eye movement (REM) sleep (ISCD-3 2014). Palliative care populations may have a combination of a pre-existing primary sleep disorder and insomnia that occurs in response to diagnosis or treatment (acute or adjustment insomnia) but is usually chronic in cancer and other chronic or advanced diseases. In clinical practice, differentiating between sleep disturbance and insomnia is less important than detection of specific sleep disorders that require referral and evaluation by sleep specialists and appropriate treatment.

Later in this chapter, the assessment and management of common sleep disturbances in medical conditions and palliative care, defined in Table 2, including insomnia or insomnia syndrome, hypersomnia, circadian rhythm disturbance, specifically sleep-wake cycle reversal, and nightmares will be discussed.

3 Sleep Architecture and Physiology

Sleep influences the body's major physiological systems, including thermoregulatory, musculoskeletal, endocrine, respiratory, cardiovascular, gastrointestinal, and immune systems (Sateia and Pigeon 2004). These physiological systems are bi-directional and can be affected by disrupted sleep or influence an individual's sleep. Disruptions in sleep can all drastically change a person's thinking and behavior and negatively impact on physical, mental, and emotional health.

Sleep architecture (SA) refers to the basic structural organization of normal sleep, which is segmented into two types of sleep identified as non-rapid eye movement (NREM) and rapid eye movement (REM) sleep (Zepelin et al. 2005). NREM is associated with distinct brain activity and physiology and is divided into progressively deeper stages of sleep comprised of four stages (stage 1–4). Each stage has unique characteristics in brain wave patterns, eye movements, and muscle tone. During sleep, NREM and REM sleep alternate cyclically, and disruptions in either the cycling or stages are associated with sleep disorders. NREM stage 1 describes the transition between wake and sleep that occurs upon falling asleep and during brief arousal periods and represents 2–5% of total sleep time. Stage 2 represents 45–55% of sleep time and occurs throughout the sleep period. Stages 3 and 4 are referred to as slow-wave or deep sleep, most of which occurs during the first third of the night. Stage 4 lasts about 20–40 minutes and makes up about 10–15% of total sleep time. Both are shown on EEG as high-voltage and slow-wave activity. Whereas, REM sleep is shown on EEG as low-voltage and mixed frequency, muscle atonia, and bursts of REM and is most often associated with dreaming.

Physiological changes that occur during sleep, specifically during REM sleep, including cardiovascular (increases in blood pressure and heart rate, particularly in the morning), respiratory (ventilation and respiratory flow become increasingly faster and more erratic and less adaptive; cough reflexes are suppressed), and thermoregulatory processes. Changes also occur with NREM sleep and include reduced cerebral blood flow and metabolism, changes in renal blood flow, glomerular infiltration, hormone secretion, and sympathetic neural stimulation that is evidenced in decreased secretion of electrolytes and calcium, reduced urine flow and higher concentration of urine, and changes in endocrine functions such as secretion of growth hormone, thyroid hormone, and melatonin (influenced by light-dark cycle and suppressed by light).

Sleep-Wake Regulation The dominant model for sleep-wake regulation consists of two key processes including a homeostatic process that promotes sleep (process S) and a circadian process that maintains wakefulness (process C) (Borbely 1982). Process C is wake promoting and regulated by the circadian system, whereas process S counteracts process C to promote wakefulness and alertness in a cyclical process initiated during the day and night that is coordinated with environmental light-dark cycles. Sleep process S is regulated by neurons in the hypothalamus with transmission through molecules that shut down the arousal system, thus allowing the brain to fall asleep, the loss of which can cause profound insomnia. Inputs from other regions of the brain can also influence this sleep system such as the lower brainstem (communicates information about the state of the body, i.e., a full stomach) and emotional and cognitive areas in the forebrain.

Wakefulness is generated by two key pathways that originate in the ascending arousal system of the brainstem. The first pathway arises from cholinergic neurons in the upper pons, which activates parts of the thalamus that transmits sensory information to the cerebral cortex. The second pathway originates in cell groups in the upper brainstem that contain the monoamine transmitters (norepinephrine, serotonin, dopamine, and histamine), which enter the hypothalamus picking up inputs from nerve cells that contain peptides (orexin, hypocretin, and melanin-concentrating hormone) and from cells in the forebrain that contain acetylcholine and gamma-aminobutyric acid and are interpreted in the cerebral cortex through activation of nerve cells. Multiple factors,

alone or in combination, can impact processes C and S, disturbing the timing, duration, and architecture of sleep and potentially creating complaints of insomnia (Carskadon and Dement 2005). Additionally, there are inputs from the circadian system that enable the wake-sleep system to synchronize with the external day-night cycle or override the cycle to meet environmental needs (Waterhouse et al. 2012).

Circadian Rhythms Circadian rhythms (24-hour clock) control the sleep-wake cycle and other physiological processes such as body temperature, heart rate, muscle tone, and hormone secretion such as corticosteroids (Gillette and Abbott 2005). The rhythms are generated by neural structures in the hypothalamus that function as a biological clock and organize physiological rhythms in accord with environmental day-night cycles and through a disruption in gene products in a negative feedback loop that controls the 24-hour cycle time of circadian clocks and other body systems such as lipid metabolism. The suprachiasmatic nucleus (SCN) is responsible for regulating circadian rhythms through inputs from nerve cells in the retina that act as brightness detectors, which can reset the clock genes; these are transmitted to the brain and physiological processes in the body to bring about all the daily cycles synchronized with the day-night cycle. The SCN controls melatonin secretion, which further consolidates circadian rhythms.

Sleep Patterns The pattern of sleep changes across the life course including how sleep is initiated and maintained, the percentage of time spent in each stage of sleep, and overall sleep efficiency (i.e., how successfully sleep is initiated and maintained) (Bliwise 2005). Older individuals typically show an increase in sleep disturbance with difficulty in initiating and maintaining sleep particularly in the presence of depression, respiratory syndromes, and physical disability illness that is likely due to a gradual deterioration in the hypothalamic nuclei that drive circadian rhythms and melatonin production (Dijk et al. 2000). Decreasing sleep homeostasis can occur (time spent in stage 3 sleep decreases, increase in overnight arousals), which can be exacerbated by comorbid medical conditions such as musculoskeletal disorders and cardiopulmonary disease. Gender-based differences in sleep and circadian rhythms have also been shown. Adult men spend greater time in stage 1 NREM sleep and experience more awakenings, whereas women maintain slow-wave sleep (stage 3 and 4 NREM) longer than men and experience more difficulty falling asleep and mid-sleep awakenings.

4 Etiology and Risk Factors

Sleep disturbance specifically insomnia occurs as a comorbid problem with many medical conditions as shown in Table 3 (Schutte-Rodin et al. 2008). The causes of sleep disturbance comorbid with chronic illness and advanced disease are

Table 3 Comorbid conditions and insomnia

Body system	Comorbid condition
Neurological	Stroke, dementia, Parkinson disease, seizure disorders, headache disorders, traumatic brain injury, peripheral neuropathy, chronic pain disorders, neuromuscular disorders
Cardiovascular	Angina, congestive heart failure, dyspnea, dysrhythmias
Pulmonary	COPD, emphysema, asthma, laryngospasm
Digestive	Peptic ulcer disease, cholelithiasis, colitis, irritable bowel syndrome
Genitourinary	Incontinence, benign prostatic hypertrophy, nocturia, enuresis, interstitial cystitis
Endocrine	Hypothyroidism, hyperthyroidism, diabetes mellitus
Musculoskeletal	Rheumatoid arthritis, osteoarthritis, fibromyalgia, Sjögren syndrome, kyphosis
Reproductive	Pregnancy, menopause, menstrual cycle variations
Other	Allergies, rhinitis, sinusitis, bruxism, alcohol, and other substance use/dependence/withdrawal

Reference: Schutte and Rodin 2008

multifactorial, and both physical and psychological factors are clinically important. Differentiation of these factors into predisposing, precipitating, and perpetuating factors based on Speilman's three-factor conceptual framework is useful for guiding assessment of factors that contribute to insomnia (Spielman et al. 1996). This model known as the 3P model asserts that underlying biological or predisposing factors such as pre-existing traits interact with various situational (precipitating) factors, causing acute insomnia, whereas the detrimental beliefs, behaviors, and strategies (perpetuating factors) employed to cope with loss of sleep lead to the development of chronic insomnia. All types of insomnia, regardless of etiology, share the final common pathway of cognitive and physiologic hyperarousal, causing an individual to cross the insomnia threshold, i.e., the point at which sleeplessness occurs (Buysse 2013).

4.1 Predisposing Factors

The underlying risk or precipitating factors for insomnia vary but can include female sex; advanced age; lower levels of education; depressed mood; breathing disorders of sleep such as obstructive sleep apnea; low levels of physical activity; comorbid medical conditions, i.e., diabetes; nocturnal micturition; regular use of agents to aid sleep (i.e., hypnotics); previous history of insomnia; and high levels of perceived stress and/or anxiety (Morin and Benca 2012). Although higher rates of insomnia have been reported in younger cancer patients, this may be confounded with the high rates of psychosocial distress noted in those with life-threatening illness earlier in the life cycle (Palesh et al. 2010). Individuals presenting with insomnia syndrome usually exhibit premorbid psychological vulnerability to insomnia, characterized by higher depressive and anxiety symptoms, lower extraversion, higher arousability, and poorer self-rated mental health at baseline that pre-exists the diagnosis of a life-threatening or chronic illness (Morin and Benca 2012).

4.2 Precipitating Factors

A complex relationship exists between subjective events and neural events that can precipitate disruptions in sleep, and the biological mechanisms are not fully elucidated.

Adverse Disease or Treatment Effects Physiological response to disease or treatments such as brain radiotherapy, chemotherapy, or hormone therapies in cancer, thermoregulatory problems, or immunological changes are associated with insomnia (Berger 2009). Sleep disturbance is also common with diseases involving the central nervous system such as degenerative brain diseases, i.e., Alzheimer, or that disrupt the SCN and sleep processes such as REM sleep (e.g., dopaminergic deficit in Parkinson disease) or diseases affecting the liver, e.g., cirrhosis, and can include changes in liver function at the end-of-life that can disturb the sleep-wake cycle or the central nervous system, i.e., the brain (DeCruz et al. 2012). Shorter sleep time, increased lighter sleep with multiple arousals, and lower sleep efficiency have also been reported in those with chronic obstructive lung disease or congestive heart failure (McSharry et al. 2012).

Symptoms and Symptom Clusters In advanced disease, sleep disturbance is often associated with other symptoms, such as pain, fatigue, psychological distress, and psychiatric conditions (depression and anxiety). These symptoms are often interrelated likely due to similar underlying inflammatory mechanisms as part of a symptom cluster making this a complex symptom to manage in clinical practice (Berger 2009). Insomnia in palliative care populations is often identified as part of a symptom cluster of insomnia, pain, and depression or symptom clusters of pain, fatigue, and insomnia (Davis and Goforth 2014; Beck et al. 2005).

Other symptoms associated with chronic disease or adverse effects of treatments can also disrupt sleep (e.g., menopausal or other gastrointestinal, genitourinary, respiratory symptoms, co-

occurring symptoms, or symptom clusters) (Berger 2009). A small observational study of palliative care inpatients (n = 61) found that pain, medications to treat pain such as opiates, and respiratory symptoms of dyspnea and cough contributed to severe insomnia (Renom-Guiteras et al. 2014). Larger studies (n = 209) have also shown that physical symptoms such as pain and psychological distress particularly depression contribute to insomnia in palliative care populations (Akechi et al. 2007; Glynn et al. 2014).

Chronic Pain and Opiates Chronic pain is a strong predictor of sleep disturbance and attributed to disruptions in REM and slow-wave NREM sleep and characterized as symptoms of difficulty falling asleep and staying asleep, lack of restful sleep, frequent awakening, and daytime somnolence (Finan et al. 2013). Pain is highly prevalent in many chronic diseases and can be excruciating in advanced diseases such as cancer (Berger 2009). A vicious cycle of disturbed sleep due to pain followed by worsening of pain and resulting in more disruption in sleep has been noted. Of note, high pain intensity and insomnia have been shown to increase a desire for hastened death at the end-of-life (Rosenfeld et al. 2014).

Medications used to manage pain such as opiates may also disrupt sleep. Although the exact mechanism by which opioids disrupt sleep is unclear, morphine has been shown to reduce REM sleep via inhibition of acetylcholine release in the medial pontine reticular formation resulting in disruption of sleep architecture and affecting states of arousal during wakefulness (Brincat and Macleod 2007). The adverse effects of opiates on the central nervous system are complex but include a decrease in the level of consciousness (sedation, drowsiness), those affecting the thinking process and ability to react (cognitive impairment, delirium, hallucinations), and direct toxic effects on neurons (myoclonus, seizures, hyperalgesia, tolerance). The sedative effects of opioids can disrupt daytime arousal and disrupt circadian rhythms and lead to sleep-wake reversal and contribute to vivid dreams and nightmares. Many of these causes of sleep disturbance can be managed through optimization of pain management and with opioid dose reduction, opioid rotation, or use of a psychostimulant such as methylphenidate to counteract the sedating side effects of opioids to minimize sleep-wake reversal or hypersomnia (Mystakidou et al. 2009).

Psychological Distress A large body of evidence has shown associations between psychosocial distress, psychiatric conditions such as generalized anxiety disorder and depression, and insomnia. Psychological distress and psychiatric conditions such as depression is common in palliative care populations with high rates of moderate to severe depression reported (Wilson et al. 2007). Depression has been linked to disturbances in the continuity of sleep, decreased latency to the first REM sleep period, and diminished deep sleep (NREM, stage 3 and 4) (Ohayon 2011). Situational anxiety or pre-existing anxiety disorders can also contribute to nightmares and are found to be associated with sleep disturbance in palliative care populations through arousal of the primary adrenal axis (Davis et al. 2014). A recent review and meta-analysis of sleep and mental disorders showed alterations in sleep across a range of psychiatric conditions with noted changes in the arousal system, sleep depth, and REM processes with variation based on type of psychiatric disorder (Baglioni et al. 2011). Insomnia may also be a symptom of psychological distress, and effective treatment of this symptom may help to reduce sleep disturbances, although the interrelationship between these disorders is complex. Sleep disturbance is a hallmark symptom of major depression.

Medications to Manage Disease and Insomnia Any drugs that alter the balance of the neurotransmitters that regulate the sleep-wake cycle or the direct effects of disease on the central nervous symptom and other physiological systems can disrupt sleep. Drugs shown to contribute to insomnia include corticosteroids, diuretics, stimulant antidepressants, and other stimulants, such as antipsychotics, and a paradoxical response to hypnotics that can disrupt sleep has been shown (Davis

and Goforth 2014). A large systematic review of reviews with meta-analysis showed that drug classes such as DOPA agonists (for Parkinson disease and restless legs syndrome), acetylcholinesterase inhibitors (for Alzheimer disease, cognitive impairment, and dementia), SSRIs (for obsessive-compulsive disorder and premenstrual syndrome), serotonin-norepinephrine reuptake inhibitors (for generalized anxiety disorder), opioid receptor antagonists (for alcohol dependence), tricyclic antidepressants (TCAs) (for depression), COMTI (for Parkinson disease), nicotine receptor agonists (for smoking cessation), and systemic corticosteroids (for chronic obstructive pulmonary disease) are associated with impairment in sleep (Doufas et al. 2017). Moreover, psychotropic medications used to manage psychological distress or psychiatric conditions may worsen sleep disorders and may contribute to sedation and drug accumulation particularly in older individuals. As an example, mirtazapine commonly recommended in palliative care for management of psychological distress and symptoms of insomnia or insomnia syndrome has been shown to increase somnolence, sedation, and other symptoms that are associated with sleep disturbance such as hallucinations and delirium (Khoo and Quinlan 2016).

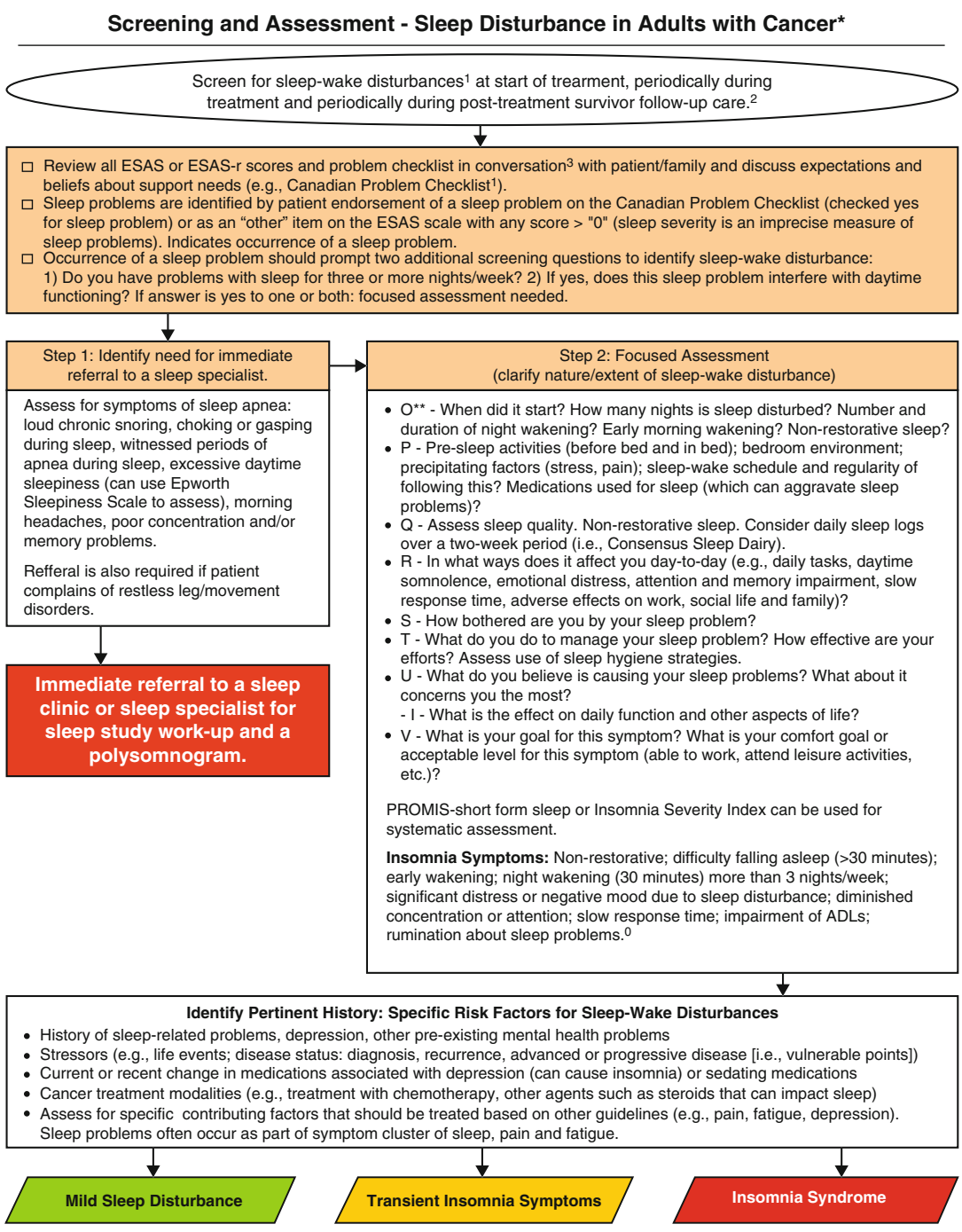
Environmental Factors Adequate levels of sleep are dependent on not only the physiological environment but also on behavioral and environmental factors. Excessive arousal in bed is a frequent cause of insomnia and may be particularly pronounced for patients with advanced disease. Nighttime rumination, fears, anxiety, and worry are profound for these patients and may contribute to hyperarousal. Environmental factors such as disruptive noise or interruption of sleep by caregivers, absence of usual light/dark cues, or temperature also play a role in sleep disruption. In PCUs, interruptions during the night by the nursing staff, noise coming from the ward or from another patient in the same room, have been shown to influence the sleep quality of palliative care patients (Hugel et al. 2004).

4.3 Perpetuating Factors

Beliefs, behaviors, or thoughts can maintain or exacerbate sleep disturbance (Buysse 2013). Behaviors including excessive time in bed, daytime napping, reduced daily activity, irregular sleep-wake times, stimulant consumption, and inappropriate use of sleep aids and beliefs including unrealistic sleep expectations, false perception of sleep time and quality, fear of sleeplessness, and difficulty discerning the cause of daytime fatigue can contribute to sleep disturbance. Negative cognitions such as uncertainty about the disease and prognosis, existential distress, and nighttime rumination accompanied by feelings of fear may all contribute to sleep disturbance in palliative care patients (Renom-Guiteras et al. 2014).

5 Clinical Assessment and Evaluation of Insomnia

Comprehensive assessment and evaluation of sleep disturbances as part of routine practice in palliative care populations is essential given its high prevalence and impact on symptom burden and psychological distress. As shown in Fig. 1, current practice guidelines recommend a three-step process for the assessment and evaluation of sleep disturbance (Howell et al. 2011, 2013; Qaseem et al. 2016). The initial step involves routine screening to identify sleep disturbance at scheduled clinic visits (Step 1). A positive screen for the presence of sleep disturbance should be followed by additional questions for detecting sleep disorders (Step 2). This step should be followed by a more focused assessment and evaluation to identify the specific parameters of sleep disturbance necessary to guide selection of interventions (Step 3). Routine screening in clinical care may be particularly important as palliative care patients may not complain of sleep disturbance. Moreover, an initial screening step can identify sleep disorders that require referral to a sleep specialist and can reduce the burden of a full assessment or completion of more lengthy sleep measures.



* Refer to the full technical guideline document for the disclaimer statement on the Canadian Association of Psychosocial Oncology website (www.capo.ca).

1 Use Screening for Distress Tool (SDT), which includes Edmonton Symptom Assessment System (ESAS-r) and Canadian Problem Checklist (CPC).

2 At initial diagnosis, start of treatment, regular intervals during treatment, end of treatment, post-treatment or at transition to survivorship, at recurrence or progression, advanced disease, when dying, and during times of personal transition or re-appraisal such as family crisis, during survivorship, when approaching death (CAPO/CPAC guideline: "Assessment of psychosocial Health Care Needs of the Adult Cancer Patient" by Howell et al., 2009).

3 The health care team for cancer patients may include surgeons, oncologists, family physicians, nurses, social workers, psychologists, radiation therapists, patient navigators and other health care professionals (HCPS).

** Fraser Health Symptom Assessment Acronym OPQRSTU(I)V: O = Onset; P = Provoking/Paliating; Q = Quality; R = Region or Radiating; S = Severity and Duration; T = Treatment; U = Understanding/I=Impact; V = Values

Fig. 1 (continued)

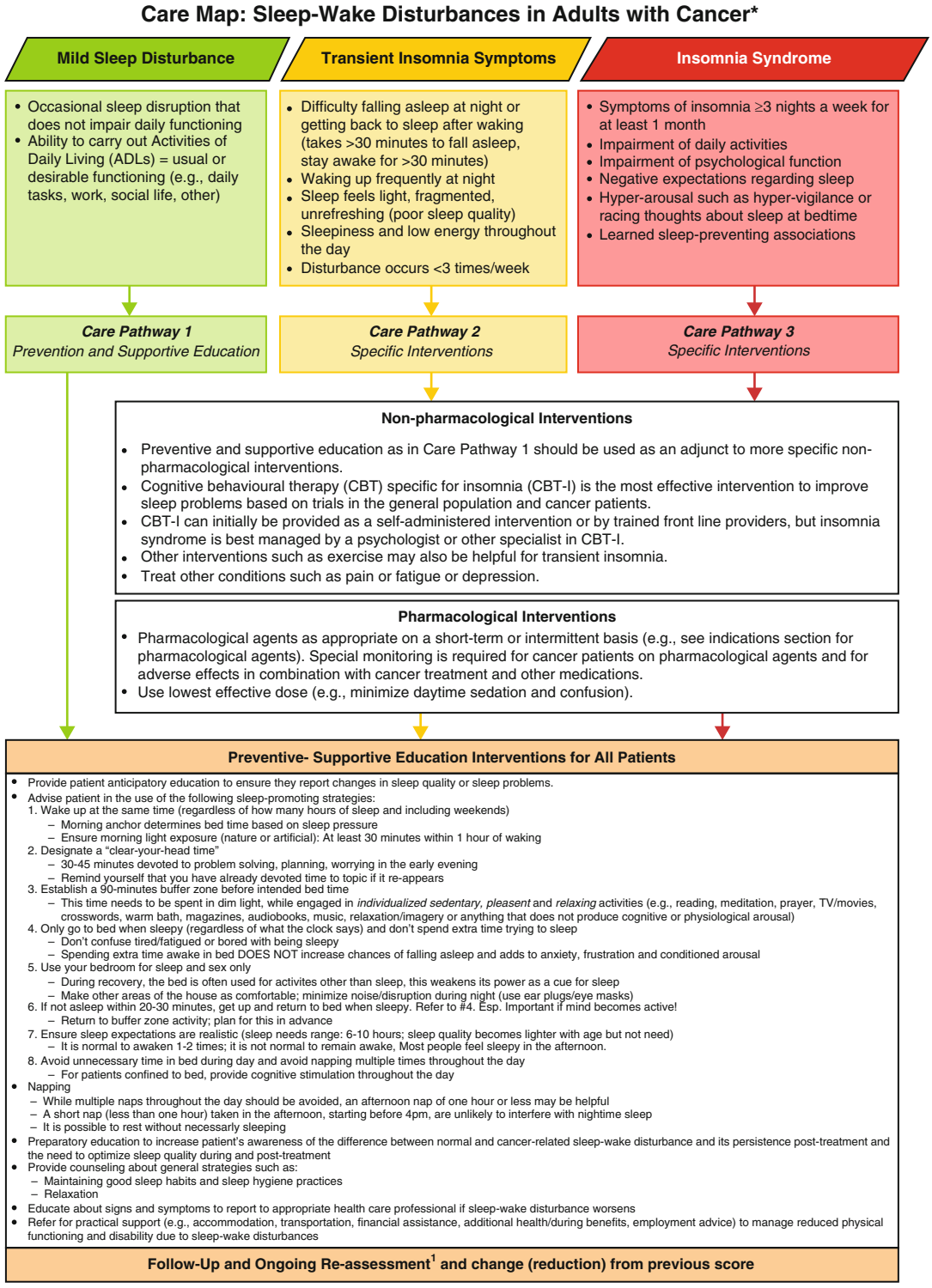


Fig. 1 Screening and assessment for insomnia in adults with cancer (Source: Howell et al. 2013)

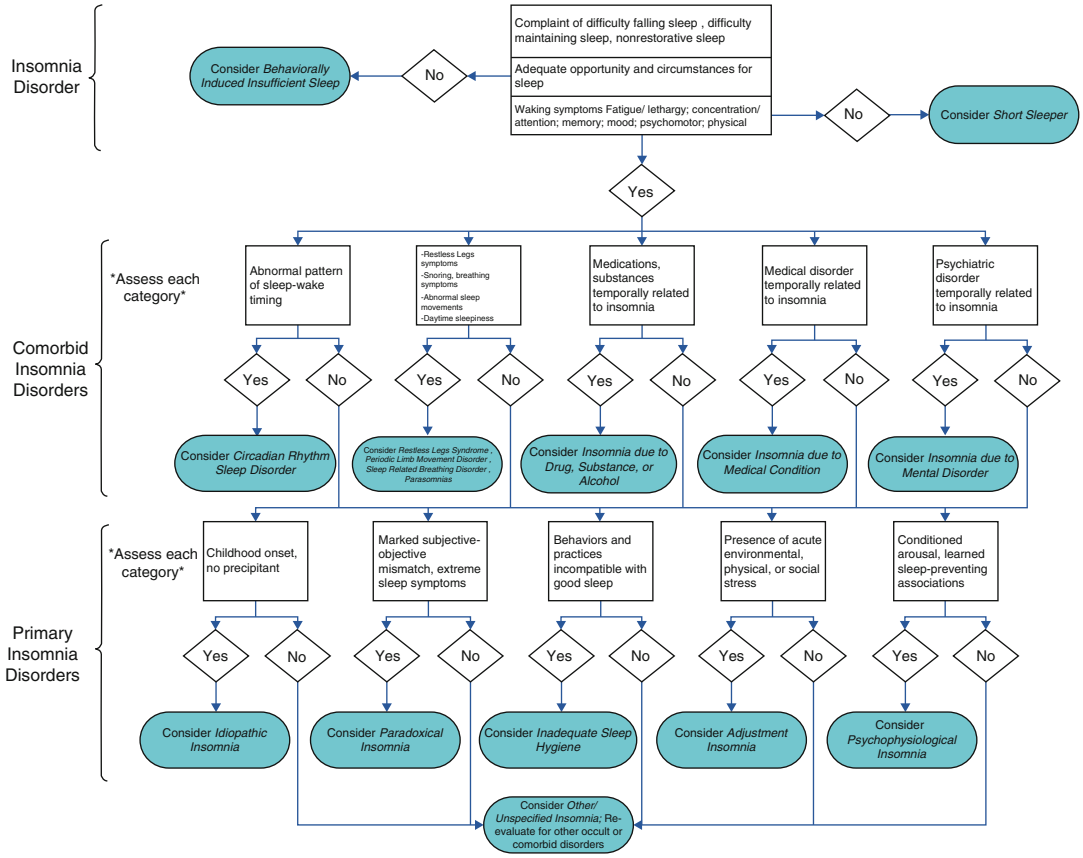


Fig. 2 Screening for sleep disorders (Reprinted with permission. Source: Schutte-Rodin et al. 2008)

Screening for Sleep Disturbance Screening for sleep disturbance (Step 1) typically involves several questions that can accurately detect the presence of sleep disorders. Although the specific questions or tools used for screening for sleep disturbance may differ across organizations, this step is useful to identify patients with the presence of sleep disturbance and to detect sleep disorders such as obstructive sleep apnea, narcolepsy, or restless leg syndrome that require more immediate referral for evaluation by a sleep specialist as shown in Fig. 2 (Schutte-Rodin et al. 2008).

Simple numerical rating scales (0, no sleep problem, to 10, worst sleep problem) may be sufficient such as the inclusion of sleep anchors on the "other" scale of the Edmonton Symptom Assessment System (ESAS) as an initial screen for sleep disturbance, particularly since ESAS is commonly used for symptom screening in cancer and palliative care (Gilbert et al. 2012). In a study of palliative care patients, exploratory and validation samples suggested that a cutoff value of ≥ 4 on an ESAS sleep item provides good sensitivity with reasonable specificity (Yennurajalingam et al. 2017). These authors suggested that all patients who score ≥ 4 on an ESAS sleep item should undergo a focused assessment for diagnosis of a sleep disorder. More recent research using the revised version of ESAS (ESASr) identified a score ≥ 2 on the ESAS-drowsiness item had a sensitivity of 61.5% and a specificity of 75.4% as a screen for sleep disturbance (Savard et al. 2016). When used in combination, the best option was scoring positively on a single question (endorsement of yes for problems with sleep) on a problem checklist and a score ≥ 2 on the ESAS-drowsiness item (sensitivity, 84.2%; specificity, 69.7%). Sleep

experts have recommended the use of two key questions to standardize the screening process for insomnia using items from the Patient-Reported Outcomes Measurement Information System (PROMIS) (Buysse et al. 2010) as follows:

1. Do you have problems with your sleep or sleep disturbance on average (routinely, in the past month, etc.) for three or more nights a week?
2. If yes, does the problem with your sleep negatively affect your daytime function or quality of life?

If the patient answers positive (yes) to both questions, a more focused assessment and comprehensive evaluation of sleep disturbance is recommended. The PROMIS short form 8A can also be used as a valid and reliable "sleep thermometer" to identify the presence of sleep disturbance.

Clinical practice guidelines have also recommended the use of a more comprehensive screening tool such as the Sleep Disorders Screening Checklist-25 (SDS-CL-25) that can be used to accurately screen for six sleep disorders including insomnia, obstructive sleep apnea, restless legs syndrome/periodic limb movement disorder, circadian rhythm sleep-wake disorders, narcolepsy, and parasomnias (Klingman et al. 2017). Ideally, screening in palliative care populations should also include screening measures for delirium and psychological distress given that insomnia is a key clinical marker for these conditions.

Focused Assessment and Evaluation Depending on the health status of the patient, a focused assessment of sleep disturbance should include specific parameters for identification of all sleep-related symptoms and disruptions in the sleep-wake cycle using self-reports of patients and their caregivers and clinician interviews. The underlying causes and comorbidities that can contribute to sleep disturbance, inclusive of recent stressors, can be assessed by taking a detailed history, doing a physical exam to identify physical conditions or comorbidities that contribute to insomnia, and taking a drug history (prescribed, recreational, caffeine, alcohol, nicotine). Identification of predisposing, precipitating causes, and perpetuating factors and the key parameters for assessment and evaluation are recommended as follows:

- Any underlying cause of insomnia or an associated comorbid condition, i.e., psychiatric or medical conditions such as COPD.
- Sleep history including patterns in the sleep-wake cycle.
- Previous treatments used and their effectiveness.
- Sleep hygiene practices and negative learned associations.
- Duration of symptoms.
- Emotional status and other symptoms.
- Person's beliefs and negative cognitions about sleep, perception of sleep quality, or other distortions about sleep (i.e., I will die in my sleep).
- Impact that insomnia has on the person's quality of life, cognition, ability to drive, employment, relationships and mood, and other daytime activities.
- Impact on caregivers particularly in the setting of home palliative care.
- Substance use (alcohol and drugs) and other medications including over-the-counter sleep aids.
- Consider the sleep requirements of the patient, variation with age, and normal pattern.
- Use a sleep log or diary covering 2 weeks to complement the history.

It is essential to characterize the complaint in terms of difficulty initiating sleep, recurrent nocturnal awakening, insufficient total sleep, nonrestorative sleep, advanced or delayed sleep onset, excessively long sleep, chronic drowsiness, and sleep attacks. At a minimum, a sleep history should capture domains of sleep including total sleep time, sleep latency, awakenings during sleep, wake time after sleep onset, napping during the day, excessive daytime sleepiness, quality of perceived sleep, circadian rhythm, and sleep efficiency (Woodward 2011). Patient-reported outcome measures (PROMs) that are psychometrically valid can help to standardize the assessment process, reduce the burden on the patient, and are a more efficient use of a clinician's time,

Table 4 Recommend domains and measures for sleep disturbance

Sleep efficiency (SE)	Ratio of actual sleep to time spent in bed × 100 reported as a percentage
Sleep latency (SL)	Time in minutes measured from intention to sleep (turn the lights out) to the actual onset of sleep
Waking after sleep onset (WASO)	The number of times a person wakes up during sleep, which increases with age
Pittsburgh Sleep Quality Index (PSQI)	PSQI is a 24-item self-report measure of sleep quality (global score > 5 is indicative of poor sleep quality (Buysse et al. 1989)
Insomnia severity index (ISI)	ISI is a seven-item rating scale to assess the patient's perception of insomnia and severity. Optimal cutoff score of 8 in cancer patients = optimal sensitivity and specificity (Bastien et al. 2001)
Epworth Sleepiness Scale (ESS)	ESS is an eight-item self-report questionnaire used to assess subjective sleepiness (score range 0–24, normal <10). Useful for measuring frequency of daytime sleepiness and associations between daytime sleepiness and insomnia (Johns 1991)
Sleep Disorders Screening Checklist-25	Screens for six categories of sleep disorders: insomnia, obstructive sleep apnea, restless legs syndrome/periodic limb movement disorder, circadian rhythm sleep-wake disorders, narcolepsy, and parasomnias. Takes 1–3 minutes to complete and is based on the ICSD criteria. Includes 17 statements clustered by disorder, summing responses in each subscale. Sensitivity and specificity for diagnosed sleep disorders (0.64 to 0.88) (Klingman et al. 2017)
Sleep diary	Useful in identifying circadian rhythm disorders and poor sleep hygiene. Self-reported record of a person's sleeping and waking times with related information, usually over a minimum of 2 weeks. It is self-reported or can be recorded by a caregiver (Carney et al. 2012)
Dysfunctional beliefs and attitudes about sleep questionnaire	A 28-item scale that evaluates sleep-related beliefs, respondents' expectations, and attitudes regarding the causes, consequences, and potential treatments of sleep issues (Morin et al. 1993)
Actigraphy	A small device that monitors and analyzes wrist movements during routine daily activities to estimate time spent in sleep vs. awake. Not used in diagnosis but can serve as a useful objective adjunct to routine evaluations of insomnia, circadian rhythm disorders, restless legs syndrome (RLS), or periodic limb movement disorder (PLMD) (Litner et al. 2003)
Polysomnogram (PSG)	Gold standard measure for assessments of sleep structure and for objective validation of the effects of treatments; not currently recommended for routine screening or diagnosis of insomnia in clinical practice (Pressman 2002)

References: Buysse et al. (1989), Bastien et al. (2011), Johns (1991), Klingman et al. (2017), Carney et al. (2012), Morin et al. (1993), Litner et al. (2003), Pressman (2002)

particularly in the context of palliative care (Howell et al. 2015). As shown in Table 4, several PROMs with valid cutoffs have been recommended for assessment of sleep disturbances such as the Pittsburgh Sleep Quality Index (Buysse et al. 1989) and the Insomnia Severity Index (Bastien et al. 2001) and for measurement of excessive daytime sleepiness using measures such as the Epworth Sleepiness Scale (Johns 1991). Objective measures for sleep are also summarized in Table 4. The Clinical Sleep Assessment for Adults (CSA) can also be a useful tool for guiding the clinical interview for sleep disturbance (Lee and Ward 2005).

Family and friends and particularly the patient's bed partner may also be an important source of assessment information, as they may be able to provide information about sleep and wake patterns, daytime napping, and frequency of symptoms (snoring or nocturnal limb movements). Daily sleep logs and sleep diaries are considered a "gold standard" for subjective sleep assessment and monitoring of response to treatment that is completed by individuals over several

days (e.g., 2-week period). Ideally, sleep diaries should be collected at baseline and throughout the course of insomnia treatment and for long-term evaluation in the case of relapse or reevaluation (Carney et al. 2012). A sleep diary should include information about sleep quality, sleep parameters (e.g., sleep duration, frequency and duration of nocturnal awakenings), napping, daytime impairment, medications, activities, time of evening meal, caffeine and alcohol consumption, and stress level before bedtime for each 24-hour period.

Sleep diaries can also provide data about sleep routines and may help identify environmental or behavioral factors contributing to insomnia. To achieve more consistency, a consensus sleep diary has been developed and proposed for use in insomnia research (Carney et al. 2012). There is agreement that such self-monitoring should yield information about relevant metrics including nightly sleep onset latency (SOL); wakefulness after initial sleep onset (WASO); total sleep time (TST); total time spent in bed (TIB); sleep efficiency (SE), defined as the percent of the time asleep out of amount of time spent in bed; and sleep quality or satisfaction, which includes a subjective global appraisal of each night's sleep from the perspective of the patient.

Objective Measures Findings from a physical exam and laboratory data may also be important to identify factors contributing to sleep disturbance. Polysomnography (PSG) is a major diagnostic tool and gold standard for identification of sleep disorders indicated in the evaluation of suspected sleep-related breathing disorders and periodic limb movement disorder and when the cause of insomnia is uncertain or when behavioral or pharmacologic therapy is unsuccessful (Pressman 2002). PSG assesses sleep parameters, stages, and architecture and is usually conducted in sleep medicine clinics overnight and supervised by sleep specialists. PSG includes the monitoring of electroencephalography, electrooculography, electromyography, effort of breathing and air flow, oxygen saturation, electrocardiography, and body position.

Actigraphy, which uses a small wrist or leg accelerometer to measure body movements, is also used to objectively evaluate activity-rest patterns and response to treatment of sleep disturbance (Littner et al. 2003). The use of objective measures in palliative care should take into consideration patient factors such as stage of illness, prognosis, and functioning as necessary to determine the specific type of sleep disorder and direct appropriate treatment.

6 Management of Sleep Disturbance

The goal of treatment for sleep disturbance and insomnia disorders is aligned with the principles of a palliative care approach, that is, to identify and treat any reversible or underlying cause(s) that are contributing to sleep disturbance. This includes optimizing the management of other symptoms, pain, and psychological distress (anxiety and depression) that can precipitate and exacerbate sleep disturbance.

The nature of the specific sleep disorder should also guide treatment approaches since each type of sleep disorder may require a different treatment approach. Primary sleep disorders such as insomnia and insomnia syndrome, sleep apnea, restless leg syndrome (RLS), and circadian rhythm disturbance may all require specific treatments, which have been shown to improve sleep quality. The algorithm developed for the identification and management of sleep disorders is shown in Fig. 2.

Given the multifactorial nature of sleep disturbances in palliative care, management strategies may require a combination of psychological interventions or non-pharmacological interventions and pharmacological treatment that is individualized to the patient and takes into consideration predisposing, precipitating, and perpetuating factors and illness severity and prognosis. The overall goal of treatment of insomnia is to improve sleep quality and minimize associated distress and daytime dysfunction if possible.

7 Non-pharmacological Management

As shown in Fig. 1, general treatment measures for management of insomnia include the treatment of comorbid medical and psychiatric conditions, modifying sleep-interfering medications and substances; changing sleep behaviors, i.e., sleep hygiene; and optimizing the sleep environment (Howell et al. 2013). Simple strategies such as changing the timing of medications such as corticosteroids, adjusting doses of opiates, or switching of opiates or antidepressants, sleep hygiene, and environmental manipulations may be an initial step in a tiered approach to management of insomnia and may be helpful in specific sleep disorders such as circadian rhythm disorders.

7.1 Sleep Hygiene Strategies

All patients should receive supportive education and information, including coaching in sleep hygiene strategies, as a health promotion approach for populations at risk for insomnia and as an adjunct to cognitive behavioral therapy. As summarized in Table 5, the patient should be advised and coached in the use of specific sleep hygiene behaviors to reduce insomnia, although the efficacy of sleep hygiene alone has not been established (Dietrich et al. 2016). Some aspects of sleep hygiene such as avoidance of daytime sleeping and increasing daytime activities may be difficult in very ill palliative care patients. If possible daytime napping should be kept short, and a prolonged uptime prior to bedtime and a focus on increasing tolerable daytime activities will be important.

7.2 Cognitive Behavioral Therapy for Insomnia (CBT-I)

CBT-I is now recommended as the standard of care and first-line treatment for primary insomnia and insomnia syndrome (Sateia et al. 2017). CBT-I is a multicomponent intervention that targets the behavioral and cognitive factors that are believed to perpetuate insomnia over time including poor sleep habits and negative thoughts, attitudes, and beliefs about sleep that contribute to hyperarousal (Savard and Savard 2017). The interrelated and most common components of CBT-I include stimulus control, sleep restriction, relaxation therapies, sleep hygiene, and cognitive restructuring are shown in Table 6. While a combination of these components has been shown to be most effective on sleep outcomes, single components such as relaxation therapy have also shown effects on insomnia and may be more feasible and acceptable to palliative care patients who may be too ill to participate in CBT-I programs.

A large body of evidence including systematic reviews and meta-analysis of CBT-I have demonstrated the short- and long-term efficacy of CBT-I for primary insomnia in general populations (Trauer et al. 2015) and cancer (Savard and Savard 2017). CBT-I has also been shown to be effective for distress and insomnia and other medical conditions including Parkinson disease (Humbert et al. 2017) and multiple sclerosis (Majendie et al. 2017). There is extensive review evidence for the efficacy of CBT-I in cancer with medium to large effect sizes shown and statistically and clinically significant gains on sleep measures (Johnson et al. 2016). CBT-I has been shown to improve sleep onset latency, wake after sleep onset, sleep efficiency, and sleep quality in the general population, and in cancer populations, improvements in SOL, WASO, and self-perceived severity (Johnson et al. 2016). CBT-I has produced larger effects than treatment as usual (TAU), compared to waitlist control groups, pharmacotherapy +/− medication placebo, relaxation therapy and behavioral placebo, and sleep hygiene education. Of the studies with long-term follow-ups, the effects of CBT-I have been remarkably durable lasting up to 2 years in a substantial proportion of participants, and, on several measures, patients continue to improve (if not reach remission) long after treatment is discontinued (Savard and Savard 2017). However, evidence in older adults (>60) is more mixed, and CBT-I may be less beneficial in older individuals versus younger patients with less durability of the long-term effects (Montgomery and Dennis 2003).

Table 5 Strategies for sleep hygiene

Behavior	Rationale
Wake up at the same time (regardless of how many hours of sleep and including weekends)	Sleeping in after a night of disrupted sleep, or on weekends, tends to perpetuate sleep problems by preventing the accumulation of sleep pressure, leading to more difficulty falling asleep or maintaining sleep
Ensure light exposure soon after waking	Exposure to natural or artificial light is an important regulator of sleep-wake rhythms. Light exposure can help "set" a patient's circadian clock, making it easier for them to continue with the same wake-up time
Designate a "clear-your-head time"	Establishing 30–45 minutes devoted to problem solving, planning, and worrying in the early evening can help patients deal with the concerns that may contribute to mental activity at night. It may be helpful for patients to write these concerns down to avoid mental rehearsal and remind themselves that they have already devoted time to a topic if it reappears
Establish a 90-minute buffer zone before intended bedtime	Implementing a designated time to unwind in the evening before bed allows patients to create an environment that is conducive to sleep. Dim lighting and a relaxing, pleasant, and sedentary activity promote sleep and activities that do not produce cognitive or physiological arousal, i.e., reading
Go to bed only when sleepy and don't spend extra time trying to sleep	Spending extra time awake in bed and trying to sleep does not increase the chances of falling asleep. In fact, this strategy can be counterproductive because it can contribute to performance anxiety, frustration, and eventually conditioned arousal
Use your bedroom for sleep and sex only	Preserve the bed as a strong environmental and psychological signal for sleep; and make the other areas where a patient spends time during the day as comfortable as their bed
If you are not asleep within 20–30 minutes, get out of bed and return when sleepy	If a patient is not asleep and their mind becomes active after being in bed for 20–30 minutes, it is recommended that they interrupt the tendency to try harder to sleep by getting out of bed and returning to their buffer zone activity. Returning to bed when sleep feels imminent. This may need to be planned for in advance or repeated several times until the disruptive sleep cycle is broken. The goal of this strategy is to reinforce the association between the bedroom and sleep
Ensure sleep expectations are realistic	Address inaccurate sleep beliefs that can contribute to increased patient anxiety surrounding sleep. One of the most common is that 8 hours of sleep is optimal for everyone; normal sleep needs range from 6 to 10 hours. Sleep quality changes with age, and it is normal to wake one to two times but not remain awake
Restrict napping	Patients should avoid multiple naps, especially in the evening; however, a short nap (less than 1 hour) in the afternoon, starting before 3:00 pm, may be helpful and is less likely to interfere with nighttime sleep. If resting, rather than sleeping, it should be done in a room other than the bedroom
Restful environment	Minimize noise and disruptions during night. Use earplugs and eye masks, cool temperature

References: Howell et al. (2013, 2015), Dietrich et al. (2016)

Positive benefits have been reported across various modes for delivering CBT-I, including face-to-face individual therapy, in-person group therapy, telephone-based modules, web-based or Internet modules, and self-help books (Zachariae et al. 2016). Web-based modules or self-help books may be particularly valuable in palliative care populations who can complete these strategies at their own pace. A recent review presented evidence from 15 trials, finding improvement in

Table 6 Cognitive behavioral therapy: insomnia components

Component	Definition	Approach
Stimulus control therapy	Promotion of a consistent sleep-wake schedule (sleep patterns) and behavioral strategies to reinforce association between bed and sleep	Go to bed early when sleepy, get out of bed if unable to sleep, use the bed for sleep only, arise at the same time of day, and avoid napping
Sleep restriction therapy	Limiting the time spent in bed as possible to actual sleep time to produce mild sleep deprivation and more consolidated sleep	The sleep window is gradually increased over a few days or weeks until optimal sleep duration is achieved
Sleep hygiene education	Behavioral or environmental practices that positively or negatively affect sleep including avoiding stimulants such as caffeine or alcohol several hours before bedtime and other behaviors and keeping the sleep environment dark, quiet, and comfortable	Manipulation of sleep environment and behaviors to promote sleep
Relaxation training	Strategies aimed at reduction of somatic tension, e.g., progressive muscle relaxation, or intrusive thoughts, e.g., imagery training or meditation	Usually require professional guidance initially and daily practice for a few weeks

References: Savard and Savard (2017)

the severity of insomnia and sleep efficiency, with the duration of treatment and the degree of support as moderators of sleep efficiency for web-based interventions (Seyffert et al. 2016). Larger effects have been shown for longer treatment duration and personal clinical support as part of web-based interventions. Self-administered CBT-I could be feasible in palliative care populations but with smaller treatment effects (Savard and Savard 2017).

The application and feasibility of CBT has emerged for the management of psychological distress (anxiety and/or depression) in advanced disease (Campbell and Campbell 2012). However, there is less research on CBT-I for management of insomnia in palliative care. CBT-I may be particularly beneficial in palliative care populations given that adverse effects are not reported for this approach. However, CBT-I involves a considerable time commitment and energy from the patient to acquire the new skills and behaviors that are emphasized. Some elements of CBT-I such as sleep restriction may also be difficult to achieve in palliative care patients who may be too ill to participate or experiencing hypersomnia due to adverse effects of disease or treatment and other disruptions in the sleep-wake cycle. Simple strategies such as environmental manipulation such as increased exposure to natural or artificial light during the days and reduced exposure during nighttime alongside behavioral strategies such as increased activity or engagement in pleasurable activities during the day if tolerable may be helpful. Another component of CBT-I, relaxation therapy, may also be difficult for a patient with severe weakness or pain from bony metastases. Adaptations of CBT to the palliative care setting have been suggested including offering guided assistance to patients in practicing skills such as talking an individual through the relaxation techniques; the use of pleasant activities as a sleep restriction strategy and brief CBT may be more tolerable.

Research is needed to establish the predictors of success with CBT-I and other psychological and behavioral interventions in palliative care populations. Kvale and Shuster (2006) recommended that CBT-I only be used with a patient whose prognosis exceeds the length of time required to benefit from this treatment, usually at least 4–6 weeks. Access to CBT-I may be problematic in palliative care, but there is emerging evidence that it can be delivered by appropriately trained and supervised community health nurses, primary care counselors, and primary care physicians. Ideally a clinician who is trained in

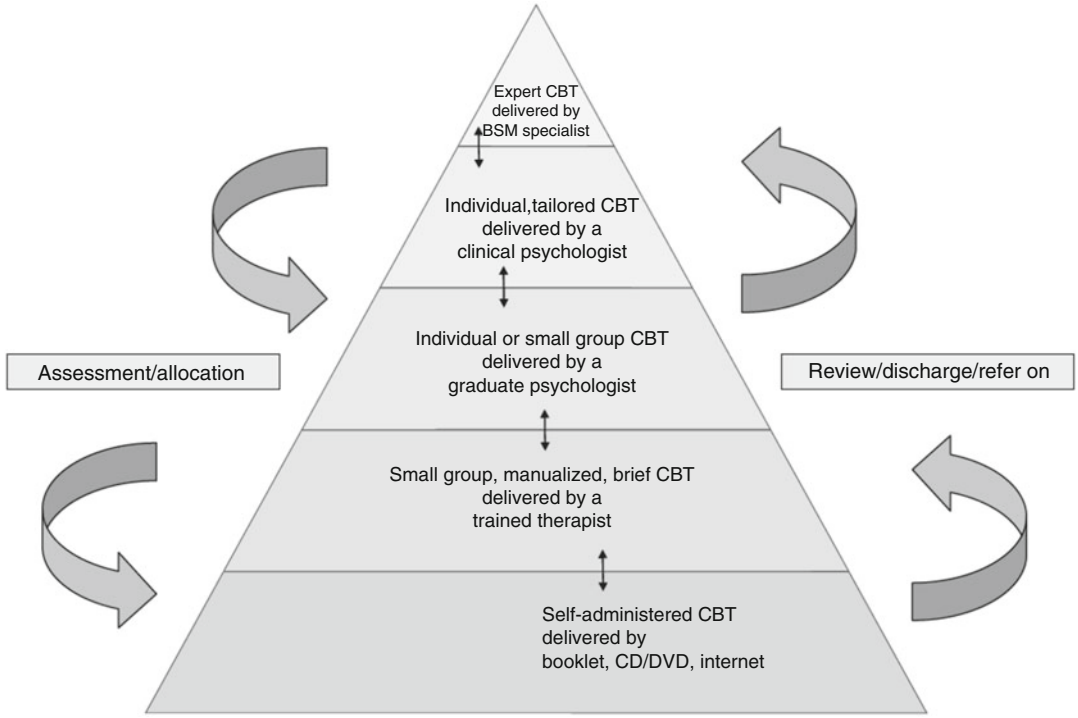


Fig. 3 Stepped care (Reprinted with permission. Source: Espie 2009)

psychological or behavioral therapies should deliver cognitive behavioral therapy; however when this level of care is not available, training of front-line staff guided by a manual has shown effectiveness (Espie 2009). To achieve best clinical care and utilize existing resources, an approach called stepped care has been proposed as shown in Fig. 3. Depending on the severity and complexity of the sleep disturbance, individuals could be allocated to different levels of psychological treatment with self-administered cognitive behavioral therapy (e.g., reading materials or bibliotherapy) as Step 1, brief cognitive behavioral therapy delivered by nurses following a manual as the next level (Step 2), and involvement of specialized health professionals such as psychologists experienced in delivering CBT-I in later steps (Step 3) in combination with pharmacological treatment on a short-term basis until CBT takes effect. Stepped care will still require practitioners to be trained, and implementation in routine practice may still not feasible based on available resources.

7.3 Mind and Body Therapies

Mind/body therapies such as yoga and Mindfulness-Based Stress Reduction (MBSR) may be helpful in reducing insomnia in medical illness and in palliative care populations (Neuendorf et al. 2015). A randomized non-inferiority trial comparing CBT-I with Mindfulness-Based Cancer Recovery (MBCR), an adaptation of Mindfulness-Based Stress Reduction (MBSR) in a heterogeneous sample of posttreatment cancer patients ($n = 111$), found this intervention to be inferior to CBT-I (Garland et al. 2014). CBT-I produced larger improvements in diary-measured sleep latency and sleep efficiency, but both interventions significantly reduced the amount of time spent awake after sleep onset and increased total sleep time. Significant improvements in symptoms of stress and psychological functioning were also reported, regardless of assigned treatment. MBCR/MBSR since it is focused on an acceptance-based treatment approach may be a viable alternative for palliative care patients.

8 Pharmacological Management

When behavioral approaches do not resolve sleep problems, the addition of medications is usually warranted, and a combination of these may be necessary in the context of palliative care. The goal of pharmacologic treatment is to improve sleep quality and quantity, to minimize impairment in daytime functioning and distress, to reduce sleep latency and wakefulness after sleep onset, and to increase total sleep time or sleep efficiency.

Numerous reviews and meta-analysis have been conducted on the effectiveness of pharmacological agents in the management of insomnia in adult populations with small to moderate effects shown with both benzodiazepines (BZDs) and non-benzodiazepine receptor agonists (BzRAs) (De Crescenzo et al. 2016). A recent systematic review and meta-analysis conducted to inform evidence-based recommendations in the American Academy of Sleep Medicine (AASM) 2017 guideline suggested the use of several medications for management of insomnia in adult populations, and recommendations from this guideline are summarized in Table 7 (Sateia et al. 2017). Small to moderate effects were shown for BZDs, BzRAs, anticonvulsants such as tiagabine, orexin receptor agonists, melatonin agonists, and heterocyclics in adult populations. Medications including diphenhydramine, melatonin, L-tryptophan, and Valerian were not recommended noting the harmful adverse effects of these drugs since their anticholinergic effects outweighed the benefits. It was also noted in the guideline that there was insufficient high-quality evidence regarding the overall efficacy of pharmacotherapy for insomnia and adverse effects that may preclude their use in some medical conditions and particularly in the elderly.

Drugs commonly used in the management of insomnia in palliative care include the benzodiazepine group of drugs, benzodiazepine receptor antagonists, sedating antidepressant drugs (Davis et al. 2014). The BZDs are commonly used in palliative care for their anticonvulsing properties and can reduce sleep latency, reduce nighttime awakenings, and increase total sleep time and a feeling of restorative sleep. However, they are recommended for short-term use, i.e., 4 weeks, and then should be tapered to discontinuation due to dependence. Intermediate-acting BZDs are preferred, but their active metabolites in the elderly and those with altered liver function can result in excessive drowsiness, sedation, and dizziness and need to be used cautiously when combined with opiates due to increased sedation and paradoxical agitation. Other drugs such as sedating antidepressants may be a useful option for depressed patients with insomnia, whereas some of the SSRI group of antidepressants are more stimulating and can increase insomnia and are not recommended as first-line treatment for insomnia in palliative care.

In the medically ill, it is recommended that medications should be prescribed at the lowest possible dose for the shortest amount of time and considered mainly in patients who are unable to participate in CBT-I, who still have symptoms despite participation in such treatments, or in select cases as an adjunct to CBT-I or as a short- term solution while waiting for CBT-I to take effect. This approach may not be feasible in patients with advanced disease, and these populations may require longer-term use and are unable to wait for CBT-I to take effect or may be unable to tolerate behavioral approaches given the number of sessions required depending on prognosis.

Little research has been conducted on the effectiveness of these drugs for insomnia in palliative care populations except in cancer. Sedating tricyclic antidepressants in lower doses that are recommended for depression have been used as adjuncts to treat insomnia in palliative care, but the daytime sedation and anticholinergic side effects can lead to adverse effects particularly in the elderly. Other medications such as trazadone may also be helpful to improve restorative sleep. Consensus recommendations to guide practice by the American Academy of Sleep Medicine (AASM) recommendations for prescribing medications for management recommend the following approach (Schutte-Rodin et al. 2008, p. 498).

- Short-intermediate-acting benzodiazepine receptor agonists (BZD or newer BzRAs) or

Table 7 Pharmacological agents recommended for insomnia

Agent	Type of agent	Dose (mg)	Onset of action-minutes/half-life hours	Effectiveness	Adverse effects/ caution
Recommended for treating sleep onset insomnia					
Eszopiclone (Lunesta)	BZD receptor antagonist	1–3 1 mg in elderly/ debilitated or hepatic impairment	10 minutes/ 5–7 hours	Doses of 2 mg and 3 mg reduced sleep latency by 14 minutes (SL), improved sleep quality (SQ)	Metallic taste in mouth, nausea and vomiting, dizziness, somnolence, rebound insomnia, low mood
Temazepam (Restoril)	BZD	7.5–30 7.5 mg elderly/ debilitated	30–60/8–15	Doses of 15 mg reduced SL by 37 minutes, small improvement in SQ	Somnolence, dizziness, hangover effect into next day, diarrhea
Ramelteon	Melatonin antagonist	8	45 minutes/ 2–5 hours	Doses of 8 mg reduced SL by 9 minutes; no improvement in SQ	Low mood (depression), anxiety, hallucinations, memory loss, nightmares, nausea and vomiting
Triazolam (Halcion)	BZD	0.125–0.25 0.125 in elderly/ debilitated	7–27 minutes/ 1 hour	Doses of 0.25 reduced SL by 9 minutes, improved SQ	Somnolence, dizziness, hangover effect into next day, diarrhea
Zaleplon (Sonata)	BZD receptor antagonist	5–20 5 mg in elderly/ debilitated	30 minutes/ 1 hour	Doses of 5–10 mg reduced SL by 10 minutes. No improvement in SQ	Not suitable for long-term use in elderly, similar to other BZD
Zolpidem (Ambien)	BZD receptor antagonist	5–10 5 mg in elderly/ debilitated	7–27 minutes/ 2–3 hours	Doses of 10 mg reduced SL by 5–12 minutes	Somnolence, fatigue, drugged state
Recommended for treating sleep maintenance insomnia					
Doxepin	Heterocyclic	3–6	3.5 hours/ 15 hours	Doses of 3 and 6 mg improved total sleep time 26–32 minutes longer, WASO reduced by 22 minutes, small improvement in SQ	Drowsiness, dizziness, dry mouth, blurred vision, constipation, or trouble urinating, sedating effects
Eszopiclone	BZD	1–3	10 minutes/ 5–7 hours	Doses of 15 mg improved total sleep time by 28–57 minutes, increased total sleep time, WASO not reported, small improvement in quality of sleep	Metallic taste in mouth, nausea and vomiting, dizziness, somnolence, rebound insomnia, low mood
Temazapam (Restoril)	BZD	7.5–30	30–60/8–15	Doses of 15 mg reduced SL by 37 minutes, small improvement in SQ	Somnolence, dizziness, hangover effect into next day, diarrhea
Suvorexant	Orexin receptor antagonist	5–20	60 minutes/ 12 hours	Doses of 10 to 20 mg improved total sleep time by 10 minutes, reduced WASO by 16–28 minutes, SQ not reported	Based on trials of 10–20 mg doses. Not used for narcolepsy. Hepatic insufficiency
Zolpidem	BZD receptor antagonist	5–10	7–27 minutes/ 2–3 hours	Doses of 10 mg improved total sleep time by 29 minutes, WASO reduction of 25 minutes, moderate improvement in SQ	Somnolence, fatigue, drugged state

References: Sateia et al. (2017), Schutte and Rodin (2008)

ramelteon: examples of these medications include zolpidem, eszopiclone, zaleplon, and temazepam.
- Alternate short-intermediate-acting BzRAs or ramelteon if the initial agent has been unsuccessful.
- Sedating antidepressants, especially when used in conjunction with treating comorbid depression/anxiety: examples of these include trazodone, amitriptyline, doxepin, and mirtazapine.
- Combined BzRA or ramelteon and sedating antidepressant.
- Other sedating agents: examples include antiepilepsy medications (gabapentin, tiagabine) and atypical antipsychotics (quetiapine and olanzapine). May only be suitable for patients with comorbid insomnia who would benefit from the primary action of these drugs.

Several factors should be considered in the use of medications for insomnia in palliative care specifically the differential diagnosis and etiology of sleep disturbance, short- and long-term effectiveness of the drug, its rate of absorption and metabolism, and potential risks and side effects. The elderly and seriously ill patients may be particularly at risk for adverse effects given the alterations in drug sensitivity and pharmacokinetics, and this must be taken into consideration in prescribing and weighing of the benefit to risks. Other drugs recommended in guidance documents for management of insomnia include hypnotic drugs such as lorazepam, temazapam, and zopiclone, but these should be used with caution particularly in combination with other medications (Davis and Goforth 2014). Discontinuation and rebound insomnia must be considered when pharmacological agents such as benzodiazepines such as lorazepam are discontinued.

When pharmacotherapy is utilized, the choice of a specific pharmacological agent within a class should be directed by (1) symptom pattern; (2) causative factors; (3) patient age, illness severity, and prognosis; (4) treatment goals; (5) past treatment responses; (6) patient preference; (7) cost; (8) availability of other treatments; (9) comorbid conditions; (10) contraindications; (11) concurrent medication or treatment interactions; and (12) side effects (Matheson and Hainer 2017). Additionally, absorption, time to maximum concentration, elimination half-life, receptor activity, ability to cross the blood-brain barrier, dose and frequency, and short-acting versus long-term formulation.

A goal of pharmacologic treatment is to achieve a favorable balance between therapeutic effects and potential adverse effects; and the use of one drug that may have a crossover effect for managing other palliative care symptoms such as psychological distress is an important principle. Pharmacological agents for patients with insomnia comorbid with other illnesses must consider the concomitant use of these agents with agents being used for disease management, as well as the type of condition (e.g., involvement of the central nervous system may preclude their use and aggravate insomnia). A large review of Cochrane Database of Systematic Reviews corresponding to 274 RCTs examined the effects of 109 drug and condition pairs and identified five drugs that were associated with a decrease in sleep disturbance including budesonide (inhaled corticosteroid), triazolam (benzodiazepine hypnotic), olanzapine (atypical antipsychotic), sulfasalazine (anti-inflammatory), and zopiclone (non-benzodiazepine hypnotic) with ORs of 0.50 or less (Doufas et al. 2017). Whereas many other drugs were associated with increased sleep disturbance or adverse effects, few of these were concordant with descriptions of adverse effects on sleep in drug formularies.

9 Management of Specific Sleep Disorders

Sleep disorders such as obstructive sleep apnea, restless leg syndromes, or narcolepsy require referral and management to sleep specialists and are beyond the scope of this chapter. Patients with advanced disease can have a single primary (premorbid) insomnia or other sleep disorder or secondary insomnia due to their medical or psychiatric condition. Common sleep disorders in

palliative care populations include hypersomnia, circadian rhythm disorder such as sleep-wake reversal or inversion of sleep-wake cycles, and nightmares. The characteristics of these disorders and strategies for management are described below. Sleep disorders are best managed in consultation with sleep specialists with strategies tailored to the specific sleep disturbance and causative factors.

Hypersomnia Hypersomnia (also labeled somnolence) is a neurological disorder and type of circadian rhythm disturbance that results in an abnormal increase in sleep duration (10 or more hours at a time) and difficulty staying awake during the day that is not relieved by daytime napping (Reynolds and O'Hara 2013). Hypersomnia is also characterized by symptoms of excessive daytime sleepiness, excessive amounts of deep sleep, trouble staying awake during the day, and sundowning which refers to agitation or a delirium-like state (wandering, agitation, aggression) mainly at night and is related to changes either in NREM or REM sleep or could be more central in origin. Hypersomnia can be due to brain and central nervous system tumors, cancer that has spread to the brain or other organs, and has been associated with some types of chemotherapy or radiotherapy (Berger 2009). Hypersomnia is frequently seen in elderly patients with Parkinson disease (PD), Lewy body dementia (DLB), or Parkinson disease dementia (PDD) and dementia (Weldemichael and Grossberg 2010).

Pain medications, anti-nausea medications and some antidepressants, sedatives and sleeping pills, and other medications to control agitation at night can also cause hypersomnia. Fluid and electrolyte disturbances (hypokalemia, hypothyroidism, or hypercalcemia) and hormonal disturbances in the endocrine system or superimposed delirium may also be causative factors. In addition, the use of anticonvulsants and anticholinergic drugs such as antihistamines, antidiarrheals, and drugs used to reduce bladder irritability can cause daytime sedation and sleepiness. Behavioral problems such as lack of participation in stimulating daytime activities can also lead to daytime sleepiness, and at times caregivers may promote daytime sleeping to ease the burden of caregiving.

Recommendations for measurement of hypersomnia include the Epworth Sleepiness Scale (Johns 1991) and the Stanford Sleepiness Scale (SSS) (Maclean et al. 1992) as subjective measures of sleepiness alongside PROMs for evaluating changes in insomnia parameters. Additionally, a complete medical examination and full evaluation for potential disorders such as sleep apnea should be excluded in the differential diagnosis.

Management of this condition may include adjustment in medications to reduce their toxic effects or interactions, behavioral/environmental approaches including sleep hygiene behaviors, and increase in physical activity or daytime activities. Pharmacological approaches are considered as a last resort and medications such as trazadone, zolpidem, mirtazapine; and the use of specific agents for behavioral dyscontrol such as carbamazepine or risperidone or mediations such as methylphenidate for excessive daytime sleepiness may be helpful but may be associated with other adverse effects and used with caution (Ouslander et al. 2006). Psychostimulants such as modafinil have proved clinically useful in the treatment of narcolepsy and other causes of excessive daytime sleepiness, such as idiopathic hypersomnolence (Ballon and Feifel 2006).

Caregiver burden should be carefully assessed with referral to home care resources or respite care in the context of hypersomnia and other sleep disturbances.

Nightmares Several studies have reported a significant relationship between nightmare frequency and sleep disturbances including insomnia, sleep onset latency, frequent nighttime awakenings, and restless or fitful sleep in adult populations (Hansen et al. 2013). Drugs which alter the normal synaptic activity of serotonin, norepinephrine, and dopamine may lead to nightmares. Opioids, beta-blockers, levodopa, ketamine, and BZDs have been found to the associated with nightmares. Nightmares typically occur during the first hours of stage 3–4 non-rapid eye movement (NREM) sleep and are differentiated from night terrors, which is a

type of primary sleep disorder that causes feelings of terror or dread and inconsolability like the experience of patients during a panic attack (Hochenbury and Hochenbury 2010).

Nightmares or disturbing dreams are reported in about a third of patients at the end-of-life and may occur independent of opioid analgesics (Davies et al. 2017).

Nightmares are often a symptom of trying to work through unresolved feelings and fears in palliative care. Nightmares may also be a symptom of post-traumatic disorders (Krakow and Zadra 2006). Nightmares occur as an outcome of almost any traumatic experience, and frequent nightmares are also reported by a sizable proportion of individuals without a trauma history. Nightmares are characterized by repeated awakenings, usually from late-night REM sleep, with clear recall of frightening dream content. On awakening from the disturbing dream, the person is quickly alert with little to no confusion or disorientation. The newer ICSD-3 criteria specify that although nightmares usually involve fear or anxiety, other dysphoric emotions may be implicated. The DSM-5 explicitly states that nightmares must cause "clinically significant distress or impairment in social, occupational, or other important areas of function" to be classified as a sleep disorder (DSM-3; ICSD-5).

In addition to adjustment of medications and attention to other causative factors that may be contributing to nightmares, simple behavioral measures such as sleep hygiene may be helpful in reducing the frequency of bad dreams alongside strategies such as mindfulness or imagery to promote more positive images prior to sleep.

Management of nightmares focuses on nightmares either as a learned sleep disorder or a learned behavior or considers nightmares as a symptom of a damaged imagery system. Sleep disturbance and nightmares are often associated with post-traumatic stress disorder, and mixed findings have been shown for CBT with reduction in nightmares noted (Krakow and Zadra 2014). Cognitive behavioral therapies, nightmare-focused CBT, desensitization, imagery rehearsal, and relaxation techniques have been reported as beneficial; however, large prospective studies are lacking (Krakow and Zadra 2014). The feasibility and efficacy of these approaches in palliative care has not been established, and the time required for these types of therapy to manage nightmares (8–9 hours of contact time) is substantive and must be taken into consideration. Medications such as Prazosin or propranolol have also been shown to be helpful for nightmares in PTSD (Krakow and Zadra 2014). Referral for psychotherapy should also be considered for treatment of PTSD, and treatment should be primarily aimed at managing psychological distress or psychiatric conditions such as PTSD.

Sleep-Wake Cycle Reversal Sleep-wake cycle reversal also called sleep-wake inversion is considered as sleep disorder that is characterized by involuntary reversal of sleeping tendencies, whereby patients exchange diurnal habits for nocturnal habits such that they are active at night and sleep during the day (Fitzgerald et al. 2017). The main reason for the alteration in sleep-wake cycle is related to alterations in the suprachiasmatic nucleus (SCN) and melatonin secretion.

Disturbances in the sleep-wake cycle are common in older medical inpatients with dementia and/or delirium and can be exacerbated by stress and psychiatric disorders such as depression that can impact on the circadian timing system, but the relationships between these conditions are not fully clarified. Disturbances in the sleep-wake rhythm are a hallmark symptom of depression and widely appreciated as a key symptom of delirium (Ryan et al. 2013).

Management of sleep-wake cycle reversal includes altering medications that may trigger this sleep disorder, behavioral treatment such as good sleep hygiene, incremental and gradual changes in sleep and wake times if appropriate, manipulation of the environment to promote circadian rhythms timed to external light and dark, and optimizing management of psychological distress and screening for delirium or other sleep disorders such as OSA. Exposure to bright light during the day and physical activity or other stimulating activities may be helpful. Pharmacological

treatment may be required. Light therapy has also been suggested as an option.

9.1 Conclusion and Summary

Sleep disturbance and sleep disorders such as insomnia and insomnia syndrome are common in palliative care populations with serious consequences on daytime functioning, quality of daily living, and overall quality of life. Early identification of sleep disturbance through routine screening in palliative care followed by more comprehensive evaluation is essential as this symptom is often poorly managed in clinical care. Palliative care patients may have a combination of a primary sleep disorder and comorbid insomnia with multiple causative factors including pain and psychological distress. Treatment should include identification of the specific sleep disorder and use of appropriate strategies in consultation with sleep specialists.

Simple strategies such as sleep hygiene may be helpful for improving sleep disturbances as part of a supportive care approach, but the strongest evidence for efficacy has been found for CBT-I for insomnia which may require adaptation for administration in palliative care. A combination of psychological and pharmacological interventions will likely be necessary to manage the multifactorial nature of sleep disruption in palliative care. The adage of using one medication to manage many symptoms in palliative care may be particularly relevant since insomnia is usually interrelated to other symptoms such as pain and psychological distress as part of a symptom cluster. Additionally, optimizing management of other symptoms may be helpful for reducing disruptions in sleep. The efficacy of medications to manage insomnia is not well established, particularly in advanced disease populations. Moreover, the harms of medications to treat insomnia may outweigh the benefits, and this must be considered in the context of palliative care. Considerations for pharmacological treatment include the nature of the insomnia; the expected duration of treatment; the potential side effects; the possibility for reactions with other medications, i.e., disease treatment or other symptom management medications; and the impact on daytime functioning and patient tolerance as well as prognosis. Insomnia and other sleep disorders are a serious symptom in palliative care that warrant impeccable assessment and management with treatment approaches tailored to the individual, causative factors and the specific sleep disorder that is identified such as insomnia, hypersomnia, sleep-wake reversal, and nightmares in the population. Sleep disturbances can worsen symptom burden and distress and the potential suffering for both palliative care patients and their caregivers. Thus, appropriate treatment of this neglected symptom is critical to reduce morbidity and maximize quality of life.

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Psychological Symptoms

25

Gregory B. Crawford

Contents

Abstract

Psychological symptoms are highly prevalent in people requiring palliative care. They are much more challenging to elicit, and more controversy exists about what is normal and what might require intervention than physical symptoms. There are significant issues in determining what is normal and what is not. Sadness, distress, anxiety, and depression can coexist and require careful assessment.

Management of psychological symptoms and conditions can broadly be considered in terms of non-pharmacological and pharmacological therapies, "the talking and the drug therapies." These are not mutually exclusive, and for people with limited energy, failing cognition, and limited time, some pragmatic decisions may be necessary. To be distressed and immobilized by emotion is not normal. Depression is not a normal part of dying. There should be discussion about the nature of psychological issues and conditions,

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_21

explanation of common somatic symptoms, and a plan for intervention and support.

The burden on the carer, both professional and personal, in such situations should not be underestimated.

1 Psychological Symptoms

Symptom control is a significant part of the healthcare interventions provided by clinicians for people facing the end of their lives. Physical symptoms are generally well recognized and have a considerable prevalence (e.g., lack of energy (73.4%), pain (63.1%), nausea (44.7%), lack of appetite (44.5%), constipation (33.6%), cough (29.4%), and shortness of breath (22.9%)) (Portnoy et al. 1994). Psychological symptoms are much more challenging to elicit, and more controversy exists about what is normal and what might require intervention. Symptoms such as anxiety and depression may not be as easily acknowledged, diagnosed, or treated by patients, carers, or healthcare providers (Derogatis et al. 1983; Razavi et al. 1990; Barraclough 1997; Dein 2000; Henderson et al. 2000; Gilbody et al. 2001). For many the label of a "psychiatric" or "mental health" issue carries a strong stigma. Some would see serious risks associated with "unnecessary pathologizing" what are possibly normal reactions (Parker et al. 2012). This can inhibit full assessment and the consideration and implementation of appropriate interventions to provide relief.

2 What Is Normal: Sadness, Distress, Anxiety, and Depression

The diagnosis of an incurable illness is associated with an expected emotional response to the loss of well-being and to a potentially limited and altered future. Sadness, tearfulness, altered sleep, and change in appetite and eating habits are a normal response to receipt of this information and the impending loss it conveys (Zisook and Shear 2009). These symptoms constitute a grief reaction (Kübler-Ross 1969; Periyakoil 2015; Grunfeld et al. 2004). The symptoms of grief and sadness, as responses to such a situation, can be seen to be on a continuum with those of an anxiety and major depressive illness. Depression is not necessarily the inevitable response to such a situation. This raises the dilemma of defining thresholds (Chochinov et al. 1994; Robinson and Crawford 2005) at which a diagnosis is made and what might be considered to be the "normal" reaction to considering the possible end of one's own life. Emotions to death and dying and reactions to such information are modified by personal beliefs and cultural factors, particularly relating to what a person might believe occurs after they die. There are cross-cultural and historical attitudes to such complex issues including belief in an afterlife with perhaps heaven and hell, to a nihilism or sense of nothingness. Kübler-Ross introduced the concept of different types of depression – a reactive and a preparatory depression – the latter being seen as a normal part of the dying process and something that should not be interrupted (Kübler-Ross 1969). She believed that "an understanding person will have no difficulty in eliciting the cause [of the depression]." This is not as easy as she has suggested but may help to explain why some clinicians feel inhibited or may fail to intervene in distress, anxiety, or depression or even to assess systematically for psychological symptoms.

3 The Person Experience

It is always useful for healthcare providers to try to put themselves in the shoes of their patients or clients. It is all too easy to forget how foreign the environments are that we work within and how vulnerable our patients are. Not only are they being given bad news and potentially life-threatening information, but there are larger issues to consider. Not only are people trying to understand the problem and ask the obvious questions about what might be done to cure, control, or modify the process, but there are physical symptoms to manage and changes in body function. There are multiple demands for healthcare appointments and relationships to navigate with multiple providers.

The need for information, clear communication, and a sense of some control in what feels like the uncontrollable all are aspects of the experience for most.

It is not surprising that there will be impacts on work and leisure. There will be disruption of home, social, and financial arrangements. There are going to be changing roles and functions within the family. And in all of this most will be dealing with the understandable fear of loss of role, function, purpose, and death. And most would wish to maintain or find a new sense of meaning and purpose in life.

4 Distress

Psychological issues may present in many ways. Some people may express distress, depression, or anxiety in terms of unrelieved physical symptoms rather than emotion. It may be that there is only limited mild intermittent distress, or it may be a severe persistent distress that can become an overwhelming anxiety (National Comprehensive Cancer Network 2003). And there are questions about whether anxiety leads to depression or vice versa. And it is reasonable to consider that these issues are not simply binary, i.e., both can coexist and feed into the expression of psychological distress and vary over time. Exploring a person's experience of their illness and understanding the context and meaning ascribed to that illness and the physical, social, emotional, and spiritual influences and components of their distress are all vital to more fully assess and understand the person's experience (Clayton et al. 2007).

5 Demoralization

Within palliative care literature, demoralization as a syndrome has been proposed by Kissane et al. (2001) as having core features of hopelessness, loss of meaning, and existential distress. It is believed that this syndrome can be differentiated from depression and is recognizable in people facing the end of their lives. It is associated with chronic medical illness, disability, bodily disfigurement, fear of loss of dignity, social isolation, and feelings of greater dependency on others or the perception of being a burden.

Because of a sense of helplessness, those with the syndrome are thought to progress to a desire to die or to commit suicide. Treatment is aimed at relieving or alleviating the distress caused by this syndrome. The *Cambridge Dictionary* (Cambridge University Press 2018) describes demoralization as "having lost your confidence, enthusiasm, and hope" and also suggests feelings of sadness and unhappiness. Some alternative words and phrases have included "being down in the dumps, doleful, downhearted, miserable, morose and feeling wretched." These are powerful words and feelings.

6 Anxiety

Anxiety is a feeling of worry, nervousness, or unease about something with an uncertain outcome often with an associated strong concern that something unpleasant might happen (CareSearch 2017). For people facing the end of their lives, it would seem entirely reasonable that there is a fear or threat of separation and loss. It is common to hear people voice fears not only about death but also about the dying process, the manner of dying, the course of the illness, and the impact on their family. It is important to ask about suicidal thoughts or impulses in a patient experiencing significant anxiety or depressive symptoms (Hudson et al. 2006). Anxiety can accompany a depressive disorder.

The challenge is to be able to broach these difficult but important conversations. This requires a willingness to ask questions, to make connection, to have advanced communication skills, and be willing to listen. Some possible opening questions might be, "What do you feel about everything that is happening to you?"; "You seem (upset/anxious/depressed) today. Would you like to talk about how things are going?"

A full assessment requires specific questions about anxiety, depression, and likely symptoms. An exploration of physical symptoms such as palpitations, nausea, dizziness, shortness of

breath, trembling, sweating, and diarrhea is useful. Psychological symptoms may include feelings of apprehension, fear, and dread. You should also consider treatment-related factors; drug-induced anxiety; drug withdrawal including alcohol, tobacco, and other drugs; and disease-related factors, such as poor control of pain, nausea, dyspnea, and hypoxia (Palliative Care Expert Group et al. 2016).

It is important to assess for a depressive disorder as this may be the underlying condition when anxiety is severe, and it does not respond to supportive measures.

7 Depression

Depression is a major health issue in Australia (Wilhelm et al. 2003). There is a growing body of research about depression in palliative care populations and concern that it is a difficult and not particularly well-managed problem. This may relate to the inherent nature of depression but is possibly compounded by the difficulties of assessment and management in palliative populations, a group of people with many physical symptoms and the added burden of the existential issues associated with anticipating the end of life.

Depression has a significant and often unseen impact on the well-being and quality of life (Grassi et al. 1996; Goldney et al. 2000; Ruo et al. 2003; Smith et al. 2003) of the people it affects and on those around them. However, the construct and definition of depression is difficult. It is poorly understood. The general public and even health professionals may have quite different and divergent concepts, understandings, and beliefs about what depression is (Ng et al. 2013, 2015, 2014). The general public may consider crying, feeling sad, being melancholic, or feeling "upset" or "down and blue" to be depression. Palliative care professionals are often untrained in psychological health assessment and management. They are likely to have varied and possibly inaccurate concepts about psychological illness. A mental health professional diagnosis of a major depressive illness requires a constellation of specific symptoms that may include feelings of sadness and feeling "down and blue" that are pervasive and persistent (World Health Organization 1993; American Psychiatric Association 2013). Symptoms are on a spectrum of severity and can extend to a psychotic illness with loss of contact with reality and with loss of hope for the present or the future. Even the diagnostic systems proposed by specialist psychological authorities vary in the symptom constructs that are described to make a diagnosis, and the instructions and advice offered may be difficult to interpret and implement.

Depression is a prevalent problem in our society (Chochinov et al. 1994; Hotopf et al. 2002; Lloyd-Williams and Riddleston 2002; Durkin et al. 2003; Meyer et al. 2003). Depression is poorly recognized and poorly treated (Lloyd-Williams 1999; Wilson et al. 2000; Durkin et al. 2003; Lloyd-Williams et al. 2003a, b) within palliative care patients, causing increased suffering and hardship for these patients and their carers and families. Physical symptom control can be much more difficult to achieve in these patients (Dinan 1999). Carers' ability to support their depressed family member or friend may be diminished, at a time when there may be very little pleasure remaining in their lives. Interaction with and assistance from healthcare providers can be impeded, resulting in poorer health outcomes (Spiegel 1996; DiMatteo et al. 2000; Passik et al. 2002; Kelly et al. 2003; Lin et al. 2003). Depressed patients are less likely to attend appointments (DiMatteo et al. 2000). They are likely to feel bad about themselves and to make people around them feel uncomfortable, further perpetuating their isolation. They are more likely to be seen as "bad" or "difficult" patients, further reinforcing these negative feelings.

In Australia, the current 1-month prevalence of major depression in the general population is 3–5% (Wilhelm et al. 2003). This is similar to the reported prevalence in the United States and the United Kingdom (Wilhelm et al. 2003). Depression is reported to be more common in the unemployed, smokers, and those having a medical condition (Breitbart et al. 1995; Block 2000) as well as being in midlife (Fredman et al. 1988; Sorenson et al. 1991; Blazer et al. 1994), those previously married, and in females

Table 1 Comparison of symptoms assessed by DSM-5 and ICD-10

DSM-5		ICD-10	
Need one of these	Depressed affect	Depressed affect	Need two of these
	Anhedonia	Anhedonia	
Need four of these symptoms	Fatigue	Fatigue	
	Weight loss or change in appetite	Change in appetite	Need four of these symptoms
	Insomnia or hypersomnia	Sleep disturbance	
	Psychomotor agitation or retardation	Psychomotor agitation or retardation	
	Worthlessness or guilt	Guilt	
	Concentration problems or indecisiveness	Concentration or thinking problems	
	Recurrent thoughts of death or suicide ideation	Recurrent thoughts of death or suicide	

(Goldberg and Huxley 1992; Weissman et al. 1996). Depression is predicted to be one of the leading contributors to the burden of disease into the future (Murray and Lopez 1996).

In the medically unwell, the assessment of depression is more problematic, and the prevalence is much more difficult to determine. In a systematic review of the prevalence of depression in patients with advanced disease, particularly advanced cancer, and among mixed hospice populations, i.e., palliative care populations, Hotopf et al. (2002) found that depression was a common problem; however, the quality of research was poor. The prevalence of depression varied between 1% and 50%. This variation is likely to be because of small sample size, and large attrition and exclusion rates, due to deteriorating physical and mental function and death and different definitions for making a diagnosis of depression. Many studies provided limited information about participants including demographic and clinical details and failed to provide "any data on the extent or severity of the participants' disease and their survival." The generally agreed prevalence of depression in the medically unwell and in palliative care populations is 25% (Barraclough 1999). Depression in this population is greater in the young (Blazer et al. 1994) and in some particular diseases (e.g., carcinoma of the pancreas) (Holland et al. 1986). There have been studies of the interaction between asthma and diabetes with depression, showing that with increased physical symptoms there is also an increase in depression (Goldney et al. 2003, 2004).

There are accepted systems for classifying the symptoms and signs required to make a diagnosis of depression (World Health Organization 1993; American Psychiatric Association 2013). There is however no single universally agreed system to confirm such a diagnosis and no one objective measure. The "gold standard" for making a diagnosis remains a systematic, structured clinical interview followed by the judgment of a mental health professional. The two widely accepted classifications of mental illnesses are the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) of the American Psychiatric Association (2013) and the *International Classification of Diseases* (ICD) developed by the World Health Organization (1993). Many of the symptoms that might be considered may be on the continuum from normal variation to a clinical disease or condition. There is also possible overlap of symptom criteria with other known physical and psychological diseases and conditions. The diagnostic process requires the patient to have the physical, mental, and psychological capability to participate. There are clearly potential and real barriers to the assessment and diagnosis of depression, particularly in terminal illness. See Table 1.

A DSM-5 diagnosis of a major depressive episode requires that five symptoms, which may include both psychological and somatic symptoms, be present during the same period and that one of these is either depressed affect or

anhedonia (American Psychiatric Association 2013). DSM-5 diagnostic criteria for a major depressive episode include somatic symptoms that are common among medically ill patients, such as fatigue, change in weight, altered sleep patterns, and concentration. These somatic symptoms of depression may overlap with the symptoms of many medical illnesses. DSM-5 instructs doctors to exclude potential somatic symptoms of depression "when they are clearly attributable to another medical condition" (American Psychiatric Association 2013). But this advice creates practical problems (Peveler et al. 2006). For a population with a large number of "somatic symptoms," this instruction is not as easily translated into practice as might be suggested. It is often impossible to determine the etiology of symptoms. There is concern that including somatic symptoms of unknown etiology may lead to overdiagnosing depression (Ouslander 1982; Endicott 1984; Rapp and Vrana 1989; Kalichman et al. 2000). Alternatives to DSM-5 and ICD-10 classifications of depression have been proposed to differentiate depression from symptoms of a wide range of medical conditions, including cancer (Endicott 1984), Parkinson's disease (Marsh et al. 2006), dementia (Vida et al. 1994), chronic pain (Wilson et al. 2001) and generally for the elderly (Rapp and Vrana 1989; Gallo and Rabins 1999). They include three approaches: "etiological" (case-by-case or blanket exclusion from diagnostic criteria of symptoms judged likely to be due to medical illness or aging), "inclusive" (inclusion of all symptoms regardless of etiology), and "substitutive" (substitution of additional psychological symptoms for most or all somatic symptoms) (Endicott 1984; Cohen-Cole and Stoudemire 1987; Rapp and Vrana 1989; Kathol et al. 1990; Chochinov et al. 1994). Judging whether a symptom is "clearly and fully accounted for" by the patient's medical condition may be impractical.

Ellis et al. (2006) compared the two extreme approaches that do not require this judgment, i.e., the inclusion of somatic symptoms regardless of etiology (i.e., the DSM-5 guideline is ignored) and the exclusion of somatic symptoms which might be caused by the patient's medical condition or aging. Somatic symptoms regardless of their etiology did not adversely affect the identification of patients who showed evidence of psychological distress warranting follow-up. In contrast, the exclusion of somatic symptoms potentially due to disease or aging led to underrecognition of psychological distress (Ellis et al. 2006). Suggestions that somatic symptoms be excluded or substituted when assessing older and medically ill adults (Yesavage et al. 1982–1983; Bukberg et al. 1984; Rapp and Vrana 1989) were not supported. Whether somatic symptoms should be included, treated in a specific way, or be excluded is still unclear, and ultimately the decision must be left to the clinician and the individual situation.

There are barriers to effective management of depression in palliative care: recognition and diagnostic and treatment barriers related to patients, clinicians, and healthcare systems (Goldman et al. 1999). Patients create an important barrier to the recognition of depression by their failure to disclose psychological distress (Hinton 1994). Reasons may include a belief that talk about emotions is a waste of doctors' time (Maguire 1985), that they are responsible for their own distress (Maguire and Howell 1995), and that depression is too common to be noteworthy (Endicott 1984) and patient "stoicism" (Endicott 1984). Indeed, patients may actively deny their psychological distress in order to avoid the stigma associated with psychological disorders, because they believe depression is a sign of weakness, to avoid causing additional worry to their families, or because they fear being seen as ungrateful for the efforts of their family and clinicians (Endicott 1984). Patient disclosure is also influenced by clinicians' conscious or unconscious use of tactics that limit the expression of emotional distress (Maguire 1985).

Clinicians also directly contribute several barriers to the recognition and diagnosis of depression. Clinicians may have low motivation to identify patients with depression (Wilson et al. 2000). Depression can be difficult to detect accurately. It is a syndromic disorder: no biological markers can be used to identify it. Diagnosis relies on emotions, behaviors, and cognitions that overlap those reported by patients with

other psychological disorders and patients with no psychological disorder. As a result, it is known that symptoms of depression may not be recognized accurately by day care staff (McIntyre 1982), nurses (McDonald et al. 1999; Passik et al. 2000; Meyer et al. 2003; Pautex et al. 2003), or doctors (Passik et al. 1998, 2000; Durkin et al. 2003; Pautex et al. 2003) who do not have specialist mental health training. Nurses recruited to palliative care services are rarely required to have mental health training, and their continuing education generally fails to focus on these issues (Lloyd-Williams and Payne 2003).

8 Assessment

A careful and considered history is always the first step in assessment (Butow et al. 2015). The clinician should not be frightened of asking difficult questions. Not exploring a situation fully will lead to misunderstandings, assumptions, and ultimately poor management. A diagnosis of major depression is based on having a depressed mood that cannot be lightened; loss of pleasure or interest, even within the limitations of the illness; an excessive feeling of being a burden to others, accompanied by a sense of worthlessness or low self-esteem and of fearfulness and/or anxiety; and avoiding others or withdrawal. There may be brooding or excessive guilt and/or remorse, a pervasive sense of hopelessness or helplessness, a persistent desire for death, or suicidal ideation with prominent and persistent insomnia and excessive irritability.

Asking a person about their mood and exploring their thoughts including specifically asking about suicidal ideation or intent are not inherently dangerous. Indeed, it is indefensible to avoid these issues. It is unreasonable to fear that raising these issues might "give the person ideas." This is not true. It is important however to explore the person's thoughts about death and desire to actively end their life, the degree of planning, and access to means and intent to die (Hudson et al. 2006). Individual jurisdictions will have different thresholds and legal requirements for clinicians to ensure a person's safety. To deprive a person of their liberty is a serious responsibility, but at times this may be indicated and even more challenging when the person in consideration has a serious and potentially life-limiting illness.

There are many questionnaires and screening tools that have been proposed to assist in making the diagnosis of a psychological disorder or condition (Beck and Beck 1972; Chochinov et al. 1997; Kramer 1999; Hickie et al. 2001; Lloyd-Williams 2001; Akizuki et al. 2003; Arroll et al. 2003; Crawford and Robinson 2008). The gold standard is a structured clinical interview. Commonly used screening instruments may only be unidimensional considering "anxiety" as a single concept or "depression" or "depressed affect" such as using a visual analogue scale. That anxiety and depression are commonly coexistent is perhaps evidenced by the popularity of the Hospital Anxiety and Depression Scale (HADS) that is commonly used in clinical and research practice (Kramer 1999).

The impact of treatment-related factors; drug-induced depression; drug withdrawal including alcohol, tobacco, and other drugs (Passik and Theobald 2000); and disease-related factors, severe uncontrolled symptoms, or fear of symptoms such as pain should be part of the assessment. Important factors can include a past personal or family history of suicide attempt, cognitive problems (e.g., delirium), and any psychotic symptoms (e.g., hallucinations, delusions). An important part of the assessment should also include the person's level of isolation and social and family support.

9 Management

Management of psychological symptoms and conditions can broadly be considered in terms of non-pharmacological and pharmacological therapies, "the talking and the drug therapies." These are not mutually exclusive, and for people with limited energy, failing cognition, and limited time, some pragmatic decisions may be necessary.

The power of the clinician's and the clinical team's therapeutic relationship should never be underestimated (Marziali and Alexander 1991).

To provide clear information and explanation of what is happening physically and psychologically can be reassuring for many to assist in coping with the personal and social impact of disease. Supportive counselling and just being willing to explore the patient's distress, fears, and concerns and to promote a realistic hope should not be minimized. Dealing with physical symptoms and trying to address social and financial concerns can offer significant reduction of distress. Promoting communication with and support from others and by involving family and carers in care of the patient are useful strategies. Helping people to remember and gather the emotional resources that have sustained them through their lives before this crisis is a useful strategy for many. These are in essence attempts to try to reframe the situation and to consider strategies that assist in finding meaning and purpose.

Cognitive and other behavioral therapies can provide benefit (Coull and Morris 2011) but may not be readily accessible, or people may not have sufficient energy, time, and clear cognition to participate. Some of the nurturing therapies so well known in hospice care can provide a place of safety and relief as well. Life review and making meaning, whether in formal dignity therapy (Chochinov 2002), structured or informal biography services, or even reviewing the family photographs, may all be useful. Therapies to induce relaxation and some sense of peace should be considered. Some gain benefit with massage, aromatherapy, visualization, and music therapies (Hilliard 2001; Krout 2001; Demmer 2004; Kyle 2006; Ernst 2009).

Medication to moderate symptoms and to improve mood should be considered and if appropriate introduced early. Antidepressants have delay in maximum onset of therapeutic benefit. Many people are commenced on such medications when there is insufficient time to gain real and meaningful benefit (Lloyd-Williams et al. 1999). There is evidence that anything other than very short-term use of benzodiazepines is a useful strategy for the longer-term management of anxiety (Palliative Care Expert Group et al. 2016). Benzodiazepine medications with very short half-lives are particularly problematic particularly at the end of life. The clinical situation, the likely prognosis, and the intensity of the symptoms will all influence decisions. Antidepressants are likely to offer better long-term relief of anxiety. It is worth considering the full constellation of symptoms and trying to maximize benefit by employing medications that might assist other symptoms such as disturbed sleep and neuropathic pain. A trial of antidepressants for those with symptoms highly suggestive of a major depressive disorder should always be considered early. Choice about individual medicines will be guided by prescriber experience, confidence, route of administration, likely prognosis, and assessment of possible side effects and their likely impact on the person's quality of life.

And it can be argued that for the management of pain, most clinicians would initiate therapies even if there is incomplete understanding of the full etiology of the pathophysiology of the symptom. For psychological symptoms, it may be equally reasonable to commence interventions to assist in ameliorating the symptom, even in the absence of a full and clear diagnosis. The best way to support someone with a major psychological issue is to provide a coordinated interdisciplinary approach that is provided by professionals with different skills, working together to form a cohesive and consistent framework for the person and their family.

10 What Does It All Mean?

To be distressed and immobilized by emotion is not normal. Depression is not a normal part of dying. One must not ignore or avoid discussing these important issues, but help people to explore, if they wish, the meaning of what is happening and to assist in formulating a plan of support and intervention. To feel abandoned in such a situation would be unthinkable.

The management of psychological issues particularly for people facing the likely end of their life is complex. It may be quite daunting. But this should not allow any to avoid assessing and

commencing a therapeutic plan – be they inexperienced or experienced clinicians. Consider what resources are available within your network to provide advice, and consider what further assessment and interventions might be available to assist you and your patients.

It is important to try to provide continuity of care and emotional support, to understand the patient's concerns and needs and those of their family. There should be discussion about the nature of psychological issues and conditions, explanation of common somatic symptoms, and a plan for intervention and support. Medications are important but not the only "answer." Adverse effects on cognition, alertness, possibly mood, and behavior should be assessed. Antidepressants may assist both anxiety and depression, with or without judicious, short-term benzodiazepine use. If they are likely to provide benefit, then prescription is better earlier rather than later.

The burden on the carer, both professional and personal, in such situations should not be underestimated. Those providing personal care are likely to require extra support as well. Clinicians should not underestimate their own personal cost of supporting patients in these circumstances. The support of a team is useful and remembering to access the strategies for personal well-being is vital.

> Slowly, I learn about the importance of powerlessness. I experience it in my own life and live with it in my work. The secret is not to be afraid of it – not to run away. The dying know we are not God. . ..all they ask is that we do not desert them. (Cassidy 1991)

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Delirium

26

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_22

Abstract

This chapter outlines how health professionals may best prevent, recognize, assess, manage, and support people with palliative diagnoses who are at risk of delirium and their families, according to best evidence and the circumstances, needs, and wishes of the person. The chapter also presents evidence-practice gaps in delirium care in palliative contexts and briefly outlines future directions for research and clinical practice development.

1 Introduction

Delirium is a great source of suffering and perplexity for people receiving palliative care and the health professionals who care for them. The opportunities to appropriately respond to the needs of people with palliative diagnoses mirror other populations at risk of delirium; and there are similar challenges to delivering this care. Additional considerations relate to the burden, benefit, and goals of care in the context of living and dying with advanced illness.

Having optimal cognition, safety, and a sense of self and relationship with others at the end of life are highly valued by seriously ill people (Delgado-Guay et al. 2016; Spichiger 2008; Steinhauser et al. 2000). Equally, when a loved one has delirium, family carers want clinicians to give more information about what is happening and show respect and sensitivity for the person and their subjective experience (Namba et al. 2007; Brajtman 2003). Family feel supported when clinicians demonstrate respect and understanding of the person's needs and preferences and address suffering in ways which support them to communicate with each other (Bolton et al. 2016; Finucane et al. 2017).

This chapter outlines how health professionals can work to optimize care to achieve these important goals for people with palliative diagnoses and their families. Best evidence for delirium prevention, recognition, assessment, management, and support for people with advanced illness is presented. Where evidence is lacking for this population, we present evidence, guidelines, and standards for optimal delirium care of older hospitalized patients. We advocate for nuanced approaches to delirium care that are based on the individual needs and wishes of the person and informed by the intent of palliative care to prevent, recognize, and impeccably assess distressing symptoms and to relieve suffering. Ethical dilemmas, complexities, and uncertainties that clinicians and teams may encounter when caring for delirious people and their families in the last months, weeks, and days of life are discussed. Lastly, we propose how delirium outcomes for people receiving palliative care may be improved through research and clinical practice development.

2 Phenomenology

Delirium is an acute neurocognitive disorder, medical emergency, and serious healthcare complication. Delirium arises from physiological disturbances related to a medical condition, substance intoxication or withdrawal, and/or a toxin and manifests as acute disturbances to attention, awareness, and cognition (American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) 2013). Disturbances present variously in each patient, each delirium, and even during the course of one episode (Meagher et al. 2012a).

Cognitive changes include memory deficit; disorientation to time, place, and/or person; language and visuospatial disabilities; and perceptual disturbances, such as illusions, hallucinations, or delusions. Perceptual disturbances are almost always frightening for the person experiencing them, and this fear may cause him or her to become withdrawn, suspicious, and/or aggressive toward others, including family and clinicians (Breitbart and Alici 2008). Labile mood and altered sleep-wake cycle frequently occur but are not required for a diagnosis (Meagher et al. 2011). The intensity of delirium symptoms may range from mild to severe; and episodes may be brief (i.e., last for hours to days) or sometimes continue for weeks, even months (American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) 2013).

2.1 Diagnostic Criteria

Delirium was first included within the American Psychiatric Association Diagnostic and Statistical Manual (APA-DSM) in 1980. There have since been five iterations of delirium diagnostic criteria, reflecting evolving understanding of core features. Current criteria are:

1. Disturbed attention (i.e., reduced ability to focus, sustain, or shift attention) and awareness (reduced orientation to the environment).
2. Disturbance developed over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of the day.
3. An additional disturbance in cognition, e.g., memory deficit, disorientation, language, visuospatial ability, or perception.
4. The disturbances in criteria A and C are not better explained by another pre-existing, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.
5. Evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication, or withdrawal (i.e., due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies (American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) 2013).

While classified as one disorder, delirium is further categorized as three subtypes according to the level of psychomotor activity:

(i) Hyperactive delirium: increased motor activity, agitation, and heightened states of arousal
(ii) Hypoactive delirium: decreased motor activity, delayed response, and drowsiness
(iii) Mixed delirium: fluctuation between hyperactive and hypoactive states in the 24-h period (American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), 2013; Gupta et al. 2008)

Whereas in a study of patients receiving palliative care, a small proportion (6%) experienced no particular subtype, and around 40% experienced a varied subtype, across the course of a delirium episode (Meagher et al. 2011).

3 Pathophysiology

The understanding of the pathophysiology of delirium is evolving. Hypotheses include those that primarily are theoretical and others that are being empirically investigated. The main theoretical models are as follows:

Neuronal Ageing: This model proposes that, with aging, central nervous system (CNS) immune cells undergo excessive production of pro-inflammatory cytokines in response to peripheral stimulation, providing a possible pathway for CNS dysfunction and consequent delirium. According to this model, elderly patients are

more at risk of developing delirium, because of age-related cerebral changes in stress-regulating pathways (Maldonado 2008, 2013).

Oxidative stress: In which physiologic insults, such as tissue damage, trauma, hypoxia, severe illness, and infections, cause decreased oxidative metabolism, leading to cerebral dysfunction with associated cognitive decline and behavioral symptoms seen in people with delirium (Berr 2000).

Neurotransmitter: Relates to deficits in central cholinergic functioning. This hypothesis suggests that excess release of dopamine, glutamate, and acetylcholine (Ach), as well as altered levels of serotonergic and gamma-aminobutyric acid (GABA) activity, may underlie clinical presentations of delirium (Maldonado 2008, 2013). It has further been proposed that decreased tryptophan and increased melatonin may result in decreased serotonin in people with delirium (Van Der Mast et al. 1991; Karlidag et al. 2006).

Circadian cycle: Disruptions to the 24-h circadian cycle and usual sleep-wake cycle have long been linked to development of delirium. This hypothesis suggests that alterations in the metabolism of melatonin (a hormone involved in the regulation of the sleep-wake cycle) may also play a role in the development of delirium (Maldonado 2008, 2013).

Neuroendocrine model: Suggests that sustained high levels of glucocorticoid levels occurring with acute stress can impair neurons in the brain and in turn may trigger and/or sustain delirium (Maldonado 2013; Olsson 1999).

The models with developing empirical evidence are

Neuroinflammatory: Altered neurotransmitter levels are commonly implicated in delirium. Higher serum levels of interleukin (IL)-6 and IL-8 (Van Munster et al. 2008) and raised S100 calcium-binding protein B (S100B) (van Munster et al. 2010) have been reported in people with delirium. Low levels of anti-inflammatory markers, such as insulin-like growth factor 1, are also reported (Adamis et al. 2009). As these studies report no correlation with clinical outcomes, with the exception of cognitive changes during delirium, it is therefore difficult to ascertain whether the altered levels are etiological or simply an epiphenomena (Caplan et al. 2010).

Glucose metabolism hypotheses: Lower cerebrospinal fluid (CSF) neuron-specific enolase (NSE) and higher CSF lactate are reported in people with delirium, suggesting the following hypotheses: (1) disrupted glycolysis, with switching from aerobic to anaerobic glucose metabolism by neuronal cells; (2) suppression of the glycolytic pathway in neurons; or (3) disrupted lactate uptake by neuronal cells (Caplan et al. 2010). Recent research further revealed widespread reduction in glucose metabolism in older inpatients with delirium and levels returning to baseline following delirium resolution (Haggstrom et al. 2017).

Most of these hypotheses are complementary and intersecting (Maldonado 2013). Ideally, further research into the complex neurochemical cascades leading to delirium will inform future development and testing of novel therapeutic approaches.

4 Epidemiology

4.1 Risk Factors

Epidemiological data indicates that people most at risk of developing delirium are those who are older, have advanced illness, and/or prior cognitive impairment (National Clinical Guideline Centre for Acute and Chronic Conditions 2010). Other predisposing factors are visual or hearing impairment, poor functional status, current hip fracture, and impaired nutrition. Yet any person – adult or child – can experience delirium when physiological insults are sufficiently great. Precipitants associated with illness, injury, and medical treatment are many and include (but are not limited to) polypharmacy, metabolic disturbance, presence of an indwelling catheter, dehydration, infection, and use of physical restraints. Additional precipitants related to advanced cancer are psychoactive medication (benzodiazepines, antipsychotics, and corticosteroids) and bone, liver, and brain metastases (Caraceni 2013) (Table 1). People receiving inpatient palliative care are

Table 1 Delirium risk factors

Predisposing factors	Precipitating factors	Additional risk factors in patients with cancer
Potentially modifiable • Sensory impairment (vision and hearing) • Diminished function/performance status • Malnutrition **Non-modifiable** • ≥65 years • Advanced illness • Prior cognitive impairment • Multiple comorbidities • Current hip fracture	**Potentially modifiable** • Polypharmacy • Anticholinergic load • Indwelling catheter • Use of physical restraints • Drug intoxication • Dehydration • Infection • Hypoxia • Pain • Anemia • Emotional stress • Prolonged hospital stay **Less modifiable** • Metabolic disturbance • Low albumin • Environment • Drug or alcohol withdrawal	**Potentially modifiable** • Benzodiazepines • Opioids • Corticosteroids • Other psychoactive medications **Non-modifiable** • Prior delirium • Bone metastases • Liver metastases • Hematological malignancies • Metastases to brain or meninges

National Clinical Guideline Centre for Acute and Chronic Conditions 2010, Caraceni 2013, Clinical Epidemiology and Health Service Evaluation Unit Melbourne Health 2006, Canadian Coalition for Seniors' Mental Health 2010, and Ahmed et al. 2014

likely to have multiple causes, up to as many as six (Meagher et al. 2011); a multimodal model of delirium risk proposes that predisposing and precipitating factors for delirium are cumulative (Inouye and Charpentier 1996).

4.2 Prevalence and Incidence

Delirium occurs frequently in palliative care contexts, where people are highly vulnerable through often having several predisposing and precipitating factors. Prevalence in studies conducted in adult palliative care units and hospices ranged from 13.3 to 42.3% at admission, 26% to 62% during admission, 58.8% in the weeks prior to death, and for almost all participants (88%) within six hours of death (Hosie et al. 2013; Rainsford et al. 2014). In the studies that screened participants at least once daily, incidence was 33–45%, compared to studies where daily screening did not take place (3–7%) (Hosie et al. 2013).

Hypoactive delirium is the most prevalent subtype, occurring in 68–86% of delirious inpatients in one study (Hosie et al. 2013) and in 58% in another of inpatients with advanced cancer (Uchida et al. 2015). Meagher et al. (2012b) reported a lower proportion of patients in a palliative care unit with hypoactive delirium (35%), likely because the study applied a different subtype categorization of motor behavior than that of the current APA-DSM 5 (American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) 2013) and these other studies.

There are no data on delirium prevalence or incidence in children receiving palliative care. A retrospective chart review of pediatric oncology admissions reported a 1-year incidence of 10%, which was likely an underestimate, as no prospective structured screening or diagnosis methods were used to detect cases (Combs et al. 2014). There are also minimal data on delirium prevalence or incidence in people having palliative care in their home or a residential aged care facility. One study reported an estimate of confusion occurring in 50% of US hospice patients in the previous week, measured by nurses' retrospective clinical report rather than a standardized tool (Nowels et al. 2002). Another reported delirium

prevalence of one in three people with pre-existing moderate to severe cognitive impairment in seven long-term care facilities in Canada (McCusker et al. 2011). Delirium is elsewhere reported to be present in almost one in five older people on arrival to the emergency department and almost half of people who reside in a nursing home (Inouye et al. 2014). The acute onset of delirium in an older person may be a key reason why emergency hospital care is sought.

4.3 Adverse Outcomes

Delirium adversely impacts on the individual, their family, clinicians, and the healthcare system.

During delirium, acute decline in attention and cognitive function reduces the person's capacity to make decisions and communicate with others, which suddenly and often unexpectedly compounds the other physical and functional losses of advanced illness. A delirious person may be reluctant or unable to verbally communicate his or her disturbed thinking, and feelings of fear, confusion, and isolation are common (O' Malley et al. 2008). While not always unpleasant, altered perception most often has a nightmarish, hellish quality, including visions of snakes, spiders, and ants crawling on walls and bedclothes, and beliefs that doctors and nurses plan to murder, experiment on, and sexually assault themselves and/or other patients (Boodman 2015). Being delirious also makes it harder for the person to verbally communicate other distressing symptoms, such pain or breathlessness, which may lead to inadequate management of those symptoms and greater discomfort and distress (Gagliese et al. 2016). In studies of people with advanced cancer who had experienced delirium in hospital, the majority remembered the experience (Breitbart et al. 2002; Bruera et al. 2009). Memories generated feelings of distress, embarrassment, humiliation, and ongoing fear, including that the delirium will return (Breitbart et al. 2002; Bruera et al. 2009; Teodorczuk et al. 2011).

Adverse effects of delirium are increased risk of falls, pressure areas, longer-term cognitive and functional decline, longer hospital stay, and mortality (National Clinical Guideline Centre for Acute and Chronic Conditions 2010; Australian Commission on Safety and Quality in Health Care 2013). An episode of delirium more than doubles the cost of an older patient's healthcare in the following year, due to spending a greater number of days in hospital or a nursing home (Leslie et al. 2008).

During delirium, family members experience high levels of distress (Breitbart et al. 2002). A review of 33 studies of family caregivers of patients with delirium in palliative care contexts found that they experienced anxiety, fear, helplessness, embarrassment, anger, disappointment, sadness, and guilt (Finucane et al. 2017). Delirium adversely impacted on relationships with the person, other family members, and health professionals. Caregivers wanted the person's suffering to be relieved, but did not want the possibility of communication to be thwarted because of sedation (Finucane et al. 2017).

Health professionals, particularly nurses, find identifying and appropriately responding to delirium challenging and experience uncertainty, strain, and distress (O' Malley et al. 2008; Leventhal et al. 2013). Nurses working in palliative care reported feeling compassion, distress, surprise, puzzlement, and frustration when delirium occurred (Agar et al. 2012; Hosie et al. 2014a). In one study, delirium severity and presence of perceptual disturbances were most significant predictors of nurse distress (Breitbart et al. 2002). In another of palliative care team members' experiences of caring for family of people dying with agitated secondary to delirium, participants felt the suffering of patients and family, tried to maintain control of the situation (usually through use of medication), felt ambivalent about the use of sedation, and valued communication to inform the family about the rationale of interventions and to reduce conflict (Brajtman 2005).

5 Prevention

There is growing evidence that the most effective way to improve delirium outcomes for people in hospital is to prevent it from occurring. Meeting

basic human needs, such as for physical and cognitive activity, sleep, hearing, vision, and hydration, significantly reduced delirium incidence in older hospitalized patients by up to 50% (Hshieh et al. 2015; Siddiqi et al. 2016). In contrast, a delirium prevention intervention for people with advanced cancer in seven Canadian specialist palliative care inpatient units reported a negative result (Gagnon et al. 2012), possibly because this intervention was not sufficiently targeted at these fundamental physical and cognitive needs. Instead, physicians were notified about delirium risk factors for each patient and asked to consider medication changes in response; while nurses orientated patients to time and place and gave patients and family information about early delirium symptoms. Despite almost 90% adherence to the study protocol, the intervention made no difference to delirium incidence, severity or duration, or dosage of psychotropic medication received by patients (Gagnon et al. 2012).

Psychoactive medications (Table 1) are commonly prescribed in palliative care to manage symptoms, such as pain, breathlessness, nausea, and fatigue, and may contribute to the increase risk of delirium (Gaudreau et al. 2005a; Clegg and Young 2011). It is important to discuss the potential risks with the person prior to commencing new psychoactive medication, so that they may make informed decisions about which means of symptom control are best for them. For example, some people would prefer to forgo some degree of pain relief to maintain optimal cognition. Choice of psychoactive medication should consider the side effect profile, pharmacokinetics and pharmacodynamics for the individual, and possible non-psychoactive alternative therapies and also pay close attention to drug-drug interactions. It is important to use the lowest effective dose and ensure ongoing regular review of the dose, necessity for ongoing treatment, and possible adverse effects.

Whether multicomponent delirium prevention interventions specifically targeted to risk factors and proven elsewhere are feasible and effective during receipt of palliative care is yet to be established. That the strategies address fundamental human needs does warrant that they are valued for all people in every care setting. Yet a potential barrier to routine implementation in palliative care is that people with advanced illness are frequently frail and fatigued and may be unable to fully participate in activities such as exercise. To make informed decisions about participating in these interventions, people first need to also understand the risks associated with delirium. They need accurate, timely, and sensitively delivered information about delirium and preventative strategies from clinicians at key points in the illness trajectory, such as on admission to a service and when deterioration occurs. Integrating delirium prevention into palliative care requires health professionals to view delirium as serious and potentially preventable in advanced illness, value this care, and offer and deliver preventative interventions in a safe, supportive, and informed way that is tailored to the individual.

6 Recognition

Early recognition of delirium risk and symptoms by all who are caring for the affected person, whether in primary care, the emergency department, or specialist palliative care settings, is essential so that his or her needs and those of their family can be assessed, a diagnosis or differential diagnosis made, and appropriate interdisciplinary care planned and implemented.

Historically, delirium is under-recognized and misdiagnosed across settings, including palliative care (National Clinical Guideline Centre for Acute and Chronic Conditions 2010; Barnes et al. 2010). Hypoactive delirium, which can easily be mistaken for depression or fatigue, is the least well-recognized subtype. One study in a palliative care unit reported a one-in-five detection rate of patients with hypoactive delirium by any member of the multidisciplinary team, significantly lower than detection of those with hyperactive and mixed delirium (Fang et al. 2008; Spiller and Keen 2006).

Poor recognition of delirium is due in part to it being a complex and fluctuating condition that manifests in various ways, even within one episode. Other reasons are health professionals' inadequate knowledge of delirium, particularly its

diagnostic criteria (Jenkin et al. 2016); attitudes that poor cognition is normal in older age and serious and advanced illness (McCarthy 2003); and lack of routine use of delirium screening, assessment, and diagnostic tools ("tools") and organizational direction (Hosie et al. 2014b). There are additional challenges to recognizing delirium in people with limited ability to speak, such as young children (Smith et al. 2013), those with an existing cognitive impairment (Morandi et al. 2016), and during intubation and sedation (Girard et al. 2008) and dying (Bush et al. 2014).

Timely recognition is supported by evidence-based knowledge of delirium as an abnormal condition, its seriousness, and who is most at risk (together denoting "awareness") and routine screening of those at risk using brief, validated tools and/or diagnostic criteria to confirm the diagnosis (National Clinical Guideline Centre for Acute and Chronic Conditions 2010; Australian Commission on Quality and Safety of Healthcare 2017).

Awareness requires evidence-based understanding of delirium that aligns with accepted diagnostic criteria, as in the APA-DSM-5, provided earlier. Across settings and time, numerous misnomers for delirium have been used in different areas of clinical practice and research, with examples being *ICU psychosis*, *sundowning*, and *confusion.* Increasingly these terms are being discouraged in the literature (Girard et al. 2008; Morandi et al. 2009) because they are imprecise, downplay the significance and severity of delirium, and contribute to under-recognition. Likewise, *terminal agitation* and *terminal restlessness* are widely used by palliative care practitioners to describe what may be delirium or other unspecified sources of distress (Hosie et al. 2014a; Brajtman 2005; Heyse-Moore 2003). Use of these terms has similarly contributed to under-recognition of delirium and delayed assessment and intervention for delirious patients in palliative care units (Hosie et al. 2014a), likely because the prefix 'terminal' implies that a delirious person is in the last days of life and communicates a presumption that interventions aimed at reversal are no longer the priority. Nurse participants in this study reported clinical incidents when they challenged their nurse colleagues' use of these terms, whereupon a more comprehensive assessment found that their delirious patients had reversible causes such as urinary retention and infection, which were successfully treated and these patients' delirium and distress resolved (Hosie et al. 2014a). To ensure an evidence-based approach to assessment and intervention when delirium symptoms occur, whatever the person's stage of illness trajectory or likelihood of reversal, it is recommended that use of *terminal agitation* and *terminal restlessness* be discontinued in palliative care practice and literature in preference for the more diagnostically precise "delirium."

Awareness also incorporates knowing the *general risk* of delirium to people with advanced illness, older age, and/or cognitive impairment (including the seriousness of its outcomes) and assessing the *specific risk* for an individual. General awareness is knowing that delirium is moderately to highly prevalent in people receiving palliative care, having "a high index of suspicion" that delirium is the cause of acute attentional and cognitive changes (LeGrand 2012), and understanding that all subtypes of delirium are a medical emergency that require urgent intervention (see ▶ Chap. 84, "Delirium as a Palliative Care Emergency"). While there is no tool to assess specific risk for people receiving palliative care, a simple and pragmatic approach outlined in evidence-based guidance is for any person with one or more risk factors (i.e., "age $\geq$ 65 years, known cognitive impairment/dementia, severe medical illness and current hip fracture" or any others) be asked, along with their family, on admission to hospital about any recent changes to behavior or thinking, undergo cognitive screening, and have preventative measures put in place (National Clinical Guideline Centre for Acute and Chronic Conditions 2010; Australian Commission on Quality and Safety of Healthcare 2017). Because by definition each person receiving palliative care has life-limiting illness, it is prudent to consider all to be at risk of delirium, with risk heightened for people who are older than 65 years, have an existing cognitive impairment, and one or more precipitants present (Table 1).

Screening patients for delirium requires routine and ongoing use of a structured tool by trained

clinicians. Delirium screening tools that are brief and low burden and/or include family observations include the:

- 4AT (McLullich 2015)
- Nursing Delirium Screening Scale (Nu-DESC) (Gaudreau et al. 2005b)
- Brief versions of the Confusion Assessment Method (CAM), such as the CAM-ICU (Ely et al. 2001) and short-, 3D-, or bCAM (Han et al. 2013; Hospital Elder Life Program 2015; Marcantonio et al. 2014)
- Single Question in Delirium (SQiD) (Sands et al. 2010)
- Recognizing Acute Delirium As part of your Routine tool (RADAR) (Voyer et al. 2015)

These tools were developed for various settings and users, and none have been tested or are routinely used in palliative care (Barnes et al. 2010; Irwin et al. 2008). Testing delirium tools and integrating them into current systems for symptom and problem screening (Palliative Care Outcomes Collaborative 2014; Cicely Saunders Institute 2012) is therefore an important area for palliative care practice development.

Confirmation (diagnosis) of delirium is best achieved by applying a validated confirmation tool, such as brief version of the CAM (as above) and/or diagnostic criteria (American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) 2013). Confirmation of delirium is not solely the responsibility of physicians; the process can be shared with other clinicians in the team who are trained in the use of the tool and have knowledge of the criteria (Australian Commission on Quality and Safety of Healthcare 2017). Potential differential and concurrent diagnoses, such as dementia or depression, need to be considered during the diagnostic process.

7 Comprehensive Assessment

Comprehensive assessment of a delirious patient is structured, multifaceted and interdisciplinary, and broader than a diagnostic assessment (Canadian Coalition for Seniors' Mental Health 2010; Australian Commission on Quality and Safety of Healthcare 2015). Given that delirium is a medical emergency, when symptoms are present and a diagnosis suspected, it is essential to determine likely causes through history taking, physical examination, and various investigations, aligned with the patient's goals of care. Understanding the experience from the patient's perspective, his or her level of distress, and need for information and reassurance are key components that are valued by patients and family (Day and Higgins 2015; O' Malley et al. 2008). Communicating the implications of delirium and the possible options for investigation and management and relative success rates expected helps people to make informed choices about the level of investigation. Understanding also informs any decisions for admission to hospital or a palliative care unit if the person is at home.

Elements of assessment of a person with suspected or confirmed delirium are several and include:

- History, including reported symptoms of delirium and precipitating medical conditions, baseline cognition, and previous episodes of delirium (some which may be from collateral history)
- Physical examination
- Likely causes and potential for reversibility
- Predicted prognosis
- Immediate, intermediate, and longer-term goals of care
- Decision-making capacity
- Level and cause of distress
- Safety: risk of falls, wandering, pressure areas, and injury to self or others
- Preference for location of care
- Social, psychological, cultural, or spiritual needs
- Family information and support needs
- The need for referral to appropriate psychiatric or geriatric specialists or specialist services if delirium is severe and/or persisting

Comprehensive assessment also involves the person and his or her family, and results in a plan of care that addresses identified needs, priorities, wishes, and short- and longer-term goals (National Clinical Guideline Centre for Acute and Chronic

Conditions 2010; Canadian Coalition for Seniors' Mental Health 2010; Australian Commission on Quality and Safety of Healthcare 2015).

8 Management

The goals of palliative care of a delirious person are to reduce distress, maintain function and physical and emotional safety, and resolve the delirium, wherever possible. These goals are best achieved through targeting the causes, effective communication, and practical strategies to meet patients and families' immediate needs.

While clinical decision-making about intervention to resolve delirium often contains elements of uncertainty about effectiveness, treating the identified causes is the most logical medical route to relieving distress. Potential for reversal of delirium remains even in far-advanced illness when modifiable precipitants, such as infection, dehydration, and psychoactive medication, are treated (Lawlor et al. 2000). Some people will have less modifiable causes of delirium, such as metabolic disturbances related to organ failure (Lawlor et al. 2000; Leonard et al. 2008). Ethical decision-making with the patient and family about treatment therefore requires consideration of and discussion about the likely success of the treatment (both for the precipitant and the delirium), where it would need to occur (e.g., hospital, home or palliative care unit), and the degree of invasiveness (e.g., oral versus intravenous antibiotics). As there are usually several precipitants for each episode of delirium (Meagher et al. 2011), treatment is often multifaceted.

Further details of the investigative and intervention approach to treat delirium are outlined in ▶ Chap. 84, "Delirium as a Palliative Care Emergency"

8.1 Pharmacological Treatment

There are no approved or proven pharmacological interventions that directly prevent or treat delirium. Rational pharmacological treatments for delirium are those which target the identified cause and any associated discomfort, for example, antibiotics to treat infection, rectifying polypharmacy, discontinuing or reducing the dose of suspected medication precipitants, paracetamol to relieve fever, and ensuring adequate analgesia for pain (Canadian Coalition for Seniors' Mental Health 2010).

Antipsychotics have for many years been recommended in clinical guidelines and commonly prescribed to relieve delirium symptoms within both palliative care and other settings, yet there is growing evidence that this medication is not effective. A recent systematic review and meta-analysis of 19 randomized controlled trials and cohort studies of antipsychotics to prevent or treat delirium found no association with reduction of delirium severity or duration (Neufeld et al. 2016). Clinical trials conducted in intensive care settings report that use of antipsychotics did not increase participants' number of days without delirium (Page et al. 2013; Girard et al. 2010). Most recently, the first adequately powered trial of antipsychotics (risperidone vs haloperidol vs placebo) in patients receiving palliative care found that, at three days, participants in the risperidone and haloperidol arms had delirium symptom scores significantly higher than those in the placebo arm. Participants in the active arms had significantly more extrapyramidal effects, while participants in the placebo arm received significantly lower doses of rescue midazolam and had the best overall survival (Agar et al. 2016).

Benzodiazepines, such as midazolam and lorazepam, are recommended and used as a second-line pharmacological palliative intervention for delirium when the patient is highly distressed (Palliative Care Expert Group 2016), with an absence of robust trials to evaluate efficacy and toxicity, and are also a class of medication which can contribute to or worsen delirium. A 2009 Cochrane review found no evidence that benzodiazepines improved delirium outcomes (Lonergan et al. 2009). The review authors highlighted that participants in the lorazepam arms had unacceptable side effects in two included studies, including severe sedation, which caused one randomized controlled trial to be prematurely discontinued (Breitbart et al. 1996).

A recent Cochrane review investigating the benefit of palliative sedation on quality of life, survival, and refractory symptoms in terminally ill adults in the last days of life examined 14 studies (12 in hospice and palliative care units and primarily of midazolam) and reported insufficient evidence that palliative sedation improved quality of life or symptom control (Beller et al. 2015). Of the eight included studies measuring sedation for delirium, none reported improved delirium symptom control, and four reported worsening of delirium symptoms; the one study measuring unintended adverse effects reported 6% of participants experienced drug-induced delirium (Beller et al. 2015).

Based on current evidence, antipsychotic and/or benzodiazepine medication should therefore be viewed as an emergency, last resort, and short-term intervention for a severely distressed or agitated delirious person, after all other therapeutic strategies to relieve distress and maintain safety have been trialled and when the immediate risks to the patient are assessed as greater than these pharmacological interventions. Wherever possible, the principle of informed consent requires that the affected person or their surrogate decision-maker be fully advised of the intent, potential for benefit, possible adverse effects, and plan for use of these medications, before they are prescribed and administered.

8.2 Communication

People with delirium value verbal and nonverbal language that communicates respect for them as a person and understanding of what they are experiencing, while family members feel supported when they are consulted and given timely information by health professionals (Finucane et al. 2017; O' Malley et al. 2008).

Delirium is usually frightening and alienating, and many people struggle to communicate its symptoms, even more so for those who speak a language other than English or have other pre-existing barriers to communication. Being alert to the person's fears and difficulties; using simple, concise, and slow-paced ways of speaking; sensitively asking about the experience; respectfully promoting orientation (e.g., using the person's name, introducing self, referring to the day and place in conversations) without directly contradicting the person's altered reality; and obtaining the help of interpreters where required are the recommended ways of communicating with a delirious person (Canadian Coalition for Seniors' Mental Health 2010).

People affected by delirium also appreciate knowing that it is common during medical illness, usually short in duration and often treatable. Highlighting that the causes are physiological clarifies that symptoms do not mean that the person is suddenly developing dementia or a mental illness, which is a common misunderstanding (Breitbart and Alici 2008). Naming symptoms as 'delirium' is therefore important. However, explaining that delirium is common should not be intended to communicate that it is normal, because delirium is always an abnormality for the person (Hosie et al. 2016). Communication instead seeks to understand the experience of delirium from the person's and family's perspective, identify the level of distress, and acknowledge the real impact. Informing family about delirium, including with written information, and involving them in practical and emotional care of the person are desired and acceptable to them and potentially beneficial for both (Finucane et al. 2017). As outlined above, communication with the person and family members includes discussion about treatment options and likely outcomes.

An episode of delirium, particularly subsequent episodes, may also signal that the person's prognosis is grave and death is near. At this time, interdisciplinary reassessment of the person's circumstances and needs, and honest, sensitive communication with the patient and family about the possible significance of delirium, enables a clear and agreed upon plan of care.

Effective team collaboration, communication and functioning improve processes and outcomes for people receiving palliative care (Tieman 2007; Abernethy et al. 2013). However, communication between team members, especially between

nurses and physicians, can be a barrier to optimal delirium care in palliative care contexts. Nurses do not always clearly report observed symptoms as delirium, and then perceive a lack of respect or listening from physicians and nursing managers (Hosie et al. 2014a). When delirium occurs, interdisciplinary communication is best enabled by shared use of diagnostic language, understanding of delirium and the rationale for a plan of care, established roles for each discipline, and more frequent and focused discussion at the bedside; in other words, informed, explicit, structured, and whole team consideration of delirium symptoms, with the person and family placed at the center of assessment, decision-making, and care (Vasilevskis et al. 2010).

8.3 Practical Strategies

There are numerous practical strategies recommended in clinical practice guidelines for care of a delirious person. Examples include:

- Continuation of care that helps the person maintain optimal movement, vision, hearing, cognition, hydration, and sleep.
- Optimizing the environment:
  - Natural day and night lighting, noise levels, and activity.
  - Avoid transfers and maintain familiar surroundings and belongings.
  - Orientating equipment such as clocks, calendars, and wall schedules.
- Assess and minimize risk of falls and injury while avoiding restraints and allowing the person to move as freely as possible.
- Supporting those who are familiar to and trusted by the person to remain with him or her, including family members, friends, and professional carers.

The reader is referred to relevant guidelines for more comprehensive details of these strategies (Canadian Coalition for Seniors' Mental Health 2010; Australian Commission on Safety and Quality in Health Care 2014).

8.4 Delirium in the Last Days of Life

Delirium is very common when someone is dying, although not inevitable. When delirium occurs in the last days and hours of life, there remains the need for a prompt and individualized response to the meticulously assessed needs of the person and his or her family.

Numerous studies have consistently reported what is most important to patients and family at the end of life. In the hospital setting, patients and family highly valued expert, respectful, and compassionate care, effective communication and shared decision-making, an adequate environment, involvement of family, support with financial affairs, and trust and confidence in clinicians (Virdun et al. 2015, 2016). Patients also wanted to maintain a sense of self and not be a burden to others; and family further valued preparation for death, the patient to be safe and enabled to make choices, and family care continuing past the death of the person (Virdun et al. 2016). A study of the end of life wishes of people with advanced cancer, conducted in the United States, reported the ten most important as being, in this order: to be at peace with God, pray, have family present, free of pain, not be a burden to family, trust in the doctor, maintain a sense of humor, say goodbye to those who were important to them, have family prepared for death, and be able to help others (Delgado-Guay et al. 2016). Studies in Japan with bereaved family members of people who had delirium when they were dying from cancer reported that family experienced high levels of distress; more than half believed clinicians should have shown more respect for the person, explained what was happening on a daily basis, helped to relieve the physical and psychological burden on family, and better prepared them for death (Namba et al. 2007; Morita et al. 2007).

Given the consistency of the descriptive data over time and setting, and the growing evidence for ineffectiveness of pharmacological interventions to reduce delirium duration, severity, or distress, it is clear that physical, emotional, and spiritual care to help people who are delirious in the last days of life to be seen as a person; connect and communicate with family, health

professionals, and God; and prepare for death ought to be the focus of both clinical practice and future interventional research.

Palliative care for a person who is delirious in the last days of life, and their family, therefore continues all appropriate strategies to relieve suffering, as outlined above. If agitation is present for a dying person, all potential contributors, such as pain, urinary retention, fecal impaction, and psychological and spiritual distress, should be assessed and managed accordingly. If any level of sedation is considered for a person who is suffering from refractory agitated delirium in the last days of life, or other symptoms, health professionals should be guided by the European Association for Palliative Care (EAPC) framework for palliative sedation (Bush et al. 2014; Cherny and Radbruch 2009). Briefly, this framework includes that the person is comprehensively assessed by experienced palliative care physicians and teams, and any other appropriate specialist; that patients and family members are fully informed and provide consent; that sedation is proportional to the person's needs and wishes, that the person's physical, hydration, nutrition, and concomitant medication needs are considered and met; that supportive care of the family continues; and that the views and well-being of team members with respect to decision-making and intervention are also considered (Cherny and Radbruch 2009). Care must also be taken that any sedating intervention is given primarily for the wellbeing of the person, and not for that of family or team members.

9 Future Approaches to Improving Palliative Care of People at Risk of Delirium

Improving delirium outcomes for people receiving palliative care requires greater empirical evidence in every domain: prevention, recognition, assessment, treatment, and support, including for family in bereavement (Lawlor et al. 2014). Numerous descriptive data exist, but proven interventions are lacking. Next steps to improving palliative care of people at risk of delirium are therefore to develop interventions that are based on the aspects of care that have consistently been reported as the most important to people at the end of life and test them in well-designed studies (Finucane et al. 2017). Interventions proven to be effective for other patient groups and settings, such as delirium prevention through meeting fundamental human needs, can also be tailored and tested in palliative care (Hshieh et al. 2015; Siddiqi et al. 2016). Novel therapeutic targets based on pathophysiological evidence of pathways to delirium ideally will guide future trials of pharmacological prevention and treatment therapies. Theories of grief and bereavement could be developed and tested as interventions to support family of people with delirium in advanced, life-limiting illness. For example, the theory of ambiguous loss acknowledges and addresses the loss experienced by family when a living person is physically present yet psychologically absent – as can occur during delirium – to find greater meaning, mastery, connection, hope, and resilience in the difficulty of the situation (Boss 2010; Day and Higgins 2016).

At the health system level, patients receiving palliative care require equitable access to organizational initiatives to improve delirium systems and practice. For example, in Australia, a new delirium clinical care standard will include people receiving palliative care in its remit (Australian Commission on Quality and Safety of Healthcare 2017).

Delirium education for health professionals should be based on those known to be most effective in changing attitudes, knowledge, and practice. Examples include interprofessional education (Sockalingam et al. 2014) and spaced education (Phillips et al. 2014).

10 Conclusion and Summary

This chapter has outlined how health professionals may best prevent, recognize, assess, manage, and support people with palliative diagnoses who are at risk of delirium, and their families, according to best evidence and the circumstances, needs, and wishes of the person. The chapter also

presented evidence-practice gaps in delirium care in palliative contexts and briefly outlined directions for future research and clinical practice development.

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Neurological Symptoms

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Contents

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Abstract

Neurological disease is a major cause of disability and death across the world. There is increasing evidence that palliative care is effective in managing symptoms, maintaining and improving quality of life and helping patients

R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_23

and families cope with the deterioration. As the disease progression varies, both between diseases and for individuals. palliative care may be involved for varying periods of time, and may need to be involved episodically throughout the disease progression. Careful assessment of all the issues – physical, psychosocial and spiritual – will allow appropriate management and support for patients and families. Carer support is very important as families face all the issues of coping with a progressive disease. Recognition of the later stages of life is helpful in enabling patients, families and professionals to be able to prepare for the dying phase and manage all the issues appropriately.

1 Introduction

The assessment of neurological symptoms may be particularly complex. It is essential that there is very careful assessment of the symptom, before any treatment, as for all palliative care. However there may be many interactions between the symptom and the psychosocial and spiritual aspects of care. Moreover there may be issues of communication and cognition, as many symptoms are experienced by people with complex progressive neurological diseases as well as other comorbidities.

The difficulty of communication – maybe due to severe dysarthria, dysphasia, or respiratory dysfunction reducing the power of speech – may make the assessment of the symptom more difficult as the patient may not be able to express themselves clearly or may not even be able to express the distress caused by the symptom. This may also be seen when there is cognitive change. The patients may be less able to express their concerns and to discuss their problems and the symptom. The assessment of the patient and symptoms may be by careful observation of the person, looking for signs of distress or evidence of symptoms, but may also include the assessment and comments from family and carers. This has been used widely for the assessment of pain, and the DisDAT assessment has been widely used for pain assessment in intellectual disability and PAINAD for pain assessment in dementia (Regard et al. 2007; Warden et al. 2003). For both of these assessments, there is close observation and discussion with the carers, and if distress is present, the cause is looked for. If there is evidence for pain, analgesia may be given, and careful reassessment will see if the distress has reduced and the diagnosis of pain has been correct.

Thus neurological symptoms may require even greater "impeccable assessment" (WHO 2002), as they may be part of a wider neurological disease, with variable progression. However the same symptoms may be seen in patients with other diseases, such as paraneoplastic syndromes in patients with cancer, autoimmune disease, or related to medication (Panzer and Dalmau 2011). It is important to differentiate the cause of the symptom, and to look at the comorbidities, if the management is to be the best for that particular patient.

2 Dizziness and Vertigo

Dizziness is a term that is used to explain different sensations, such as light-headedness and spinning (vertigo) accompanied by an involuntary, rapid, rhythmic eye movement (nystagmus); giddiness; and feeling as if one is going to faint (syncope) (MD Guidelines 2017). Vertigo, dizziness, and unsteadiness are often reported as similar symptoms even though they may have different causes involving different organs and pathophysiology (Bisdorff et al. 2013).

Dizziness is a general term for a sense of disequilibrium; vertigo is commonly due to the involvement of the vestibular system and is reported as the illusion of motion, usually rotational motion. Other causes of these symptoms can be due to lesions in the brain stem and cerebellum and can be associated or not with nystagmus, migraine, ataxia or nausea or vomiting, and falls. Systemic disorders, like vascular or neurovegetative (postural hypotension), can cause dizziness as well as psychological psychiatric conditions like anxiety and depression.

The most common causes of vertigo are benign paroxysmal positional vertigo, acute vestibular

neuronitis or labyrinthitis, Ménière's disease, migraine, and anxiety disorders. Less common causes include vertebrobasilar ischemia and retrocochlear tumors (Swartz and Longwell 2005). In cancer patients, dizziness is common in patients with a direct involvement of the brain (primary or secondary tumors), secondary to cancer complications like hypercalcemia, hypoglycemia, and general electrolyte disorders. This symptom is common in neurological disorders like multiple sclerosis, Parkinson's disease, or multisystem atrophy.

In palliative care dizziness is often a side effect of symptomatic drugs. The palliative care formulary (2016) reports dizziness as side effects in almost all drug categories used in palliative care, starting from opioids to anticonvulsants, benzodiazepines, mood stabilizers, dopaminergics, sedatives, and in general all drugs which can act in the central nervous system.

The evaluation of a patient with dizziness requires attention to the nature and the characteristics of the symptoms that can suggest a possible diagnosis (e.g., onset, triggers, duration) and clinical features (general and neurological examination, e.g., orthostatic blood pressure and cardiac rhythm, oculomotor function, and balance) (Kerber and Baloh 2011).

Management of dizziness and vertigo depends on the underlined primary cause. Drug treatments are not presently recommended for benign paroxysmal positional vertigo (BPPV), and bilateral vestibular paresis, but physical therapy treatment can be very useful in both (Hain and Uddin 2003). Non-pharmacological techniques are effective like vestibular physical therapy in vestibular neuritis or canalith repositioning procedure for BPPV.

Corticosteroids can be effective in inflammatory causes, and therapies to reduce intracranial hypertension can ease when cerebral edema is present in brain tumors. In Parkinson's disease dopaminergic doses, adjustments can improve this symptom. Therapies for specific electrolyte disorders can play a role. In migraine-associated dizziness, specific antimigraine drugs can be helpful (Neuhauser et al. 2003).

For vertigo in both Ménière's disease and vestibular neuritis, vestibular suppressants such as anticholinergics and benzodiazepines are used. In Ménière's disease, salt restriction and diuretics are used in an attempt to prevent flare-ups. In vestibular neuritis, only brief use of vestibular suppressants is now recommended (Hain and Uddin 2003).

Drug treatments are not presently recommended for BPPV and bilateral vestibular paresis, but physical therapy treatment can be very useful in both (Hain and Uddin 2003).

In palliative care it is very important to consider the role of palliative drugs throughout a cautious titration, attention to the drugs interaction (opioids and neuroleptics but antiemetic also), and possibly a reduction of futile treatments.

Since dizziness and vertigo can have anxious or mood disorders origin, a careful psychosocial assessment should be considered and proper treatment provided. Family carers are to be involved explaining the meaning of this symptom, reassuring them about the causes, and, when appropriate, involved in the daily assessment and treatment.

3 Hearing Loss

Hearing loss is an age-related condition affecting 80% of adults over age 80. It is often denied by patients, sometimes for sociocultural reasons, as they fear of being labeled deaf. The condition can appear slowly overtime, and patients can be unaware of their loss of hear. The prevalence of this disturbance is unknown in palliative care, even though it can be assumed higher of the general population, due to the high age, comorbidity, and the treatment received (Smith et al. 2015). Hearing can be affected by specific treatments, like antibiotics or anticancer drugs.

Promotion of communication, shared decision making, and empowerment, even in the case of people with mild cognitive impairment, can enhance patient autonomy and dignity, helping to improve the quality of remaining life (Feinberg 2014). Hearing loss can have emotional impact including social isolation, loss of self-esteem due to communication mistakes, and frustration at the difficulty with communication. People may withdraw and/or become depressed and may

experience anger and frustration at the effort it takes to communicate (Bade 2011). Hearing impairment therefore can be a barrier for many palliative care outcomes and interventions, if not recognized.

Often, in a medical consultation, hearing-impaired patients tend to look absentminded and inattentive, whereas they are only unable to follow the conversation. This happens frequently when more participants attend and the carers tend to attract the discourse and, finally, make decisions about the care process.

Audiologists can play a role in helping the palliative care team, through an accurate assessment and suggesting solutions to reduce the impact of hearing loss (Weinstein 2015). In order to assess a hearing impairment, some authors suggest a single-item question along with a whisper test (Bagai et al. 2006) or a finger rub test (Smith et al. 2015). If these tests are positive, an audiological and/or speech and language consultation should be performed. Since this can be difficult for patients in palliative care, some general approach can be adopted, like an ear inspection to see if cerumen is obstructing the ear.

The treatment in case of a defined hearing loss can involve hearing aids, which unfortunately do not resolve most of the problems in palliative care patients. These devices are expensive, their provision can take time, and patients are not always compliant. They are usually prescribed when patients' expected life span is higher than 3 months. In the literature tips and techniques to improve communication with persons with hearing loss are reported (Smith et al. 2015; Weinstein 2015) including attention to the setting, positioning, language, aids, and documentation.

Some patients can have acquired deafness from the infancy; in these situations, usually they are able to communicate via sign language. The lack of knowledge of this form of communication can be a barrier to palliative care for deaf patients (Maddalena et al. 2012). It can be useful to identify someone in the staff, or among the patient's family, able to perform with this language in order to be able to fully involve the patient in the clinical assessment and therapeutic decisions.

4 Visual Disturbance

Visual disturbance is not very often reported in palliative care papers as a prevalent condition. This does not mean that patients do not suffer of visual loss, but indicates that probably they tend to focus on other specific palliative care issues and professionals do not assess and consider visual problems in routine practice.

The literature shows that the main causes of sight disturbances are primary eye tumors, ocular metastases, and some paraneoplastic syndromes. Sight alteration can also be associated with asthenia, fatigue, anemia, and hypovitaminosis (Saita et al. 1999). A visual drop is frequent in other conditions related to palliative care such as multiple sclerosis as a consequence of optic neuritis, with blurred, double, or graying of vision, nystagmus, or blinding of one eye. HIV/AIDS patients can lose their capability to see for concurrent infections, mainly cytomegalovirus retinitis, but from other pathogens including varicella zoster virus and herpes simplex virus retinitis, ocular syphilis, ocular tuberculosis, cryptococcal meningitis, and HIV-related ischemic microvasculopathy, ocular toxic, or allergic drug reactions (Kestelyn and Cunningham 2001). Other common causes are glaucoma and the consequences of diabetes.

Hypoglycemia can be a cause of temporary visual loss in non-diabetic patients and in palliative care settings, but in this case the drop of vision is to be considered a symptom of the metabolic condition, potentially very risky for survival and therefore appropriately treated (Kok and Lee 2016).

Visual impairment can hinder people from accessing appropriate services, limit relationships, and increase the sense of social isolation. As the general conditions worsen, frail patients tend to have limited resources to communicate. In specific situation, the eye function remains the only possibility to express any personal need, for example, in the locked-in syndrome, but also in ALS/MND tracheostomized and mechanically ventilated patients using eye-controlled communicators, called "augmentative/alternative communication" (AAC).

Ophthalmologists can play a role in palliative care (Yorston 2004). Interventions range from assessment and diagnosis of eye-related disorders, local and systemic treatments, and other symptoms managements such as reducing painful eye pressure pain in glaucoma, even when a total visual loss has occurred. This can be obtained with a daily dose of a 1% solution of atropine, topical steroids, or topical nonsteroidal anti-inflammatory drugs. More invasive intervention are retrobulbar chlorpromazine and alcohol injections (Galindo-Ferreiro et al. 2016) up to the evisceration or enucleation of the eye bulb that is performed mostly after a trauma, but can play a role in glaucoma (Balta et al. 2016).

5 Anosmia

Smell disorders can markedly affect the quality of life. The four main causes of smell disorders are trauma, viral infections, nasal causes such as sinusitis or polyposis nasi, and smell disorders associated with aging or neurological illnesses such as Parkinson's disease (Hummel et al. 2011). Anosmia is a non-motor feature of PD that, with other smell dysfunction, occurs in 90–96% of cases (Doty et al. 1988; Haehner et al. 2009). This symptom can anticipate the motor signs of the disease and is more prevalent than tremor, usually considered as principal indicator of PD (Alves et al. 2008). The olfactory bulb is implicated in the dysfunction. Damage to the dopaminergic, cholinergic, serotonergic, and noradrenergic systems is likely involved, and the origin is multifactorial and includes the same determinants as those responsible for other non-motor symptoms of PD, such as dysautonomia and sleep disturbances (Doty 2012). Anosmia is associated with autonomic failure and constipation (Ramjit et al. 2010). Anosmia is present in atypical parkinsonian syndromes like MSA, where autonomic dysfunctions are pathognomonic, whereas normal olfaction seems present in PSP and CBD patients (Wenning et al. 1995).

MS can cause impairment of the olfactory system, since half of the patients can have a reduced sense of smell or hyposmia (Uecker et al. 2017). Dementia with Lewy bodies is another neurodegenerative condition associated with impaired odor detection (McShane et al. 2001). Moderate hyposmia is present in Huntington's disease (Nordin et al. 1995) and in ALS (Hawkes 2006).

There are only limited treatments available for smell disorders. A proven effective treatment is only available where nasal illnesses cause the smell disorder (Hummel et al. 2011).

Treatment of odor dysfunction secondary to neurological conditions is difficult due to the progressive nature of the disorders. Rasagiline showed a positive effect on the processing of olfactory information in early PD patients (Haehner et al. 2015).

6 Movement Disorders

Movement disorders include:

Tremor is an unintentional, rhythmic, oscillation of a body part in a fixed plane and results from contractions of agonist and antagonist muscles entrained by a signal pattern originating from an oscillator in the CNS (MD 2017). The commonest cause is Parkinson's disease, due to the degeneration of neuromelanin containing neurons in the brain stem and particularly the substantia nigari. Careful assessment and consideration of the other symptoms of PD – rigidity, akinesia, and changes in postural reflexes – support the diagnosis, and treatment is by the use of levodopa and dopamine receptor agonists.

Tremor may also be "physiological" and exacerbated by stress and may be eased by beta blockers; essential tremor may be seen and there is often a family history and beta blockers are often helpful; cerebellar damage from inflammation in multiple sclerosis tremor is mild at rest and increases on activity and may respond to propranolol or isoniazid.

The use of medication may be helpful, but there is also the need to help patients cope with their tremor and for families and carers to understand the disability and anxiety associated with tremor.

Chorea is an abnormal involuntary movement characterized by brief, abrupt, irregular, unpredictable, non-stereotyped movements (MD 2017). This may be seen in:

- Huntington's disease – a genetic neurological degenerative disease where there is increasing movement issues, swallowing problems, and cognitive change. The chorea may be reduced by tetrabenazine, a monoamine depletor, and amantadine and atypical psychotics may be helpful.
- Paraneoplastic chorea may be seen with small cell lung cancer and thymoma and is associated with antibodies to CRMP5. Treatment may be more for the underlying cancer.
- Sydenham's chorea may be seen. It follows an autoimmune response to group A beta-hemolytic streptococcal infection, and symptoms may continue for years, although they usually resolve in a few months. Benzodiazepines, valproic acid, and neuroleptics are used in management.

Spasticity may occur when there is upper motor neuron damage – due to degeneration, as in MND; damage, as in nerve compression; or damage by tumor, cortical damage in stroke, or cerebral palsy. The main management will be with physiotherapy and positioning, to maximize comfort, prevent contractures, maintain joint range of movement, and enable as much mobility as possible. Muscle relaxant medication can be useful, and there is little evidence of the effectiveness of any medication. It has been suggested that quinine sulfate may be used initially, monitoring cardiac function, followed by dantrolene, tizanidine, baclofen, and gabapentin (NICE 2016). Injections of botulinum toxin into spastic muscles can be helpful for severe spasticity.

Dystonia is characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both. The movements are typically patterned and twisting and may be tremulous, and they often initiated or worsened by voluntary action. Dystonia may be inherited but can be due to infection, including encephalitis and HIV; drug induced, including levodopa and neuroleptics; and vascular, with ischemia, brain tumors, or trauma (Albanese et al. 2013). Some people are particularly prone to dystonic reaction due to phenothiazine or metoclopramide and may require anticholinergic medication, such as benztropine.

Treatment of localized dystonia may be with injections of botulinum toxin. Medication can be helpful including levodopa, tetrabenazine, reserpine and benzhexol, or baclofen (Pall 1999).

A **tic** is an involuntary movement or vocalization which is usually of sudden onset, brief, repetitive, stereotyped, but nonrhythmical in character. This may frequently imitate normal behavior and often occurs against a background of normal activity (MDS). Tourette's syndrome is characterized by tics and is first seen in childhood. Tics may be related to intellectual disability and autism or be seen in degenerative disease, in particular HD (Shprecher and Kurlan 2009).

Management will include a behavioral approach or the use of alpha-2-agaonists, such as clonidine, or neuroleptic antipsychotics, such as haloperidol, risperidone, or aripiprazole (Shprecher and Kurlan 2009; Cuenca et al. 2015).

7 Seizures Including Myoclonus

A seizure is a transient occurrence of signs or symptoms due to abnormal excessive or synchronous neuronal activity in the brain (Fisher et al. 2005). They may occur in 13% of people, with cancer, receiving palliative care. They may be:

- Simple partial seizures – with normal consciousness but an area of the cortex is stimulated, and the corresponding functional area is affected.
- Complex partial seizures – focal symptoms with an altered state of consciousness. Although the person may seem to be awake, they cannot respond and they may show repetitive behavior and eye movements. Afterward they may be sleepy, have delirium, or complain of headache.
- Generalized tonic–clonic seizures with loss of consciousness and muscle rigidity. Afterward they may be in a deep sleep and recover slowly.

About 25–50% of people in palliative care who have a seizure have brain metastases and of people with primary brain tumors 20–45% will present with a seizure, and this is commoner in slow-growing tumors, such as oligodendroglioma (Tradounsky 2013). The common causes of seizures are damage to the brain, from tumor, abscess, and hemorrhage, and systemic causes include metabolic causes, such as hypoglycemia, uremia, hypercalcemia, hepatic failure, and hypo-, or hypernatremia. Medication may cause a seizure including ondansetron, antipsychotics, and some chemotherapy agents, either by a direct effect or lowering the seizure threshold (Tradounsky 2013).

Assessment should be to determine the cause, with careful physical examination to find focal neurological signs, and a review of the patient's medication and biochemistry may be helpful. If a brain tumor, primary or metastases, is suspected, radiological investigation, usually a MRI, is necessary. An electroencephalogram is only necessary if the diagnosis is not clear or there is only subtle seizure activity (Tradounsky 2013).

Medication will usually be needed but careful discussion with both the patient and their family is essential. There is a need for explanation of the possible implications of seizures – the need to stop driving and inform the relevant authorities; possible effects of cerebral damage and the psychological implications, particularly for children, of observing a seizure; the risks of aspiration; respiratory obstruction; and even death. Patients with a brain tumor may also feel that they are losing control of their body and face the risk of stigma and marginalization that may occur as society may still feel uneasy with the diagnosis of epilepsy (Maschio 2012). There is also the need to explain the benefits of medication – corticosteroids and anticonvulsants.

The management of seizures may include primary treatment of the causative factor – such as the correction of a metabolic abnormality or radiotherapy or chemotherapy for a cerebral tumor, although anticonvulsant should be prescribed prophylactically as there may be initial peri-tumor edema and a risk of seizures. For a single cerebral tumor, particularly more benign forms, local excision may stop the seizure activity. Any medication that may be lowering the seizure threshold should be carefully evaluated and the dose reduced or stopped, if appropriate.

For many patients with cerebral tumors, management is with corticosteroids and anticonvulsant medication. Corticosteroids will reduce peri-tumor edema and may be used to reduce raised intracranial pressure and ease symptoms. There may be a reduction in seizures. Careful titration of the dose is ended to ensure that side effects are minimized but the therapeutic effect is maintained (Malik et al. 2004). For a patient with a cerebral tumor, this may involve increasing the existing dose or commencing administration. The usual corticosteroid used is dexamethasone, at a dose of up to 16 mg daily, although higher doses are considered. There are many side effects and patients need to be counseled carefully to look for these, especially the symptoms of a raised blood sugar. There may need to be discussions of whether to continue or reduce the dose, as although there may be a reduction of seizures and headache, there are risks of continuing with increasing disability and poor quality of life. These issues may require very careful discussion with patient and family (Oliver 2004).

7.1 Anticonvulsant Medication

A patient who has a seizure and for whom there is no obvious remedial cause requires anticonvulsant medication. However there are side effects and interactions with other medication that need to be taken into account. The blood levels of medication may need to be monitored carefully and evaluation of all other medication – both prescribed and "over the counter" or "complementary" medication – to check for interactions.

The anticonvulsant will vary according to the seizure type:

	First line	Second line
Partial (with or without secondary generalized seizure)	Carbamazepine Phenytoin Valproic acid (for secondary generalized seizure)	Phenobarbital Clobazam Gabapentin Topiramate Lamotrigine Levetiracetam

(*continued*)

	First line	Second line
Generalized		
Absence	Sodium valproate Clonazepam	Clobazam Topiramate/ lamotrigine
Myoclonic	Sodium valproate Clonazepam	Clobazam Topiramate
Tonic/clonic	Carbamazepine Phenytoin Sodium valproate	Phenobarbital Topiramate

Taken from Tradounsky (2013)

If possible monotherapy should be used, but with complex seizures two or more anticonvulsants may be required.

It is essential that the reasons for the anticonvulsant treatment are discussed with the patient and family, and the importance of continuing on medication is emphasized. It is also important to discuss how to cope with a seizure, as families and carers may become frightened and very anxious if they witness a seizure. It can be helpful to discuss with the family and carers possible interventions that they could take – including consideration of providing rectal diazepam or buccal midazolam preparations, which can be given by family members if the seizure is prolonged (Tradounsky 2013).

Status epilepticus is usually defined as seizure activity over 30 min or 3 episodes without return of consciousness in 30 min. This can be as tonic–clonic seizure, epilepsy partialis continua with clonic jerking of distal muscles continuing for weeks, or complex nonconvulsive status, presenting as a confusional state without any obvious seizures. There is appreciable mortality of 11% to 34% and the risk of cerebral damage.

Treatment within a hospital setting is with intravenous benzodiazepines – lorazepam or diazepam. If this is not effective, sodium valproate, phenytoin levetiracetam, and phenobarbital can be used. Midazolam is effective intravenously or intramuscularly. In severe status propofol or phenobarbital may be used, but intensive care involvement may be necessary to allow intubation and ventilation if there is profound respiratory depression (Tradounsky 2013).

In palliative care the use of intravenous medication may be difficult within the home or hospice setting. Diazepam can be given rectally and is unlikely to cause respiratory depression. Midazolam can be given buccally or by intramuscular injection, and phenobarbital can be given subcutaneously. Careful consideration may need to be given before proceeding to more invasive treatment within the intensive care setting.

The support of family and carers is essential if a patient has status epilepticus and the continuous or continual seizures are distressing for all involved. Professional carers may also need support and debriefing afterward.

After an episode of status, careful reassessment of the patient, including reassessment of the anticonvulsant regime, is essential, so that the risk of recurrence is minimized.

When a patient deteriorates and maybe becomes unconscious at the end of life, oral medication may no longer be possible. Phenytoin and sodium valproate have long half-lives (22 and 20 h), and a therapeutic level may be maintained for 12–24 h, but it is essential to maintain anticonvulsant medication during this final phase, as a seizure at the end of life is very distressing for family and carers. Midazolam or phenobarbital may be continued as a continuous subcutaneous infusion or diazepam may be given rectally (Oliver 2004).

8 Restless Legs

Restless legs syndrome (RLS) is a neurological disorder that causes the urge to move the legs due uncomfortable sensations to the lower limbs, sometimes extended to other body parts. The symptomatology appears above all during the night, and therefore it is commonly considered a sleep disorder.

RLS is very common in the general population; its prevalence can be up to 15% in primary care (Nichols et al. 2003; Allen et al. 2003). Females suffer RLS rates twice as high as compared to males (Ohayon et al. 2012).

This condition can be classified in a primary RLS, which usually occurs earlier in life (before age 20 years), and it has a strong genetic component (Walters et al. 2001). Secondary RLS which appears

later in adult life and its symptoms are sporadic, but regression of symptoms is slower, and it is associated with other disorders such as peripheral neuropathy, iron deficiency, end-stage renal disease, Parkinson's disease, poor health status in general, and aging (Yeh et al. 2012; Fereshtehnejad et al. 2015). The use of drugs that interfere with dopaminergic system can also cause RLS.

The essential diagnostic criteria for restless legs syndrome were developed and approved by the executive committee of the International Restless Legs Syndrome Study Group. They include (a) an urge to move the legs, often accompanied by an unpleasant sensation in the legs or other body parts; (b) symptoms aggravated by rest; (c) symptoms alleviated by movement (such as walking); and (d) symptoms which must be worse in the evening or night, with an urge to move the legs, usually accompanied by an unpleasant sensation in the legs (other body parts may be involved, in addition to the legs) (Allen et al. 2003; Yeh et al. 2012).

Dopamine agonists are the treatment of choice for moderate to severe RLS. They lower the severity of RLS symptoms and reduce reoccurrence of symptoms or augmentation. Ropinirole and pramipexole alleviate RLS symptoms by providing the effects of dopamine and stimulating most D2 and D3 receptors (Yeh et al. 2012). Rotigotine patches, releasing the drug over 24 h, can ease the daily symptoms. Levodopa was also used in the past decades; however, long-term treatment with this drug and dopaminergic agents can lead to augmentation, an iatrogenic worsening of symptoms which may require a change in treatment strategy (Hogl and Comella 2015; Mackie and Winkelman 2015).

Among the symptoms, musculoskeletal pain is associated with RLS above all in young adults (Hoogwout et al. 2015), and opioids seem to be effective in treating RLS symptoms (de Oliveira et al. 2016). In particular oxycodone/naloxone and possibly low doses of methadone (above all for the action on the NMDA receptors) can play a role as non-dopaminergic drugs for RLS (Hogl and Comella 2015).

Benzodiazepines are often prescribed as a coadjuvant therapy to improve the quality of sleep, but their effectiveness is unclear, and side effects and long-term dependence are to be considered (Carlos et al. 2017). Other used drugs are anticonvulsants (carbamazepine and gabapentin), and also non-pharmacological strategies can be effective (Yeh et al. 2012).

RLS should be considered in palliative care because it can be related to poor health status, neurological and renal conditions, and age and can aggravate pain and suffering. The quality of life of untreated RLS patients is affected by poor sleep, daily somnolence, and pain. It is often underestimate and not recognized. Drug interaction can worsen the symptoms or cause severe side effects.

9 Muscle Weakness

Muscle weakness may occur due to:

- Changes within the muscle itself – from genetic or metabolic disturbance (including drugs such as corticosteroids).
- Altered transmission at the neuromuscular junction.
- Abnormalities of the nerve supply to muscles.
- Disuse atrophy occurs if there is immobility/the muscles are not used, due to pain or fracture.

The weakness may recover, such as in Guillain-Barre syndrome, where there is weakness over a period of time, usually with recovery, or permanent if there is nerve damage, in paraplegia or ALS. The weakness may also be generalized or localized – for instance, in a progressive neurological disease, there may be initial localized weakness that increases more widely as the disease progresses.

There are few specific treatments that improve weakness itself. However physiotherapy may help to maintain the movements that remain and help to prevent stiffness, joint changes, spasticity, or deformity. In ALS a Cochrane Review concluded that there was no evidence that strengthening exercises were helpful, but there was also no evidence of harm (Dal Bello-Haas et al. 2013).

Transcranial magnetic stimulation has been shown to be helpful in stroke rehabilitation (Hosomi et al. 2016). A Cochrane Review suggested that neuromuscular electrical stimulation may be an effective treatment for muscle weakness in advanced progressive disease and used within rehabilitation (Jones et al. 2016).

The main aim of management will be to maintain movement and mobility as much as possible, and physiotherapy and occupational therapy enable patients to maintain as good a quality of life as possible. This may involve exercises or passive physiotherapy to reduce stiffness, advising patient and carers on the most appropriate way of moving and being moved and providing aid to mobility such as a stick, crutches, or wheelchairs, and to reduce pain and enable function such as splints or supports.

As a person deteriorates and comes to the end of life phase, they may be less able to alter their position and will be at risk of pressure area damage and pain and discomfort. Special mattresses and aids to maintain movement may be helpful, together with careful assessment and management of pressure and continence. Analgesia may be needed if there is increasing pain, and benzodiazepines, such a diazepam or midazolam parenterally, may be helpful in reducing stiffness and providing comfort.

10 Ataxia

Ataxia is a syndrome of incoordination, with changes in balance, coordination of movement, and often speech and swallowing problems. It is often due to damage or changes in the cerebellum and the main causes are:

- Hereditary ataxia – the commonest being Friedreich's ataxia and ataxia telangiectasia
- Nonhereditary degenerative ataxia – multiple systems atrophy, cerebellar ataxia, multiple sclerosis
- Acquired ataxias due to neuronal damage – head injury, alcohol, vitamin efficiency, toxins, paraneoplastic syndrome, and immune mediated causes (Klockgether 2010)

Assessment requires a careful family history, physical examination, and often investigation of the cerebellum. Genetic testing may be necessary if a hereditary cause is suspected (Klockgether 2007). Management will depend on the cause – if there is a specific deficiency or toxic factor, it may be possible to reverse or lessen the nerve damage and reduce the symptoms.

For most people with ataxia, there is no specific treatment. Physiotherapy, including the decomposition, simplification, and slowing of activity, may help the person cope with ataxia. Speech and language therapy assessment will be necessary to help with speech and swallowing issues, and occupational therapy will help maintain movement and activity as far as possible. Emotional and psychological support of both patient and family may be needed.

11 Hiccup/Hiccough

A hiccup is involuntary, synchronous clonic spasm of the intercostal muscles and diaphragm leading to a sudden inspiration, flowed by a sudden closure of the glottis causing the characteristic sound (Calsina-Berna et al. 2012). They may occur for 2–60 times per minute, and in 80% there is unilateral contraction of the left hemidiaphragm. They are commoner in males.

Hiccups are seen in the fetus and neonates but reduce in adults. It has been postulated that there is an amorphous neural network coordinating afferent inputs which act as a "hiccup center" or an inbalance of the inspiratory and expiratory neuronal circuits, caused by stimulation or damage of the brain stem or vagus or phrenic nerves (Woelk 2011).

In advanced cancer 1% to 9% of people have hiccups, and in a large study of 362 patients 14 (3.86%) patients reported hiccup – 8 occasionally, 5 persisting, and 1 continuous (Mercadante et al. 2013). Persistent hiccups continue for 48 h and intractable for over 1 month (Calsina-Berna et al. 2012). The causes of hiccups may be:

- Gastrointestinal – distension, reflux, tumor mass
- CNS – intracranial tumor, trauma, MS, infection

- Thoracic – damage or irritation of the phrenic nerve, such as infection or tumor
- Metabolic – hypokalemia, hypocalcaemia, renal failure
- Ear/nose/throat – infection, tumor, foreign body
- Psychogenic – stress, conversion reaction, personality disorder
- Drugs – corticosteroids, benzodiazepines, opioids, antidopaminergics
- Chemotherapy- etoposide, cisplatinum

Assessment is important to ascertain the cause if possible, as this may affect management. There may be a specific cause which will allow appropriate treatment, such as gastric distension which may be eased by antacids and prokinetic medication. However usually there is no clear cause, or there is no treatment to remove the causative factor, such as an inoperable tumor causing phrenic nerve irritation. The management of hiccups is then complex, and there are many suggested treatments and medication, but most are from case reports and there are no controlled trials. The main treatments are:

- Folk remedies – which usually involve glottis stimulation, such as holding breath, drinking water upside down.
- If there is gastric distension/reflux prokinetics, such as metoclopramide, or antacids/proton pump inhibitors may be helpful.
- Baclofen.
- Gabapentin.
- Chlorpromazine or haloperidol – which may help via the dopaminergic pathways
- Amantadine, nifedipine, valproic acid, and midazolam have all been suggested (Calsina-Berna et al. 2012; Woelk 2011).
- Surgery – including cervical phrenic nerve block for severe intractable hiccups (Smith and Busracamwongs 2003).

Support for the patient and family is important in helping them cope with the difficult symptom, which can adversely affect quality of life, as well as affecting sleep, eating and drinking, and speech and causing pain, fatigue, and depression (Calsina-Berna et al. 2012).

12 Delirium

Delirium is a complex syndrome with disturbance of cognition, arousal and attention of acute onset, and with fluctuation of symptoms. Factors include attention deficit, abnormalities of thought processing, disorientation, memory deficit, sleep–wake disturbance, behavioral changes, and language disturbance, but there may also be disturbance of perception, delusions, and affective change. This is usually related to physiological disturbance and may be reversible.

Delirium is common in palliative care with estimates of 13–42% of patients on admission to a unit showing evidence of delirium and 3–45% developing changes after admission (Hosie et al. 2013). It is also increasingly common bear to death, with estimates up to 88%.

Many neuronal pathways have been implicated in the causation of delirium, and it would appear to be a response to both an insult to the brain and stress reactions. A full assessment is essential to exclude a reversible cause – such as infection, alcohol/drug withdrawal, metabolic changes (such as hypercalcemia), hypoxia, and medication – including opioids and corticosteroids. There may be predisposing factors, such as deafness, visual loss, frailty, and comorbidities, including dementia, particularly in the elderly. Regular assessment of patients may be helpful, to detect early evidence of delirium, and allow treatment before severe symptoms develop, such as the regular monitoring using the Memorial Delirium Assessment Scale. Over 33% of people with advanced cancer on admission to a palliative care unit were found to have a raised score, and this reduced with careful assessment and treatment, with reduced cognitive change and symptoms (Mercadante et al. 2017).

The effects of delirium can be severe, with increased morbidity and mortality, longer hospitalization, longer-term cognitive decline, and distress for both the patient and family. Families may find the changes particularly distressing and explanation of the causation and management is important. The family may need support in helping to reduce the symptoms and in coping with the changes (Finucane et al. 2017).

Management of delirium includes:

- Non-pharmacological interventions – correcting any causes, ensuring the patient is in a well-lit room with a clock and calendar and supported by family and friends
- Pharmacological intervention – low-dose haloperidol, lorazepam, and atypical antipsychotics, such as olanzapine or risperidone, have been suggested. There may be pronounced sedation and side effects and possible increased mortality. Moreover a trial of risperidone and haloperidol showed that symptoms were reduced and improvement quicker with individualized management (Agar et al. 2017).
- Sedation may be necessary if there is severe distress at the end of life – see ▶ Chap. 87, "Palliative Sedation: A Medical-Ethical Exploration"

Further details are in ▶ Chap. 26, "Delirium."

13 Cord Compression

Malignant cord compression is spinal cord or cauda equine compression by direct pressure and/or induction of vertebral collapse or instability by metastatic spread or direct extension of malignancy that threatens or causes neurological disability (NICE 2008). It may occur in up to 2.5% of people with advanced cancer, most commonly breast, prostate, lung, or renal cancer. Sixty percent are in the thoracic spine, 30% in lumbosacral spine, and 10% in cervical spine (Pi et al. 2016).

The main symptoms are of pain (83–95%), motor deficit (60–95%), sensory deficit (40–90%), ataxia, and bowel and bladder dysfunction (Pi et al. 2016). Pain may be localized or radicular and may increase over a period of several weeks. Up to 80% may be unable to walk or only walk with assistance at the time of diagnosis (Levack et al. 2002), and they had suffered backache for an average of 3 months.

There is a need for suspicion of cord compression for all patients with bone metastases, particularly if there is back pain (NICE 2008). There is a need for urgent investigation and treatment. Careful neurological assessment and a MRI of the whole spine should be undertaken as soon as possible (NICE 2008).

Treatment should be started urgently to help control pain, minimize complications, and preserve or improve neurological function. The options include:

- Corticosteroids – there is limited evidence for the use of steroids, and an intravenous dose of 10 mg, followed by 16 mg daily orally, has been suggested, with proton pump inhibitors to reduce the risks and the dose reducing as soon as possible (Kumar et al. 2017).
- Surgery is the only treatment that will immediately improve the symptoms, but there are increased risks of morbidity and mortality. Surgery may be considered if it is felt that irradiation will be ineffective; the spine is unstable, an unknown primary, where diagnosis at surgery can be made by biopsy and previous radiotherapy (Pi et al. 2016; NICE 2008).
- Radiotherapy – should be offered, if the patient is well enough to cope with this, and will be effective in controlling pain in over 70% (Pi et al. 2016).
- Analgesia should be provided at all times.

The effectiveness of treatment will depend on the state at diagnosis – with 95% of patient mobilizing independently remaining independent or requiring only a stick but 51% of patients who were bedbound at diagnosis remaining independent (Savage et al. 2014). Careful rehabilitation, monitoring of the general physical state, ensuring thromboprophylaxis, and preventing bed sores are all essential (NICE 2008). Survival is low after cord compression – with bedbound patients having a median survival of 1.9 months and mobile patients only 11 months (Savage et al. 2014).

14 Coma

Coma is a state of prolonged unresponsiveness and unconsciousness from which the patient cannot be aroused. Impaired consciousness refers to similar, less severe disturbances of consciousness. A state of coma can be caused by a variety of

problems – traumatic head injury, stroke, brain tumors, drug or alcohol intoxication, or even an underlying illness, such as diabetes or an infection. To distinguish coma from brief transient states of unconsciousness (syncope or concussion), it is required a state of loss of arousal of at least 1 h.

Diagnosis is mainly clinical whereas the identification of the causes needs laboratory tests and neuroimaging techniques. The Glasgow Coma Scale (GCS) grades coma severity according to three categories of responsiveness: eye opening, motor, and verbal responses. It is not used for the diagnosis of coma, and its use is limited by intubation and use of sedating drugs that interfere with its utility (Bryan Young 2015). The GCS was developed to assess patients with head trauma and is scored between 3 and 15, 3 being the worst and 15 the best. It is composed of three parameters: best eye response (E), best verbal response (V), and best motor response (M). The components of the GCS should be recorded individually. A score of 13 or higher correlates with mild brain injury, a score of 9 to 12 correlates with moderate injury, and a score of 8 or less represents severe brain injury. The FOUR score provides greater neurological detail than the GCS, recognizes a locked-in syndrome, and is superior to the GCS due to the availability of brain stem reflexes, breathing patterns, and the ability to recognize different stages of herniation (Wijdicks et al. 2005).

Coma is different from vegetative state which happens when a person is able to be awake, but is totally unaware. A person in a vegetative state can no longer "think," reason, relate meaningfully with his/her environment, recognize the presence of loved ones, or "feel" emotions or discomfort. The higher levels of the brain are no longer functional. A vegetative state is called "persistent" if it lasts for more than 4 weeks. Patients in persistent vegetative state (PVS) have sleep–wake cycle and can cough, sneeze, scratch, and even cry or smile at times and be responsible to touch. However, all of these are automatic behaviors that do not require any functioning of the thinking part of the brain (Arenella 2017).

A state of coma is frequent in palliative care. It can be confused with the therapeutic or palliative sedation, which is the result of an active intervention adopted in those cases where patients develop intolerable pain and suffering despite excellent palliative care. In such patients, sedation is used to treat pain, dyspnea, nausea and vomiting, delirium, and myoclonus in order to relieve symptoms while the patient is to dying and to ensure the appropriate management of distress, so that the patient may die comfortably. In other cases coma is secondary to the disease progression or due to the progressive increase of drugs, like pain killers or neuroleptics, aimed at controlling symptoms, but not intended to explicitly suppress the consciousness.

There is not a specific treatment for coma. If the loss of consciousness is secondary to an endocranial hypertension, an attempt with steroids and/or osmotic diuretics can be used. If the cause is metabolic (e.g., hypercalcemia), parenteral hydration or the use of bisphosphonates can be attempted; in case of suspect of drug accumulation (opioids or other neuroactive drugs), a dose reduction can be done, but the aim must be clearly balanced with the possible outcome: will the result be transient and temporary? will the quality of life be better? and will a distressing symptom reappear?

In general patients in coma do not appear to suffer. There is no indication to force the arousal of a patient affected by a terminal condition, since it could trigger agitation or delirium and would not improve the quality of life. When a patient loses the capability to maintain attention, the focus of care must be kept on comfort care, prevention of bedsores, and symptoms. Time is required to talk to the family and explain that the person is not experiencing any suffering and is probably going to die soon.

Often family member ask if patient can hear, see, or perceive their presence. A reassuring approach can be to discuss the fact that even though the odds are that the patient does not feel or perceive external input, in case he or she could feel something a positive if someone close to them is present and talking to them. This means, for example, saying at bedside just the words one would have said if the patient were awake and avoid those that would not be appropriate. At the same time, encourage to give caress or kisses as if

he or she could feel it. It is also important to reassure that the patient does not feel hunger or thirst and will not starve to death even though he/she cannot swallow.

15 Locked-In Syndrome

The locked-in syndrome (LIS) is a rare neurological condition characterized by a complete paralysis of the voluntary muscles and intact state of consciousness and the sensory system. Usually some eye movements are spared, like vertical gaze and upper lid control. There are also incomplete form where some other muscular areas remain functional and a total form where even the eyes and lids are fully paralyzed (Bauer et al. 1979).

The most common cause is a stroke of the basilar artery and consequent bilateral damage of the pons, which may cause this catastrophic clinical state. A famous example of this condition is described in the book "The Diving Bell and the Butterfly" (original French title: Le Scaphandre et le Papillon) by the French journalist Jean-Dominique Bauby. It describes what his life is like after suffering a massive stroke that left him with locked-in syndrome. The patient was able to communicate blinking his left eyelid and created a code, shared with the speech and language therapist, that allowed him to write the book.

Life expectancy in LIS is usually not longer than few months (Thadani et al. 1991), but in rare cases can be of some decades (Haig et al. 1987).

Possible causes of LIS are poisoning (curare, snake bites, and neurotoxins) or trauma. LIS can occur as a complication of other progressive neurological conditions such as in severe Guillain-Barre syndromes or neuromuscular disorders like amyotrophic lateral sclerosis. In the latter LIS can be the consequence of the disease progression after that the patient is tracheostomized and mechanically ventilated. If the eye movement remains spared, it is possible to communicate through electronic computer-based alternative communication aids, but if the progression leads to a total LIS (Schnakers et al. 2009), it can be impossible to detect the consciousness of the patient and assess symptoms and sensations, since there are no commercially devices available for this purpose.

One important challenge is to differentiate between the coma, the persistent vegetative state (PVS), and the LIS. Clinically coma state is when a patient has a complete abolition of consciousness and awareness; in the PVS the upper functions of the brain are compromised, but the lower are spared; therefore patients are in an apparent state of arousal, but their consciousness is lost. In LIS the upper brain functions are intact, patients remain conscious and awake, but the lower brain functions are damaged and patients lose movements and communication.

No specific treatments for LIS are available. The literature shows examples of recovering from acute forms of this syndrome (McCusker et al. 1982; Silver et al. 2006; Heckmann and Dinkel 2013).

The quality of life of patients in LIS was studied, and results are surprising, since authors conclude that no difference was found between totally dependent and paralyzed LIS patients and healthy adults (Rousseau et al. 2013). Several factors may have an impact on QOL in LIS patients, such as family support and patient–computer communication devices. The QoL tends to remain stable over a long period of time (Rousseau et al. 2015).

However patients in LIS are totally dependent and their care is very challenging. Most of them are institutionalized in long-term care facilities. This is very costly because patients need tube feeding via PEG, mechanical ventilation via tracheostomy, and the communication devices. Being quadriplegic they are exposed to an increased risk of bedsores and need special beds and mattress. The corneas of the patients are at risk of ulceration if blinking is reduced. Patients are often affected by cramps and spasms that can be painful. Respiratory complications, like pneumonia, are frequent and can lead to death (Lahrmann and Grisold 2004).

Carers need long-term support. Home care is very hard to organize for patients with such a degree of physical impairment. This can be arranged with the involvement of paid carers which makes the care even more expensive.

Patients are totally dependent on their carers. As shown in previous studies on other severely impaired neurological patients, the QoL of the carers can be severely impaired, sometimes even worse than the patients (Kaub-Wittemer et al. 2003). Although being very distressed by the burden of care, discussion about end of life is often hard to tolerate for families (Anderson et al. 2010).

LIS can raise difficult ethical dilemmas about withdrawing or withholding life sustaining procedures (Kuehlmeyer et al. 2012). Some patients can ask for euthanasia (Kompanje 2010), but most patients can find a peaceful adaptation to the situation and do not request hastened death (Laureys et al. 2005).

16 Neuropathic Pain

Neuropathic pain (NP) is a type of chronic pain that occurs when nerves in the central nervous system become injured or damaged. It is a complex, chronic pain state caused by damaged, dysfunctional, or injured nerve fibers. The result is a painful sensation at the nerve site or in the surrounding area.

In terms of painful sensations, it can be described as an excruciating pain when clothes touch the skin, spontaneous burning, bursts of "pins and needles," and a band of searing pain around the body at the level of a spinal cord injury (Costigan et al. 2009).

Multiple mechanisms are responsible for neuropathic pain. It can be caused by a peripheral or by a central nervous system damage and can be secondary to mechanical trauma, metabolic diseases, neurotoxic chemicals, infection, tumor invasion or spinal cord injury, stroke, Parkinson's disease, or multiple sclerosis (Dworkin et al. 2003, 2007; Ducreux et al. 2006; Buhmann et al. 2017).

Assessing NP requires attention and practice. An accurate neurological examination can provide invaluable information about the localization, triggers, and clinical features of pain. A number of questionnaires can help in the diagnosis of NP: the neuropathic pain questionnaire (NPQ), ID Pain, and PainDETECT rely on interview questions; the Leeds assessment of neuropathic symptoms and signs (LANSS) (Bennett 2001) and *Douleur Neuropathique en 4 Questions* (DN4) (Bouhassira et al. 2005) as well as the Standardized Evaluation of Pain (StEP) (Scholz et al. 2009) integrate questions and physical tests aiming at identifying pain subtypes and therefore leading to a more appropriate choice of treatment (Cruccu and Truini 2009).

For the treatment of chronic neuropathic pain, recommendations are available (Dworkin et al. 2010). Authors list first-line pharmacological treatments including antidepressants (Saarto and Wiffen 2010) like tricyclic antidepressants (TCAs) like amitriptyline, selective serotonin–-norepinephrine reuptake inhibitors (SSNRIs) like duloxetine and venlafaxine, calcium channel α2-δ ligands (gabapentin and pregabalin), and topical lidocaine (see ▶ Chap. 10, "Pain and Pain Management").

As second-line medications, they propose opioids (tramadol and strong opioids). For those patients who cannot use or do not tolerate first- or second-line medications, third-line drugs can be offered like bupropion, citalopram, paroxetine, certain antiepileptic medications (e.g., carbamazepine, lamotrigine, oxcarbazepine, topiramate, and valproic acid), topical low-concentration capsaicin, dextromethorphan, memantine, and mexiletine (Dworkin et al. 2007, 2010).

17 Conclusion

The careful assessment – including history, examination, and investigation – is essential in the management of neurological symptoms. These may be related to acute or progressive neurological disease or other disease processes. The ongoing management will depend on the causation.

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Genitourinary Symptoms

28

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Abstract

Genitourinary symptoms may significantly impact on quality of life. Identifying the underlying cause will help guide management. In the palliative setting, understanding the goals of treatment, the prognosis of the patient, and

R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_24

their wishes will help with decisions regarding the various treatments that may be available.

1 Introduction

Genitourinary symptoms are common in patients with pelvic malignancies. These include gynecological, urological, and colorectal malignancies as well as metastases from other neoplasms. Nonmalignant conditions occurring in patients with malignancy may require management in the palliative care context.

Genitourinary symptoms may not be readily volunteered by patients to medical and nursing personnel. Patients may be embarrassed to discuss symptoms such as urinary frequency and/or incontinence. Identifying patients who may be at risk of developing these symptoms may enable early investigation and management. Specific questions should be asked at the time of consultation or scheduled nurse reviews. The use of questionnaires may help measure the subjective grade of symptoms (e.g., Lent-Soma patient questionnaire; Livsey et al. 2002).

The history of the diagnosis, staging, surgery, and treatment, together with the posttreatment symptoms, may indicate the likely pathophysiology. New onset symptoms including fevers, evidence of inflammation, infection, or self-detected masses may lead to the diagnosis. The severity of symptoms may be graded using scales such as CTCAE (National Cancer Institute 2009).

A careful general, speculum, pelvic, and/or rectal examination in the clinic is mandatory. Urine or high vaginal swabs for culture or collection of urine or smears for cytology may be helpful. Biopsy in the clinic should be undertaken with caution.

An examination under anesthesia with consideration of cystoscopy, sigmoidoscopy, and biopsy may be indicated. Biopsy within the radiation field should be undertaken with extreme caution as healing may be impaired and new fistula formation can occur.

Renal ultrasound or CT pyelogram may be helpful with renal tract abnormalities. Magnetic resonance imaging (MRI) and FDG positron emission tomography (PET) may be required to differentiate recurrent disease from posttreatment complications. Interpretation of PET scans can be difficult as both recurrent tumor and inflammation will result in increased uptake of radiolabeled glucose.

Good communication with the patient regarding the cause of symptoms, potential treatment/management options, and the anticipated outcome of proposed treatment with the revised long-term prognosis may reduce anxiety and help manage patient expectation. For example, urinary symptom flare may occur a year after SBRT for prostate cancer and resolve to baseline by 2 years (Woo et al. 2014). Patients undergoing permanent implant prostate brachytherapy may expect resolution of urinary symptoms by 12 months, but there may be a symptom flare shortly after the implant (Ryuta et al. 2012; Talcott et al. 2003).

Ongoing follow-up at three monthly intervals with monitoring of the nature and severity of symptoms in the patient record will aid assessment. More frequent assessment may be required.

2 Vaginal Dryness

Itching, burning, irritation of genital skin, vaginal discharge, and pain may accompany this symptom. Associated urinary symptoms of frequency and urgency may also be present. Radiotherapy-related vaginal dryness may be associated with vaginal narrowing and shortening.

Atrophic vaginitis due to reduction in systemic estrogen may be physiological or treatment-related secondary to chemotherapy, endocrine therapy, or radiotherapy. Approximately 40% of women experience vaginal dryness following pelvic radiotherapy (mostly grade 1–2) (Kirchheiner et al. 2014).

Endocrine therapy such as tamoxifen or aromatase inhibitors may be associated with severe or very severe vaginal dryness in 48% of patients (Chin et al. 2009).

Pelvic, speculum, and vaginal examination will generally reveal dry, atrophic, and thinning vaginal mucosa with areas of inflammation. Petechial hemorrhages and contact bleeding may be

present. A thick white discharge may indicate yeast infection. A gray-yellow discharge is often present with bacterial vaginosis. Microscopy and culture of specimens will guide management.

Vaginal yeast infections should be treated with topical application of antifungal cream or antifungal tablets. Treatment of the gastrointestinal reservoir with single dose of oral fluconazole at the time of topical treatment will reduce the risk of recurrent candidiasis.

Bacterial vaginosis can be treated with antibiotics after collection of a high vaginal swab for culture and antibiotic sensitivity.

Treatment of non-infective vaginitis should start with water-based vaginal moisturizers or lubricants such as Replens or KY gel which are available "over the counter." They may be effective in short-term relief of symptoms.

Hormonal treatment may be considered if there is no relief with the use of vaginal moisturizers and lubricants. Hormonal treatment may be given in the form of creams, pessaries, or tablets, applied directly into the vagina three to four times weekly.

In certain endocrine-responsive breast and endometrial cancers, hormonal replacement therapy is contraindicated. However, in a patient with severe vaginal dryness, the benefits of topical low-dose estrogen in alleviating symptoms adversely impacting on quality of life may outweigh the risks. Systemic absorption is low, but discussion with informed consent regarding possible low-dose absorption of estrogen which may potentially exacerbate or reactivate cancers is mandatory. In the palliative setting with limited life expectancy, quality of life considerations may override any potential exacerbation of hormone-responsive cancers.

3 Vaginal Discharge

Vaginal discharge may be normal physiological, infective, malignant, or treatment-related. Atrophic vaginitis will usually respond to topical estrogen. Collection of a high vaginal swab for microscopy and culture using a speculum will facilitate treatment of infective causes. Rarely, retained foreign bodies such as tampons will be identified with a speculum examination. Side effects of endocrine therapy such as tamoxifen may include vaginal discharge (Jones et al. 2007).

Malignant tumors require investigation and treatment in their own right, which may include surgery, radiotherapy, or chemotherapy. Formation of a differential diagnosis will include previous gynecological history, diagnosis, and treatment of pelvic malignancy and current treatment. Examination should include a general physical examination, speculum, colposcopic, and pelvirectal examination.

Previously treated pelvic tumors require palliative measures. Tranexamic acid (1 g tds po) may be used for bleeding, while metronidazole douches can reduce the offensive discharge of infected pelvic masses.

4 Vaginal Bleeding

This may be normal physiological (menstrual) or pathological. Menstrual bleeding may be regular or irregular. Intermenstrual bleeding requires gynecological assessment as it may be secondary to gynecological pathology.

Benign causes include hormonal or hematologic abnormalities, benign tumors such as polyp or fibroids, local trauma, pregnancy-related bleeding, or medications (e.g., warfarin). The presence of foreign bodies should be excluded. In the setting of malignancy, common causes are primary or recurrent carcinoma of the uterus, cervix, or vagina, local invasion from a pelvic malignancy such as colorectal cancer, metastases from other sites, or treatment-related bleeding (primarily from surgery or radiotherapy).

History and examination, including examination under anesthetic, will usually confirm the diagnosis. An urgent gynecological review may be helpful.

Investigations include full blood count, coagulation profile, and directed biochemistry. Pelvic ultrasound should include transvaginal imaging for adequate resolution where possible. A CT and/or MRI can clarify the diagnosis. Histology from an appropriate biopsy will assist in confirming the etiology.

In the presence of active hemorrhage, the patient may need urgent support with intravenous fluids and transfusion if anemic. The underlying cause should be treated. In the case of heavy bleeding, tranexamic acid (1 g tds, oral or intravenous) may be used. Vaginal packing can temporarily slow vaginal or cervical bleeding. After insertion of a urethral catheter, a speculum is passed and the vagina packed with wide ribbon gauze coated with antibacterial cream. The packing should be removed after 24 h due to the risk of infection. For malignancy, radiotherapy should be started as soon as possible and is effective in reducing bleeding due to cancer (Kim et al. 2013). Treatment may be given with relatively low risks of toxicity using 3D CRT, IMRT, or brachytherapy. Depending on the prognosis of the patient, a "standard" fractionation regime or a hypofractionated regime may be used.

5 Vaginal Stenosis

This is defined as shortening and or narrowing of the vagina and may be graded using CTCAE. It may cause difficulty with sexual function and medical examinations. Vaginal stenosis may progress with time with chronic and irreversible tissue changes (Kirchheiner et al. 2014). It may have psychosexual impact on the patient and decrease the quality of life (Mirabeau-Beale et al. 2014) with attendant difficulties with clinical physical examination of the patient. Complete obliteration of the vagina may occur and this is difficult to remedy. Prevention with regular use of vaginal dilators is optimal.

The most common cause is pelvic radiotherapy (external beam radiotherapy to the pelvic region and/or brachytherapy). The risk may be related to the total dose delivered and the volume of vagina treated (Park et al. 2014). Stenosis is exacerbated by estrogen deprivation which may occur due to previous surgery involving oophorectomy or pelvic radiotherapy-induced menopause. Vaginal stenosis due to radiotherapy may be associated with other symptoms such as vaginal bleeding, ulceration, and pain.

6 Pelvic Pain

Pelvic pain is a common symptom in patients with malignancy and in otherwise well patients (see ▶ Chap. 10, "Pain and Pain Management"). In the acute situation, narcotic and nonnarcotic pain relief may be required until other measures can relieve the pain.

For acute pelvic pain in the setting of malignancy (primary or metastatic), radiotherapy is an effective treatment (Kim et al. 2013). As radiotherapy may take 1–2 weeks to improve pain, medical management of pain with analgesics will usually be required. Modern radiotherapy techniques (3D CRT, IMRT) are effective in relieving pain due to bone metastases (with overall RR of 58–91% with short-course radiotherapy) with acceptable toxicity (Chow et al. 2007; Caravatta et al. 2012).

7 Urinary Problems

Urinary frequency and urgency may be distressing for patients who may be coping with other symptoms related to their condition such as pain and nausea. Irritating urinary symptoms may cause sleep disturbances and depression in addition to their effect on the patient's quality of life (see ▶ Chap. 24, "Sleep Difficulties"). Severe incontinence and problems such as vesicovaginal fistula may result in total social isolation.

8 Dysuria

Dysuria may occur due to nonmalignant causes such as urinary tract infection, inflammation or trauma or malignant causes such as tumor invasion of the urinary tract or its nerve supply or from pressure effects from extrinsic bladder compression. Bladder outlet obstruction may be secondary to tumor infiltration or to inflammatory or fibrotic sequelae of treatment.

Exposure of inflamed or irritated skin to urine in the perineal region (e.g., from radiotherapy or infection) can cause dysuria. It is important to identify the cause of the symptoms to deliver appropriate management (Table 1).

Table 1 Urinary problems in palliative care

Symptom	Potential cause	Investigation	Treatment
Dysuria	Infection (UTI)	MSSU	Change catheter if present Antibiotics as per sensitivities
	Inflammation		Urinary alkalinizer
Urinary urgency	Bladder instability Infection	Urodynamics Urine culture	Behavioral modification, antimuscarinic drugs, botulinum toxin, neurostimulatory devices
Urinary frequency	UTI Bladder instability Bladder inflammation (post RT) Bladder contracture/ partial cystectomy	MSSU Bladder diary Bladder diary	Antibiotics Bladder training
Nocturia	Nocturnal fluid intake	Fluid diary	Restrict fluids after 1700
	Bladder instability	Urodynamics	As per urinary urgency
Continuous urine loss per vagina	Vesicovaginal fistula Ureterovaginal fistula	Cystogram CT intravenous pyelogram	IDC/SPC Cystoscopy and trial of ureteric stent Reimplantation of ureter if feasible
Urinary retention	Dystonic bladder	Ultrasound for residual volumes	IDC or intermittent self-catheterization
	Outlet obstruction	Examination +/− cystoscopy	Self-catheterization or IDC/SPC
	Neurogenic bladder	US for pre-voiding and residual volumes	Trial of oxybutynin IDC or self-catheterization

UTI urinary tract infection, *MSSU* midstream specimen urine, *RT* radiotherapy, *IDC* indwelling catheter, *SPC* suprapubic catheter, US ultrasound

Combined treatment modalities, such as surgery and radiotherapy, may increase the risks of urinary complications (Erekson et al. 2009). Partial cystectomy may be required during surgical treatment and the residual bladder capacity further compromised by subsequent radiotherapy or chemotherapy (especially cyclophosphamide).

9 Urinary Tract Infections/Urinary Frequency

Urinary tract infections should be treated on the basis of antibiotic sensitivities. Long-term urinary catheters should be changed every 3–6 months during treatment. Urinary alkalinizers may improve urgency symptoms. In patients with recurrent urinary tract infections, prophylactic low-dose antibiotics or antibacterial agents such as hexamine hippurate (Hiprex) may be useful.

Management of fluid intake, including avoidance of caffeine, diuretics, and fluids in the evening, should be advised. Bladder training and pelvic floor exercises should be recommended.

Botulinum toxin type A (Botox) injections may be useful in overactive bladder causing urinary frequency, urgency, and urge incontinence. In rare circumstances, nerve stimulation devices implanted under the skin may be required.

Ring pessaries may be used for uterovaginal prolapse. Topical estrogen and vaginal moisturizers such as Replens are indicated for urogenital atrophy. As above, consideration of potential systemic absorption of estrogen may need to be balanced against the patient's quality of life in the patient with endocrine-responsive cancer.

Anticholinergics together with urinary alkalinizers may help relieve symptoms of dysuria. Surgery for stress incontinence should be considered very carefully, particularly in the

post-radiotherapy pelvis. Urodynamic pressure/flow profiling prior to any surgical intervention is mandatory.

10 Urinary Incontinence

Urinary Incontinence is the involuntary leakage of urine. Urinary incontinence reduces mental and physical quality of life with attendant anxiety, reduced sense of well-being, self-esteem, ability to socialize, sleep disturbances, falls, and skin breakdown (Avery et al. 2013; Smith 2016) as well as impacting on caregivers. Urinary incontinence is more common in women (23–55%) (Botlero et al. 2009; Hunskaar et al. 2004), with increasing frequency with age, and may be temporary or chronic.

Stress incontinence is provoked by increased abdominal pressure (coughing, exertion etc.), while urge incontinence is caused by bladder instability and is marked by involuntary loss of urine after a sudden and strong urge to void. Patients may have mixed urge and stress incontinence. Overflow incontinence occurs when the bladder becomes overfull due to outlet obstruction, poor bladder tone, medication or neurological issues.

Causes of incontinence may be multifactorial, and genetic factors may increase the susceptibility to incontinence (Richter et al. 2015; Campeau et al. 2011) (Table 2).

A careful clinical history is required. A medication list may also aid the diagnosis. A physical assessment including mental status, mobility, obesity, abdominal, pelvic, perineal, and neurological examination will aid treatment. Lower limb edema suggests a component of cardiac failure. Pelvic examination may reveal a palpable bladder, uterovaginal prolapse, pelvic masses, and poor pelvic floor muscle tone. Rectal examination, including prostate examination in a male, can also assist in evaluating pelvic pathology including loss of anal sphincter tone with neurologic pathology. Examination should include urinalysis and measurement of post voiding residual bladder volumes, either with a catheter and measuring device or by ultrasound. Semiautomatic devices may give an inaccurate measurement of residual volumes in the context of obesity and where other pelvic pathology is present.

Table 2 Urinary incontinence

Type	Cause	Treatment
Stress	Urogenital atrophy	Vaginal estrogen
	Urethral sphincter incompetence	Suburethral sling procedure Suburethral bulking agents
	Excessive intra-abdominal pressure	Cough suppressants, avoid straining
Urge	Urinary tract infection	Antibiotics
	Bladder instability	Oxybutynin
Overflow	Neurogenic	Intermittent self-catheterization SPC/IDC
	Pharmacologic	Review medication
	Outlet obstruction (e.g., stricture/prostatic)	SPC/IDC Consider urethral dilatation

Incontinence may be exacerbated by extrinsic compression of the bladder, intravesical tumor, or tumor involvement of autonomic and/or somatic innervation of the bladder. The presence of a ureterovaginal or vesicovaginal fistula may be interpreted by the patient as incontinence but is intractable to conventional management. A careful history will usually provide a tentative diagnosis of fistula, and this can be confirmed with a careful speculum and/or imaging with a CT IVP or cystogram.

In women with urinary incontinence, treatment will depend on the underlying etiology. In stress incontinence (triggered by increased intra-abdominal pressure due to coughing, sneezing, Valsalva maneuver, etc.), pelvic floor muscle training may improve continence (Dumoulin et al. 2015). Bladder training and/or anticholinergic agents may also help urge incontinence.

Urodynamic studies (bladder pressure profiles obtained during bladder filling) will demonstrate bladder irritability, which can be improved with muscarinic receptor antagonists. These studies require insertion of a urinary catheter for measurement of flow/pressure profiles and bladder

stability at different filling volumes. A Cochrane review showed that urodynamic studies changed clinical decision-making but may not lead to higher continence rates. It found that there was no statistical significant difference in continence rates between women receiving treatment guided by urodynamic studies compared with women assessed by history and clinical findings (Clement et al. 2013).

Cystoscopy/imaging may be indicated if the presence of a fistula is suspected.

Conservative treatment should be used before considering more invasive treatments. Absorbent incontinence pads may be sufficient for small volume incontinence. Behavioral therapy including timed voiding, modification of high fluid intake, and bladder training (delaying voiding to increase bladder capacity where small frequent voids have become established) may be helpful.

Pelvic floor muscle training requires prolonged effort with some benefit after some months of training. Physiotherapist-directed pelvic floor exercises can augment voluntary muscle control. Benefit is not sustained without continuing use. Topical vaginal estrogen may improve mucosal integrity in postmenopausal women with vulvovaginal atrophy.

Pharmacologic methods for bladder instability include anticholinergics which may be administered orally or transdermally. The lowest effective dose should be used, and full benefit may take 4 weeks to achieve. Troublesome side effects include dry mouth, impaired gastric emptying, and constipation. They should not be used in patients with a history of urinary retention or narrow-angle glaucoma.

Surgical options require careful assessment, taking the underlying pathophysiology, previous treatment including surgery and radiotherapy, and disease prognosis into account.

Botulinum toxin type A (Botox) injections can reduce bladder instability with improved continence rates. The duration of response is limited and repeated administration is necessary (Owen et al. 2016). Neuromodulation, in which leads from a nerve stimulation device are tunneled through the S3 foramen, has been shown to provide a 28–63% cure rate for urge incontinence (National Institute for Care and Excellence Guidelines 2013). Potential complications of this surgical procedure include pain, lead migration, and bowel dysfunction. Symptoms recur on stopping treatment.

In women, injection of silicone into the external urethral sphincter can augment continence. Suburethral sling procedures should be reserved for women with severe stress incontinence as recurrence rates are significant and their efficacy is limited in the postradiation pelvis (Tommaselli et al. 2015; Habashy et al. 2017).

More invasive surgical procedures such as augmentation cystoplasty or creation of a urinary diversion stoma should only be considered in very limited circumstances in the palliative care setting.

Severe intractable urinary incontinence may be sufficiently socially isolating that catheterization is warranted. Women may be taught to self-catheterize up to eight times per day. Silicone urethral catheters with collection bags strapped to the leg can be worn under clothing. These catheters should be changed every 3 months and the catheter bags changed at least weekly.

Where a urethral catheter is not feasible, a suprapubic catheter can be inserted into the bladder through the skin above the pubic symphysis. They are available with introducer kits and can be inserted into a full bladder with local anesthetic under aseptic conditions. Care is needed to ensure adequate bladder filling prior to insertion, and ultrasound may be used to guide placement.

Suprapubic catheters may cause less pain than urethral catheters, but care should be taken to avoid infection, hemorrhage, or bowel injury. The catheter will need to be changed at intervals, depending on the type of catheter. Patients with suprapubic catheters may still leak from the urethra. Bladder spasms can be an issue.

11 Bladder Spasms

Spasms occur when the bladder muscle (detrusor) contracts suddenly and severely, causing the patient to feel the urge to urinate. Severe bladder spasms may cause urinary incontinence by

forcing urine from the bladder. Bladder spasms may cause cramping pain which may be severe, and some patients experience a burning sensation.

Causes of bladder spasm include infection, indwelling catheters, previous bladder surgery or pelvic radiotherapy, and bladder cancer. Certain foods such as caffeine, alcohol, spicy foods, and preservatives can exacerbate this symptom. Neurological causes include multiple sclerosis, strokes, spinal cord injury, and degenerative neurological conditions.

Immediate relief of severe spams can be achieved with hyoscine butylbromide injection 20 mg intramuscularly. Underlying causes should be addressed. Antibiotics should be given for UTI and anti-inflammatory agents for radiation-induced bladder spasms. Oral medications to reduce spasm include oxybutynin, tolterodine, solifenacin, and tricyclic antidepressants such as imipramine hydrochloride, alpha-blockers, terazosin, and doxazosin.

The patient should practice timed voiding (e.g., every 1.5–2 h) and avoid trigger foods or drinks. Pelvic floor exercises can be helpful as can regular analgesics.

Invasive techniques include the use of TENS devices which provide electrical stimulation through the skin. Injection of Botox into the bladder wall at cystoscopy may provide relief for 2–3 months. Patients then require a second injection which may be effective for 6 months (National Institute for Care and Excellence Guidelines 2013). Side effects include urinary retention requiring a catheter and increased frequency of urinary tract infections. Onset of relief takes approximately 1 week.

12 Macroscopic Hematuria

Hematuria may originate in the upper or lower urinary tract. Causes include urinary infections, urinary calculi, renal tract neoplasms, and surgical trauma (e.g., following instrumentation or injury to the renal tract). Infections require antibiotic use (usually oral) with change of catheter. Renal calculi may require lithotripsy or surgery. Postsurgical hematuria will often settle with conservative management including use of a large three-way indwelling catheter with the capacity for bladder irrigation. Tranexamic acid (1 g tds orally or i.v. will usually reduce blood loss).

Hemorrhagic cystitis may follow chemotherapy (especially cyclophosphamide). Radiation may cause an acute cystitis with hematuria, urinary frequency, and bladder spasms. Late radiation cystitis may occur many years after radiotherapy and is related to the dose and volume of bladder irradiated. Anticoagulation may increase the risk of hematuria.

Gross hematuria is psychologically distressing for patients. Clot-induced acute urinary retention is an emergency and may require emergency department presentation for insertion of urinary catheter to relieve the obstruction and for bladder irrigation. Patients may require blood transfusion for anemia if there is significant blood loss.

Assessment should include a history and examination including vital signs, abdominal/pelvic masses, rectal/prostate examination in males, and gynecological examination in females.

Suspected renal parenchyma disease should result in referral to a nephrologist or urologist. Urinary microscopy, culture, and cytology with a full blood count are mandatory. Urinary tract ultrasound and cystoscopy may be required. CT and MRI imaging should be performed with care due to potential toxicity of contrast agents.

Treatment should be directed to the underlying cause. Palliative radiotherapy for renal tract tumors is effective in achieving hemostasis in 75–80% of patients (Mohamed et al. 2015; Cameron et al. 2015). Gogna et al. reported on patients with locoregionally progressive hormone-refractory prostate cancer treated with palliative split-course radiotherapy (Gogna et al. 2012) with gross hematuria resolving in seven out of nine patients, five out of seven patients being able to have their urinary catheters removed, and four out of four patients had their ureteric stents removed.

Tranexamic acid can reduce severe hematuria. Dose reduction is recommended in the presence of renal impairment. Tranexamic acid has been reported to cause ureteric obstruction due to

clots where bleeding originates from the kidneys (Vujkovac 2006).

13 Urinary Retention

Inability to empty the bladder completely may be chronic or acute.

Acute urinary retention causes severe pain and is a medical emergency. Chronic urinary retention causes mild discomfort or pain, lower abdominal distension, difficulty initiating the flow of urine, weak urinary flow, and feeling of incomplete bladder emptying. Chronic unrelieved obstruction may cause distension of the urinary tract proximal to the site of obstruction with injury to the kidneys or bladder musculature and innervation. It may also predispose to urinary tract infections. Lower abdominal pain and distension may or may not be accompanied by a sensation of a need to urinate. Chronic urinary retention may result in constant discomfort, slow urinary flow, urinary frequency, and a sensation of incomplete bladder emptying.

Causes include tumor masses causing obstruction (e.g., prostatic hypertrophy or cancers of the prostate, cervix, vagina, or vulva cancers obstructing the urethra). Surgical denervation may occur during radical hysterectomy or prostatectomy.

On examination, the patient may be distressed and agitated. The bladder may be palpable superior to the pubic symphysis. Insertion of a catheter (urethral or suprapubic) will provide a measurement of the residual volume, a specimen for urinalysis, and relief of discomfort. Urinary tract ultrasound should not delay treatment of the symptomatic patient but can provide imaging of the upper renal tract after correction of the acute problem.

While acute urinary retention is most appropriately treated with a temporary catheter, chronic retention may require either a long-term urethral or suprapubic catheter or intermittent self-catheterization. The frequency of self-catheterization is determined by the degree of retention (residual volume after voiding) and will generally be one to six times per day. Residual volumes under 100 ml do not require self-catheterization.

14 Ureteric Obstruction

Obstruction may be unilateral or bilateral. Unilateral obstruction may lead to impairment of renal function or renal failure if bilateral obstruction is present.

Causes include extrinsic obstruction by tumor (e.g., prostate, cervix, ovarian, colon), nodal metastases, retroperitoneal fibrosis, and postsurgical or radiotherapy strictures.

Intrinsic obstruction may be due to tumor or calculi.

Unrelieved bilateral obstruction (or unilateral obstruction with impaired renal function of the contralateral kidney) may cause rapidly progressive renal failure, drowsiness, loss of consciousness, and death.

Patients with ureteric obstruction may be asymptomatic or may present with classical loin to groin pain. They may show signs of sepsis and renal impairment/renal failure. Symptoms include nausea and vomiting, poor urine output, and hematuria. Patients may develop dehydration due to nausea and vomiting.

Examination may reveal signs of dehydration and reduced consciousness. Abdominal examination will often reveal unilateral or bilateral renal angle tenderness. Ultrasound may confirm a dilated renal collecting system. A CT nephrogram will confirm the obstruction and the transition point.

Renal cortical thinning on CT imaging may reflect chronic obstruction. Creatinine levels should be checked prior to imaging as contrast is not usually used in the presence of raised creatinine to avoid worsening of renal function. In some circumstances, aggressive prehydration may reduce the potential for damage to renal parenchyma (Sadat 2014).

Management will depend on the underlying condition, treatment history, and the patient's life expectancy. Electrolyte disturbances such as raised potassium may need to be treated urgently

with resonium given orally or rectally. Fluid balance will require careful management. Antibiotics may be given for infection where appropriate. Analgesia may be prescribed for pain (care must be taken with nonsteroidal anti-inflammatory agents and dose adjustment of narcotic analgesia in the setting of impaired renal function/renal failure may be necessary).

Treatment to relieve obstruction should be carefully considered in the context of the patient's prognosis. If the prognosis is poor and relieving the obstruction will not improve the patient's quality of life, the option of not relieving the obstruction should be considered. This option should be discussed with the patient, together with a description of what the procedure for relieving obstruction involves, the potential toxicities, and complications weighed against the benefits that may be achieved by relieving the obstruction in the context of the patient's remaining lifetime.

If the decision is made to relieve the obstruction, cystoscopy with insertion of a ureteric stent to relieve the blockage may provide short-term benefit. If a retrograde ureteric stent(s) cannot be passed, unilateral or bilateral percutaneous nephrostomy tubes may be inserted by an interventional radiologist to relieve obstruction until the underlying cause is treated. Antegrade stents may be passed percutaneously. Complications associated with percutaneous nephrostomies and those of stent placement include retroperitoneal hemorrhage, hydrothorax, pneumothorax, and intraperitoneal urinomas. Patients find percutaneous stents cumbersome to manage with the attendant skin irritation, urine leakage, and risk of dislodgement. Complications such as infection, irritation with urinary frequency, dysuria, hematuria, urinary incontinence, and pain may also occur. They may require repositioning and may migrate. Stents will require changing at 3–6 monthly intervals if left in situ.

Ureteric stenting is reasonable in newly diagnosed patients, in whom there is a reasonable likelihood of tumor regression with either radiotherapy, chemotherapy, or surgery.

Targeted radiotherapy may be considered if there is an obstructing malignant lesion that can be identified. The use of image-guided radiotherapy and modern radiotherapy techniques enables accurate targeting of the obstructing lesion with less toxicity to surrounding normal tissues. As with ureteric stenting, patients need to be informed of the potential toxicities and the benefits of relieving the obstruction.

More invasive procedures such as urinary diversion have a limited role in the palliative setting, except in the occasional patient who would be anticipated to have a significant life expectancy with treatment of the underlying condition.

15 Ureterovaginal Fistula and Vesicovaginal Fistula

These are abnormal tracts between the ureter or bladder and the vagina, causing uncontrolled discharge of urine through the vagina. They may be associated with other symptoms such as pelvic pain, vaginal bleeding, and infection. Constant urine exposure to the skin may cause skin irritation. As the patient is incontinent, this is a cause of significant morbidity. As well as impacting on the patient's emotional and psychological well-being, it may result in total social isolation.

Prolonged obstructed labor is the most common cause worldwide. Tumor-related causes include direct invasion of the urinary tract together with complications of surgery and/or pelvic irradiation. Patients with bladder invasion by tumor are more likely to develop a fistula following radiotherapy. Surgery-related fistulas usually present within 7–30 days postoperatively. Those related to radiotherapy (rare with modern radiotherapy techniques) are usually a late complication, occurring 30 days to 30 years post-treatment. These may be associated with other signs of radiation-induced injury such as bladder contracture or hematuria. The risk is increased with combined modality treatment (e.g., surgery and radiotherapy).

Careful speculum examination may reveal the site and nature of fistula, but it may be difficult to

distinguish clinically between induration from radiotherapy or from tumor. Examination may also reveal a concomitant rectovaginal fistula or other fistulas. Indigo carmine dye given intravenously will appear in the vagina within 30 min if a fistula is present. It may require several tampons placed in the vagina to differentiate leakage per urethra from a fistula. An MRI scan may show the site of the fistula and confirm the cause as tumor recurrence or treatment complication.

Urine should be collected for culture via a catheter and infection treated. Biopsy of the fistula tract may be performed to confirm malignancy. An intravenous urogram or retrograde pyelogram should be performed to assess the upper urinary tract before cystoscopy is be performed to examine the urethra and bladder for a potential site and evaluate the condition of the bladder for possible surgical management.

Malignant fistulas are complex conditions which should be managed in the multidisciplinary setting within a specialized unit.

Radiotherapy to the pelvis to control the tumor may allow the bladder mucosa to heal. Continuous drainage of the bladder with an indwelling catheter will facilitate healing of the bladder musculature and mucosa. Where conservative management fails, urinary diversion may be considered depending on the prognosis. This is a major surgical procedure with considerable risk of morbidity.

Vesicovaginal fistulas secondary to surgical complication should initially be treated conservatively with placement of a urinary catheter for 7–30 days to allow healing of the fistula. Similarly, placement of a retrograde or antegrade ureteric stent or a temporary percutaneous nephrostomy will facilitate healing of a ureteric defect. A major ureteric leak into the abdomen may require placement of peritoneal drain under radiological guidance. A CT intravenous pyelogram (for ureteric defects) or cystogram (for bladder defects) prior to catheter removal will confirm integrity of the renal collecting system.

Minimally invasive surgical techniques may be appropriate for intraperitoneal bladder defects if conservative management has failed.

16 Rectovaginal Fistula

Rectovaginal fistula occurs when an abnormal tract develops between the rectum and vagina (Champagne and McGee 2010). This causes uncontrolled leakage of stool and gas into the vagina. Symptoms may also include purulent vaginal discharge and pain in the pelvic region. Because of the incontinence of stool and gas through the vagina, rectovaginal fistulas have a significant impact on the patient's quality of life and socialization.

Malignant or nonmalignant fistulae are a major cause of morbidity, either as a result of malignancy or as a complication of treatment.

The history will suggest passage of flatus or feces per vaginam. A careful speculum examination may reveal the site of leakage. Vaginal and rectal examination may also reveal the site of the fistulous opening, but small defects may be difficult to locate, particularly in the presence of induration from radiotherapy or active malignancy. A flexible sigmoidoscopy or colonoscopy should be performed. Gastrografin CT scan may show the fistula and demonstrate the cause such as a tumor. MRI scans should be performed by a radiologist with expertise in pelvic imaging and may show linear gas tracking along the fistula.

The distance from the external anal sphincter, the current disease process, and prior treatment will dictate potential treatment. Fecal diversion with a laparoscopic end colostomy is relatively low-impact surgery in patients with a reasonable prospect of medium-term survival.

Resection of the area of affected rectum with stapled reanastomosis and a protective temporary ileostomy is a more invasive option and one reserved for patients with likely survival beyond the medium term. It requires careful discussion with the patient who may have unrealistic expectations of the physical impact of major surgery.

17 Conclusion and Summary

Genitourinary symptoms are common in palliative care and may significantly impact on patients' quality of life. Careful assessment including

history and directed investigation will usually provide a diagnosis. Decisions on treatment must be made in the context of the severity of the problem, medium- and long-term prognosis, and the wishes of the patient. While many treatment options are available, good clinical judgment, multidisciplinary care and patient input are imperative in the decision pathway toward relieving symptoms.

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End-of-Life Symptoms

29

Christine Sanderson

Contents

Abstract

Safe care at the end of life involves much more than just prescribing for end-of-life symptoms. An approach of whole person care is one in which respect for the individuality of the dying person is fundamental, and this can sometimes present real challenges for clinicians. Diagnosis of dying is a key clinical skill, and the use of triggers can assist clinicians to recognize patients who are likely to enter the terminal phase soon. Early recognition creates the opportunity to plan care and to share decision-making about goals of care with patients, allowing more choices about how and where the dying person may wish to be cared for. Common symptoms at the end of life include pain, nausea, respiratory secretions, dyspnea, agitation, and delirium. Prescribing for the end of life involves, on the one hand,

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_105

ceasing unnecessary medications and interventions and, on the other, providing and using comfort medications appropriately and effectively. Psychosocial care of the dying person focuses on their personal and spiritual needs at the end of life. Decision-making about what interventions are appropriate at the end of life is based on weighing up the likely benefit versus the burden of such interventions, assessing this in the context of the patient's prognosis. Decision-making at every stage must include the dying person as much as they are able and wish to, as well as their family and close supporters. It is therefore essential that clinicians are able to communicate comfortably and empathically about end-of-life concerns.

1 Introduction

So come, my friends, be not afraid. We are so lightly here.
It is in love that we are made. In love we disappear.
Though all the maps of blood and flesh are posted on the door,
There's no-one who has told us yet what Boogie Street is for.

From "Boogie Street," Leonard Cohen. *The Book of Longing*. Harper Collins, New York. 2006

Care for dying people at the end of life is a core role of palliative care. It is also a responsibility that is shared with every domain of medicine, and as such it is "everyone's business." The palliative care approach acknowledges that death is a normal, inevitable, mysterious, and natural phenomenon in which the focus of care should be to comfort and support. Palliative care practitioners have played a very significant part in putting the care of dying people onto the health-care agenda as a domain requiring evidence, skills, and appropriate models of care. Being able to die a natural death with distressing symptoms treated, to have choices wherever possible about where death occurs and who is present, and to be given culturally appropriate care that supports one's individuality and dignity and is responsive to psychological and spiritual needs – these are appropriate outcomes for end-of-life care and are indicators of quality care for the dying. An example of a statement of the principles associated with safe dying (Box 1) is contained in the Australian Commission on Safety and Quality in Health Care *National Consensus Statement* (ACSQHC 2015).

Box 1 Guiding Principles for Safe and High-Quality End-of-Life Care. Australian Commission on Safety and Quality in Health Care. National Consensus Statement: Essential Elements for Safe and High-Quality End-of-Life Care (ACSQHC 2015)

1. Dying is a normal part of life and a human experience, not just a biological or medical event.
2. Patients must be empowered to direct their own care, whenever possible. A patient's needs, goals and wishes at the end of life may change over time.
3. Providing for the cultural, spiritual and psychosocial needs of patients, and their families and carers is as important as meeting their physical needs.
4. Recognising when a patient is approaching the end of their life is essential to delivering appropriate, compassionate and timely end-of-life care.
5. The prognosis and the way that people respond to medical treatment will vary between individuals. This means that there is potential for ambiguity and uncertainty at the end of life. This must be honestly and openly acknowledged, and discussed with patients, substitute decision- makers, families and carers.
6. Safe and high-quality end-of-life care is patient and family-centred. Whenever possible, it should be aligned with the values, needs and wishes of the individual, and their family or carers. Such care should consider the patient's expressed wishes regarding the

(*continued*)

Box 1 (continued)

circumstances, environment and place in which they wish to die.

7. Safe and high-quality end-of-life care requires the availability of appropriately qualified, skilled and experienced interdisciplinary teams.
8. Safe and high-quality end-of-life care requires effective communication, collaboration and teamwork to ensure continuity and coordination between teams, within and between settings, and across multiple episodes of care.
9. Care of the dying is urgent care. Timely recognition of a patient's transition to the terminal phase of life must be documented and communicated to patients, families, carers and other health professionals by the interdisciplinary team. The care plan must be specifically revised to meet the unique needs of the patient, family and carers during this phase.
10. End-of-life decision-making should be shared between the interdisciplinary team and the patient. Substitute decision-makers, families and carers should be involved, in accordance with the patient's expressed wishes and/or jurisdictional legislation.

Nonetheless, in developed countries many people die in hospitals while receiving care that is burdensome and non-beneficial, with continuing investigation, monitoring and treatment, and lack of good symptom management, and the goals of care do not shift toward comfort and palliation of symptoms until quite close to the patient's death (O'Brien et al. 2006; Wright et al. 2014; West et al. 2014; Swerrisen and Duckett 2014; Henson et al. 2016). Other settings of care (home, residential aged care facility) may allow an experience of death which is less interventional, but these present different challenges in order to ensure that care and symptom management are adequate and responsive to the patient's and family's needs. This chapter will discuss care of dying people and explore the practical implementation of principles of safe end-of-life care.

2 Whole Person Care: The Dying Person and Their World

The aim of palliative care for dying patients is to promote their comfort and dignity. However, it is important for clinicians to be aware that what is meant by comfort and dignity may be very different for different people. Their life experiences; their networks of relationships; their values and beliefs; their strategies for coping; the experience of and meaning given to their symptoms, illness, and death; their perception of death as a tragedy, as meaningless, or as the completion of life; and the story of how their illness has brought them to be dying at this particular time and place – all of these things go into the individual's own construction of what is meant by comfort and dignity. This is what clinicians must try to respond to.

Clinicians who work in palliative care inevitably become very familiar with the appearances and symptomatology of dying people. This very familiarity, however, may dull them to the mystery of this once-only process for the dying person her- or himself and for all those who care about them. Clinicians need to be able to treat each person as an individual, but meeting the very individual wishes and needs of dying people may require considerable creativity and flexibility. Sometimes this is in tension with other goals of providing good palliative care, with their focus on the provision of evidence-based care and protocol-based care planning. Negotiating processes of care with the dying person and their network of supporters requires some space to be left within protocols, guidelines, and pathways to enable clinicians to individualize their responses. This is a very fundamental tension within palliative care and particularly in inpatient settings may sometimes create ethical, clinical, and human dilemmas.

When clinicians care for patients, a degree of medicalization is inevitable. Assessment and care processes allow us to define and manage problems

within a clinical framework, but this can sometimes be experienced as an intrusion within the world of the dying person. Even when patients are cared for in their own home, this medicalizing process still occurs, changing the home environment into something more institutional, intruding on people's privacy, and taking some of the decisions about how to care for the dying person away from family and friends, putting them instead in the hands of clinicians. Great gulfs of mutual misunderstanding can sometimes arise from differences in culture or when caring for those in stigmatized or socially marginalized groups. Difficulties in relating to health-care providers which may have been present throughout the illness trajectory will often intensify at the end of life. Care for dying people ultimately requires great trust from them and from their friends and families, and this trust is needed most at the time when distress and care needs are peaking. Some dying people and their supporters may struggle with conflicting concerns – their intensifying needs for help, care, and information on the one hand, versus distress at being caught within a health-care system that is experienced as intrusive or threatening on the other (Luckett et al. 2011; Hanssen and Pedersen 2013; Francois et al. 2017).

In the intimate space of the dying person's world, clinicians have to be mindful of how their own anxieties and judgements, and the language in which these are expressed, can make people feel more or less safe and accepted. A whole person care approach requires acknowledgment of different worldviews – views that may potentially be very challenging during the intensity of the final days and hours of life, which is a time when these things matter very much to people. There may not always be a way to resolve the resulting tensions; however, care is able to be more authentic and honest if any differences are acknowledged and respected. That in itself helps to build trust. Individual and team clinical processes such as case reviews, mentoring, and debriefing are important in creating a culture of whole person care and may help clinicians to meet each dying person as a person with a new story, afresh, and still thrive while doing this work.

3 Planning for Expected Death

For most palliative care patients, death can be regarded as expected, based on the nature of their condition and the lack of curative treatment options available for them. Expectedness creates the opportunity for planning and choices about care and treatment and for dying people to focus on their own priorities in the last period of their life. However, this opportunity is largely dependent on clinicians being willing to talk clearly about prognosis, being comfortable to discuss dying with patients and their families in a timely way, and being aware of the options that are available in their own community to allow choices for people who are dying, such as referral to palliative care services (Clayton et al. 2007). Many patients and families are still shocked and unprepared for the dying process, even when this is thought by clinicians to be expected (Sanderson et al. 2013; Kehl 2015; Ek et al. 2015; Lamden et al. 2016).

For those people who would prefer to die at home, careful planning for an expected death is needed to ensure that end-of-life symptoms are able to be treated appropriately. Strategies such as the Gold Standards Framework (http://www.goldstandardsframework.org.uk/home) provide a model of care that can guide provision of end-of-life care in a primary care setting. Preemptive prescribing for end-of-life symptoms is important to allow prompt initiation of treatment in the event of a sudden deterioration, and this involves ensuring that there is ready, safe access to needed comfort medications, which is especially critical when a home death is planned (NICE 2015). Documenting an advance care plan to ensure that transitions of care (between home and hospital, or between different settings of care) can be made safely if required is another essential element in planning for an expected death. Such documentation is needed to protect dying people from unwanted and burdensome interventions such as cardiopulmonary resuscitation. Preparation of family carers to look after a dying person at home is also essential, and ongoing support and access to advice will be needed.

4 Diagnosing Dying

In order to be able to provide appropriate care and to cease treatments that are no longer beneficial, it is essential to be able to diagnose dying – yet it is not always easy to identify the point at which a patient who is approaching death makes the transition to being a dying patient (Haga et al. 2012).

Symptoms associated with the onset of the terminal phase have been identified in a number of studies. A systematic review identified the most common symptoms found in patients who are dying as dyspnea (56.7%), pain (52.4%), respiratory secretions/death rattle (51.4%), and confusion (50.1%) (Kehl and Kowalkowski 2013). Functional changes, particularly the inability to swallow, reduced oral intake, reduced level of consciousness, and becoming bedbound, have traditionally been used as criteria to identify dying patients in end-of-life care pathways, but these have not been prospectively validated in robust studies (Chan and Webster 2011; Phillips et al. 2011; Watts 2012). However, a large cohort study based on the use of standardized assessment tools for symptom burden and functional state confirmed that at the time of entering the terminal phase, more than 90% of patients were bedbound and 50% were either comatose or barely rousable. The majority (73.6%) of the patients who were identified as being in the terminal phase in this study survived no longer than 2 days, 23.2% of them dying on the same day that they were assessed as being in the terminal phase (Clark et al. 2016).

The terminal phase therefore presents with a fairly recognizable syndrome, and in acute care settings, the onset of the terminal phase is very often the main trigger for ceasing active treatments and for changing goals of care (Cardona-Morrell et al. 2016). However, given the features of this syndrome, the associated alterations in the level of consciousness, and how rapidly it may progress to death, it is important to understand that the onset of the terminal phase is far too late for many of the social, spiritual, and relational tasks that are important to dying people (Steinhauser et al. 2000, 2014; Virdun et al. 2015). In particular, for families who may wish to care for their dying family member at home, earlier planning and decision-making is absolutely essential. The diagnosis of dying is a clinical assessment, and it is important that this should be a positive diagnosis made in a timely way, rather than happening at the last hour. No single diagnostic tool or measure has been identified that can support clinicians in identifying the dying patient, particularly across different diagnostic groups and in varied settings. One evolving strategy is the use of "trigger tools" or identification of sentinel events that can prompt clinicians to consider whether a patient may be at risk of dying soon (Hussain et al. 2014) and if so to reassess their goals of care accordingly (Box 2). This allows preemptive prescribing for end-of-life symptoms and encourages earlier discussions with the patient and their family, so that they can participate in decision-making and make informed choices about their wishes for treatment and care.

Box 2 Triggers and Sentinel Events Indicating Patient Is Approaching End of Life (Adapted from ACSQHC 2015)

- Diagnosis of life-limiting conditions
- Poor or incomplete response to medical treatment, continued deterioration despite medical treatment, and/or development of new clinical problems during inpatient admission
- Repeated calls to the rapid response team, particularly if the patient has been admitted for more than 1 week
- Advanced age with increased frailty, reduced mobility and increased dependence on others to assist in performing activities of daily living
- Moderate to severe dementia
- Multisystem comorbidities (cardiovascular, pulmonary, endocrine, etc.)
- Maximal medical therapies already in place
- Decline in the patient's condition, or a clinical determination that they will not

(*continued*)

Box 2 (continued)
benefit from interventions such as surgery, dialysis or treatment in intensive care
- Multiple recent admissions to hospital for exacerbation of a chronic condition
- Unexpected or inappropriately prolonged stays in hospital
- Request by patient or family or family to review goals of care, or for palliative care input

Deciding that a patient is at risk of dying soon requires an assessment of the person's overall condition, illness trajectory, performance state and level of functioning, their past responses to treatment and the likely outcome of treatment now, and their wishes. Understanding when a patient's problems are no longer likely to be reversible, or when multiple problems have additively overwhelmed a person's ability to recover, is an important clinical skill which is rarely formally taught. Factors that impede the identification of the dying patient have been studied (Kennedy et al. 2014), and many relate to the "treatment orientation" of health-care providers. The presence of clinical uncertainty often leads health-care providers to default to continuing active management while neglecting the dying person's comfort and their human needs. The process of assessing the potential reversibility of a patient's problems may in itself lead to a cascade of burdensome treatments and investigations, particularly if a holistic assessment of the patient's overall condition and wishes has not been made. The clinical cascade in response to uncertainty often results in postponing important conversations and decisions until very late – indeed these may not happen until the patient themselves can no longer participate. Even when a situation is clinically challenging, particularly when there is a degree of clinical uncertainty, sharing decision-making processes with the patient and their family can sometimes provide a path through the available options. If it is possible to have a conversation focusing on what is important to the person now, in the context of having a short time to live, that can be extremely helpful in coming to agreement about goals of care and the tradeoffs that may be involved in different options.

5 Symptoms at the End of Life

5.1 Fundamentals of Physical Care

As death approaches, it becomes ever more important to actively and regularly assess all aspects of a dying person's physical comfort and to prescribe preemptively for the common symptoms that can be expected. Assessment of a person who is not able to respond verbally requires careful observation for signs of discomfort or pain and regular focused examination related to comfort. Frequent attention to skin and mouth care, to the eyes (e.g., by providing lubricating eye drops), to the sleeping patterns, and to the person's mental state (whether the person is aware and able to communicate, whether they appear relaxed or distressed or fearful, whether there is any evidence of hallucinations) is part of the routine of caring for patients entering the terminal phase.

Supporting bladder and bowel function should be individualized according to the person's physical needs and functional state and are essential for comfort. For many patients, the capacity to toilet themselves independently is a fundamental component of dignity, and so any intervention needs to be offered with sensitivity. Unidentified urinary retention or fecal impaction is a significant cause of distress in dying patients and should always be checked for when a dying patient is restless and agitated. In-dwelling catheters have a place – they may be required if there is urinary retention, to protect the skin of an incontinent patient, or to prevent unnecessary moves for a patient in significant pain or other distress. However, a person with minimal urinary output and none of these problems may not necessarily require a catheter. Management for the bowels changes as patients approach death. Once they are no longer able to take oral aperients, gentle and judicious rectal intervention may sometimes be needed for comfort.

The most common symptoms that need to be looked for and addressed at the end of life are pain, nausea, respiratory secretions and respiratory distress, and delirium/agitation (NICE 2015; Blinderman et al. 2015). When a person is able to communicate, it is important to check with them about these and any other symptoms regularly. When a person is unable to communicate, the assessment is based on behaviors, for example, wincing, vocalizing, or stiffening when moved. Other assessments that are important relate to adverse effects of medications and treatments, for example, the presence of frequent fleeting myoclonic jerks, particularly associated with confusion, suggests opioid metabolite accumulation, while worsening edema while fluids are being administered suggests a need to cease parenteral fluids.

Pain is a feared problem and all dying patients require access to pain medications. Being bedbound, unable to move independently, and cachexic will produce a level of discomfort in many people even if there are no specific sites of pain. As needed opioids are the most appropriate choice to deal with this and should generally be given prior to turning the person or doing other personal care. Those previously on regular pain medications should have these continued in a parenteral form to maintain pain control and prevent withdrawal, possibly with some dose reduction to adjust for the changed metabolic parameters of the dying process, but with rapid access to as needed doses for any episodes of extra pain. Regular review of pain medication use and adjustment of doses are essential. Good explanations for families are also incredibly important, as the use of opioids in dying patients can be misinterpreted. Each breakthrough dose of any medication should be explained to the family, if they are present, and families should be encouraged to help assess the person's symptoms and response to medications if they are able to do so (NICE 2015).

Nausea is often not easy to identify in a patient who is not alert. Reduced oral intake, including reduction in the number of oral medications, may reduce nausea for some patients. However, patients for whom nausea has been an ongoing problem, or who have a partial or complete bowel obstruction, should have regular parenteral antiemetics continued. When rationalizing a patient's medications at the end of life, it is helpful to be aware that a range of medications may have antiemetic properties via different mechanisms, for instance, dexamethasone, antipsychotics, and antihistamines are all reasonably effective against some types of nausea. Patients on some or all of these agents may not require an additional regular antiemetic. All patients should, however, have an as needed antiemetic available, and wherever possible this should be selected on the basis that it is an agent which has been previously effective (Glare et al. 2011).

Respiratory secretions occur commonly in dying patients, usually in association with reduced level of consciousness and consequent loss of the normal ability to manage upper respiratory tract secretions. However, lower respiratory tract secretions secondary to edema or infection may also contribute. In general, it is thought that this problem is not distressing for patients, as it occurs most often when people are minimally conscious; however, some families may find these secretions (often called "death rattles") very disturbing indeed. There is little evidence to support the use of antisecretory medications (Wee and Hillier 2008), and the preferred treatment involves frequent repositioning. Many medications used traditionally are strongly anticholinergic (e.g., atropine or hyoscine hydrobromide) and have a side effect profile that is associated with adverse effects in patients who are aware, such as dry mouth, urinary retention, and delirium. If antisecretory agents are used, they should be trialled soon after symptoms are noticed, and agents that do not enter the central nervous system are preferred (hyoscine butyl bromide, or glycopyrrolate).

Gentle suction may be appropriate if secretions are copious and visible, if the patient tolerates this. Discussion with the family is an essential part of care in relation to this problem (Wee et al. 2006) as some people will be left with distressing and traumatic memories of the person's death that are connected to this symptom.

Respiratory distress may be suggested by increased respiratory rate and/or visible effort of breathing. Abnormal respiratory patterns such as Cheyne-Stokes or Kussmaul's respirations are caused by significant dysregulation of normal breathing physiology, and families should be counselled to expect these changes. If there is any suggestion of increased respiratory drive or air hunger, opioids can be titrated to reduce the respiratory rate. The goal of oxygen therapy is comfort, not normalization of oximetry. It is not without adverse effects, such as pressure injuries from tubing or drying of mucous membranes. A patient who is dying of predominantly respiratory causes, such as upper airway obstruction or lymphangitis carcinomatosis, may sometimes require palliative sedation to relieve their respiratory distress. Any patient with risk of respiratory failure who is still aware and is afraid that they may die with severe breathlessness should be reassured that sedation can be offered to reduce their awareness, and this information will often be gratefully received. Sedation, when given, should be at an effective dose, taking into account prior medication exposure, and levels of sedation should be reviewed regularly and titrated to effect. Midazolam is often the initial agent of choice due to its rapidity of onset, and in a distressed patient commencement of an infusion of midazolam and an opioid (usually morphine, which has the strongest evidence for relief of dyspnea) should be accompanied by an appropriate loading dose so that sedation is achieved rapidly (Vargas-Bermudez et al. 2015; Barnes et al. 2016; Simon et al. 2016).

Agitation is often multifactorial. Sources of pain, distress, and discomfort should be looked for and treated. Possible causes such as severe hypoxia, seizures, or akathisia should be considered. However, agitated delirium is extremely common at the end of life, most likely due to the progressive biochemical and physiological changes associated with the dying process, and if it is due to these causes, reversal is not expected (Bush et al. 2014a). As such it should be managed as a refractory delirium. In the past this syndrome has been referred to as terminal restlessness, but this term is best avoided as it reduces the likelihood that a proper assessment of the symptom will be made. Often the picture is of a dying person who is confused and disoriented, and is struggling to get out of bed, throwing off bedclothes or needing to move continuously, and who will only settle for very short times. Another common presentation is that of a person with reduced awareness who is plucking at the bedclothes, or performing other repetitive motor activities, who may be hallucinating and calling out or vocalizing. For the imminently dying patient diagnosed with a refractory delirium, the goal of treatment is to provide enough sedation that they can be calm and safe. Sedation at an effective dose with antipsychotics and/or benzodiazepines, or with sedating antipsychotics such as levomepromazine, is appropriate to obtain that goal, and – as in all symptom management at this stage – the discussion of this plan with families is essential (Bush et al. 2014b).

5.2 Preemptive Prescribing and Crisis Medications

As needed medications should be charted for comfort, including as a minimum adequate doses for pain, nausea, and agitation or delirium. Preemptive prescribing of comfort medications that can be given parenterally, along with good documentation of when they should be given, is a hallmark of good end-of-life care (NICE 2015). They minimize the problem of distressing delays in getting symptoms under control if a dying patient deteriorates more quickly than anticipated. Providing regular background medications is also important to maintain good symptom control, especially for pain. Rationalization of medications and ensuring that comfort medications can be given by an alternative route, if a patient is not able to swallow, are important.

Most often in palliative care the subcutaneous route is used for medications (NICE 2015) because this is a minimally burdensome parenteral route of delivery. Intramuscular and intravenous routes should generally be avoided due to the associated trauma for the patient. Subcutaneous lines can be maintained at home and have a low

risk of infection. Syringe drivers can reduce the need for frequent bolus doses to be given and allow steady state to be achieved. However, occasionally an alternative route needs to be considered, for instance, in a patient who is profoundly edematous or whose subcutaneous sites break down very quickly. In these patients intravenous access might be needed, but other options might be to use sublingual, topical, or rectal medications if appropriate.

Crisis medications are usually charted for patients who are at risk of specific end-of-life emergencies, e.g., major bleeding, airway obstruction, seizure, and so on. In the hospital setting, prescribing such medications is intended to ensure that there can be a rapid and appropriate response, allowing the person to be sedated quickly to minimize distress. Doses of opioid and midazolam are most often prescribed, and they should be adjusted according to whether the person is opioid and/or benzodiazepine naïve or not. It is important to individualize and provide an effective dose to achieve sedation. Crisis medications should only be used for likely preterminal events. Prescribing crisis medications in residential aged care or for patients dying at home is more complex, as they may not be able to be rapidly administered and may take carers' attention away from the dying person at the time they most need someone with them.

5.3 Review of Medications and Proportionate Dosing

Regular review and, if necessary, titration of medications is essential. Even when a patient is dying, medication doses need to be proportionate and defensible. Good palliative care involves careful choice of both drug and dose, according to the symptoms that are being experienced, and assessment of the benefits and any adverse effects (NICE 2015). Goals of treatment should be explicit, negotiated, and documented, for example, if sedation is the goal of care wherever possible that should be offered to and discussed with the patient (if they are able to communicate) and the family. Conflicting agendas may cause difficulties. For instance, patients and families may have concerns about euthanasia, or may be seeking assistance to hasten the person's death, or alternatively may be fearful that inappropriate prescribing is causing the deterioration of their family member. Addressing these concerns is important in the palliative care context. As euthanasia and assisted death are being very widely discussed and are available in some jurisdictions, it is ever more important to be absolutely clear about the intent of all palliative treatments, particularly where they involve opioids or sedation.

5.4 Fundamentals of Psychosocial Care

A person who is aware that they are deteriorating or dying may have fears, worries, or concerns that they wish to discuss. It is important to ask about this and to identify who it is that they would most like to discuss any issues with. Another helpful question is to ask if the person has any important goals that they need assistance with. The general need for companionship and conversation varies greatly, and this should be explored, without making assumptions. Not everyone will be distressed or in need of companionship.

Supporting dying people may also involve conveying their wishes back to their family and other visitors and helping them to manage who and how many people visit and for how long. Some patients do not wish to be a burden on their family and friends and may seek to minimize time with them for that reason. It can sometimes be helpful in that situation to explain that for people who are likely to be grieving their loss, time spent now can be extremely precious and can help them to recover better during their bereavement. Some patients wish for spiritual support (Best et al. 2016) – whether it be from a minister or chaplain from their own faith community or simply a chance to discuss what is on their mind with a good listener. However, it is also quite common for dying people to have no spiritual concerns or needs.

Be aware that in among all the end-of-life concerns, what many dying people greatly

appreciate is to be treated more or less normally – to talk about what is going on in the world, in their family, to discuss the weather, or just to share a joke. As well as helping to normalize what is happening to them, such interactions can reconnect a person to their threatened sense of themselves, in a situation where much of their previous life and identity is vanishing. Many palliative care services have volunteers, pastoral care workers, or other team members who can support patients in this way, when the family struggling with their impending loss and the changes in the dying person may find it difficult to do so. Appropriately modified gym activities and diversional therapies that have the goal of supporting function are often not considered for dying patients, yet they can have great psychological value at this time, as patients may sometimes feel that they are "just waiting to die." Dignity therapy (Ostlund et al. 2012; Guo and Jacelon 2014) at the end of life can be of particular benefit for dying patients whose sense of loss of personhood might otherwise overwhelm them. Even without such a specialized response, when a person is dying in an inpatient setting, every person that steps into their room has the opportunity to recognize and behave toward them in a way that supports their personhood. This is possibly one of the most therapeutic and under-recognized "interventions" in palliative care.

6 Management Decisions

Care for dying patients is anchored in the simplest principle of all. It is helpful to return regularly to the question of whether a given treatment, investigation, or procedure contributes anything to the comfort of the dying patient: any treatment or activity that does not add to the person's comfort can be ceased. However, for many patients and families, such decisions may be difficult and confronting. Misunderstandings may cause conflict, for instance, related to a perception that a dying person is not being given the care that they need. Thus, part of the difficulty for many clinicians at this stage is how to work through these decisions with the patient and their family.

6.1 Stopping Medications and Investigations

When the irreversibility of the dying process is clear, then most long-term medications for comorbid conditions offer no benefit and indeed may create harm in terms of cost, burden of tablets, drug interactions, and greater risk of adverse effects as the dying patient becomes less and less able to eliminate medications (Stevenson et al. 2004; Currow et al. 2007). Once patients are no longer able to swallow, many of these decisions "make themselves." However, discussion with patients and families is still very important, as ceasing medications can sometimes be seen as clinical fatalism or abandonment or may act as a confronting reminder of the imminence of death. When decision-making is individualized and explained, and when the rationale is the dying person's comfort and well-being, it will usually be accepted.

Routine observations such as checking of blood pressure and pulse, or routine blood tests, also contribute nothing to the care of the dying patient, whose physiological parameters are likely to be abnormal. Investigations and observations at this time are only useful to answer specific clinical questions, and even then only if the answer that is yielded will be appropriate to act on for that patient. However, routine assessments of patients' comfort, including of their pain, mental state, and other symptoms, and of how the person's family are coping, should now become the focus of the daily care of the patient, replacing those clinical priorities which are no longer important. Some hospitals have attempted to address this shift in care processes by replacing standard patient charts with a specific "comfort chart" for dying patients.

For some medications, withdrawal or inability to take via an oral route can be associated with problems or symptoms which may need to be carefully considered, and sometimes replacement with alternative treatments may be appropriate. Common examples of medications requiring some consideration are included in Table 1.

Table 1 Alternatives to some common long-term medications which can be used in end-of-life care

Oral medication	Alternative management strategy for end-of-life care
Antineuropathic agents	Monitor for worsening of pain and titrate opioids to compensate
Anti-inflammatories or gout medications	Dexamethasone given subcutaneously may provide anti-inflammatory cover if clinically required
Anticonvulsants	A patient who is on anticonvulsants after having had seizures should be converted to a long-acting benzodiazepine such as clonazepam. If anticonvulsants were prophylactic only, as needed doses of clonazepam should be made available, but the patient may not require regular doses
Anti-parkinsonian medications	Subcutaneous apomorphine or topical rotigotine may be appropriate for patients with severe Parkinson's disease even in the terminal phase, to prevent them becoming locked-in by immobility
Oral laxative	Consider treatment per rectum if clinically indicated
Anticoagulants	It is usually appropriate to cease anticoagulants, particularly if they are prescribed for prophylaxis. However, if deep venous thrombosis is a cause of distressing pain, it may be appropriate to cautiously continue parenteral anticoagulants such as low molecular weight heparin, depending on the clinical situation
Oral hypoglycemics, long-acting insulin, or other diabetic medications	When oral intake is minimal, regular oral hypoglycemics and long-acting insulins should cease. Frequent testing of blood sugar is not required. Hypoglycemia presents a more significant risk than hyperglycemia. Check blood sugar if symptomatic, and treat with short-acting insulin for symptom control if required

6.2 Food and Fluids

Issues related to giving food and fluids in the last days of life can be extremely contentious to deal with. Families may be greatly distressed by the perception that a patient is not receiving enough nutrition, believing that this is the reason for the symptoms that the person is experiencing. The human and relational significance of food and drink should never be underestimated by clinicians, who need to be able to talk comfortably and empathetically with families and about this issue. In the past, there has been a tendency to routinely cease hydration in dying patients, and indeed this was institutionalized within some end-of-life care pathways and became one of the aspects of the Liverpool Care Pathway that caused much difficulty when poorly or inflexibly implemented (NICE 2015). Requests for parenteral hydration by families of dying patients are common (Gent et al. 2015). Little evidence exists to support any benefit of such treatment; there is some low-level evidence to suggest that it may improve nausea, but it may worsen ascites, without improving delirium or thirst or survival (Raijmakers et al. 2011). Artificial nutrition for dying patients has also not been shown to prolong life or improve quality of life (Chow et al. 2016).

As with everything else in the terminal stage, the patient's comfort is the best guide wherever possible. Most families can be helped to understand that eating is no longer a biological necessity for a dying person, but that small amounts of food and drink, when able to be tolerated, and if the patient wants them, may give some pleasure – which at this time is the main goal. Lack of appetite, nausea, swallowing difficulties, dyspnea, or fatigue may all be limiting factors in how much oral intake a dying patient will want. Families can be helped to make this assessment, recognizing that pushing a person to eat may cause them distress. Likewise fluids are for comfort for the patient. When dry mouth is a problem for palliative care patients, which it commonly is because it is such a common side effect of many palliative medications, the best treatments are good, frequent mouth care and safely offering oral fluids. Parenteral hydration does little to help with this

subjective experience (Raijmakers et al. 2011), but regular small sips of fluid, ice, mouth sprays, or topical administration of artificial saliva may be much more beneficial. Wherever appropriate, families can be encouraged to offer these, which can alleviate some of their own distress. However, it is also important to give some instruction about how to offer food and fluids safely, as many family members are unaware of the risks of aspiration for seriously ill patients. The idea of pleasure from oral intake can be further explored, encouraging the family to think about what the person might enjoy, for example, a frozen fruit or some ice cream, a sip of alcohol, or some soda water or lemonade.

Frequently in hospital, dying patients have been identified as being at high risk of aspiration and have been made "nil by mouth." In the palliative care context, this is usually inappropriate; however, some institutions have policies that are quite rigid once such an assessment has been documented in the medical record. The alternative is to allow and assist the patient and family to make an informed decision about what oral intake they wish to have, including whether and when they wish to use thickened fluids and modified texture foods or not. For patients who want to eat or drink specific things, wherever possible they should be allowed to do so with safety precautions, which include careful positioning, ensuring that the patient is alert when eating or drinking, and offering only very small amounts at a time (Pollens 2004).

6.3 Appropriate and Inappropriate Interventions for Dying Patients

Stopping treatments is often much harder than starting them. Clinicians should carefully consider clinical endpoints and prognosis whenever they offer any active interventions at the end of life. When interventions are given for non-reversible problems, it is likely that those treatments will need to be withdrawn subsequently. Consideration of how to manage that is as important as initiating the treatment itself; for example, withdrawal of ventilation can itself be regarded as a palliative intervention (Huynh et al. 2013).

Many problems are not reversible in the terminal phase, for example:

- Fatigue and weakness in the terminal phase cannot be relieved by transfusion of red cells or correction of iron deficiency.
- Metabolic derangements in patients dying of renal or liver disease are not correctable.
- Severe cachexia and hypoalbuminemia are not able to be reversed by artificial nutrition.

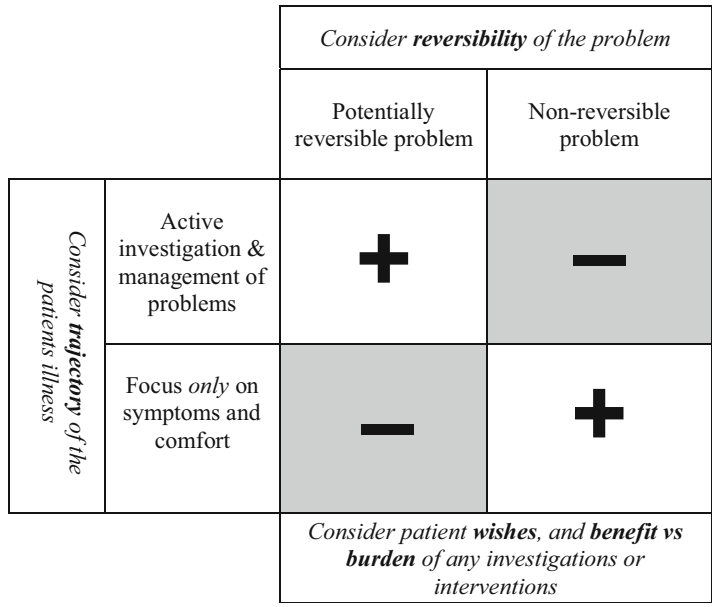
Even when it is possible to correct biochemical or hematological abnormalities, this almost invariably does not produce any meaningful clinical benefit for the patient and is not able to be sustained.

Some potentially reversible problems may be considered for treatment if they improve the comfort of the patient and treatment is not too burdensome, for example:

- Hypercalcemia causing confusion.
- Respiratory tract infection causing coughing of purulent sputum.
- Seizures affecting mental state.
- Acute intercurrent conditions – for instance, gout, atrial fibrillation, cellulitis – can all be treated for the comfort of the patient rather than to prolong their life.

Some potentially reversible problems could potentially require a significant intervention, such as spinal cord compression, or obstructive processes that may be able to be relieved by stenting. The value of any such treatment, however, will completely depend on the life expectancy of the person and their ability to tolerate the procedure itself. For the dying patient, ongoing anticancer treatment – whether with chemotherapy, immunotherapy, or radiotherapy – is only of value in the rare case that there is a defined symptom with likelihood of responding in the timeframe of the patient's life expectancy, for example, SVC obstruction that can be treated with radiotherapy (Table 2).

Table 2 A clinical approach to patient problems in end of life care



6.4 Trials of Therapy

When there is uncertainty around the reversibility of a problem, for example, a patient with sepsis or delirium, and particularly when this problem makes it unclear whether the patient is in the terminal phase or not, it may sometimes be appropriate to offer a trial of therapy. The other context in which a trial of therapy can be appropriate is when a patient or family are absolutely insistent on receiving more active treatment which is unlikely to be of benefit. A trial of therapy involves a time-limited course of treatment, and an appropriate therapeutic outcome, specified in advance. In this context, functional outcomes that are meaningful to the patient are the most helpful, for example, "to be able to comfortably spend the day out of bed." It may be important also to specify possible adverse effects of a treatment that would lead to stopping the trial. Discussing a trial of therapy for a patient who is approaching the terminal phase allows the clinician to be very clear about the context – which is that of very grave clinical concern – and thus can also help to prepare the patient and family for the possibility that death may happen soon. Often setting such clear goals gives patients and families a chance to adjust to their changing situation and can avert conflict about treatment, ultimately allowing them to be part of the decisions for a more palliative approach to care rather than fighting against them. Working through such a process carefully can help to maintain a strong therapeutic relationship, even where there is initial disbelief or great unreadiness for death.

7 Conclusion and Summary

Caring for patients at the end of life demands both clinical and human responses. This chapter has emphasized that none of the management approaches described should be allowed to become a rigid framework for care. Excellent care must always be grounded in evidence, but pathways and protocols are only ever a guide and on their own will not ensure that patients' profound human needs are met. This was an important lesson from

the implementation of the Liverpool Care Pathway (Neuberger 2013). The challenges of caring for dying people lie in how we respond to each circumstance, how we understand both the disease and the meaning of the disease, and in learning what dignity and comfort mean for each individual. Palliative care also cares for the family and loved ones of the dying person, during and after the death. This is a wide net and a serious responsibility. They too must be included in our care processes and decision-making to the very best of our ability.

Ultimately, our regular contact with death and dying should help us to be in safe hands for our dying patients, but never forgetful of the great human mystery we are witnessing. At the very end, we take them to that door, and stay with them, in order to see that they go through it safely. They depend on us to be their guide through a process that they have never experienced, but which we know familiarly.

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Part III

Palliative Care Professionals and Provision

Generalist and Specialist Palliative Care

30

Karen Ryan and Bridget Johnston

Contents

Abstract

This chapter considers the development of generalist and specialist palliative care practice and the emerging understanding of respective competences, roles, and responsibilities. Evidence relating to the effectiveness of partnership working and factors promoting (or hindering) collaboration are reviewed. Specialist and generalist palliative care practice are critically appraised through the lens of models of care. The question of whether research to date has adequately examined areas of commonality, separation, and overlap is posed, and the resultant implications for optimal palliative care practice are studied. An overview of research in the field of integrated care is provided, and it is suggested that consideration of integrated care frameworks offers opportunity

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_42

for greater conceptual and methodological clarity in the design and implementation of palliative care interventions and models of care. Worldwide ranking systems of specialist and generalist palliative care are reviewed, and variability in developmental stage between countries is highlighted. The chapter concludes that research in palliative care practice arguable remains largely siloed, considering either generalist or specialist palliative care interventions separately and failing to move to a space where consideration of the "whole" might be more advantageous than considering the sum of the parts.

1 Introduction

The ancient Greeks recognized the need to consider the respective places of both healing and treatment in healthcare. "To cure sometimes, to relieve often, to comfort always" is a phrase attributed to Hippocrates, among others. It reminds us that there has always been a need to care for the seriously ill and dying in medicine. However, the importance of comfort care was increasingly marginalized from mainstream medicine until the mid-twentieth century and the work of Cicely Saunders. When Saunders founded St Christopher's Hospice in South London in 1967, it quickly became a source of inspiration to others, and the palliative care movement spread globally. As the first "modern" hospice, it uniquely combined three key principles: education, research, and excellent clinical care that encompassed physical, psychosocial, and spiritual domains of need.

The role of specialist practitioners in the modern hospice movement was clear from the outset. Saunders explained the benefits of having skilled and experienced staff working in hospices, stating that "those working in them are specialists and from experience know how to deal with pain, fungating and eroding growths, mental distress, fear and resentment" (Saunders 1958: 40). The importance of nonspecialists in providing palliative care was also clear; indeed, Saunders said that one of the main aims of work at St Christopher's was that "... basic principles in teaching and research [should be] fed back into the health service" (Clark 2002). However, articulation of the exact role of nonspecialists and their relationship with specialists was more ambiguous. Ongoing definitional problems regarding palliative care contributed to lack of clarity over subsequent years.

As hospice and palliative care developed in the United Kingdom, interest in formally establishing it as a specialty grew. In 1987, palliative medicine became a sub-specialty of general medicine, initially on a 7-year "novitiate." Once this was successfully concluded, the specialty was established (Doyle 2005). The journey to specialty status was not without its opponents, however. Many arguments focused on whether palliative medicine was really a specialist territory and not more properly the domain of the primary care physician or treating specialist and whether specialty status would lead to further over-medicalization and marginalization of dying (Doyle 1994). Nevertheless, by 2014, 18 European countries had followed the UK's lead in establishing certification programs in palliative medicine (Bolognesi et al. 2014). The growth of palliative medicine was not confined to Europe, for example, the Royal Australasian College of Physicians created a pathway for sub-specialty training in palliative medicine with the first trainees starting supervised training in 1991. In 2006, the American Board of Medical Specialties approved the creation of Hospice and Palliative Medicine as a sub-specialty of ten participating boards.

To date, certification programs remain heterogeneous in content and structure, however, and the most appropriate certification system, not only for palliative medicine specialists but also for other disciplines, has not yet been agreed.

To a certain degree, the historic arguments about the advantages and disadvantages of specialty palliative medicine have been addressed by the model proposed by Quill and Abernethy (2013) where contributions from both specialists and nonspecialists in palliative care are valued. Quill and Abernethy argue that a care model is needed that distinguishes primary palliative care

skills (skills that all clinicians should have) from specialist palliative care skills (skills for managing more complex and difficult cases) so that they can coexist and support each other. In this "coordinated palliative care model," the primary care physician or treating specialist can manage many palliative care problems and initiates a specialist palliative care consultation for more complex or refractory problems. Patients may be returned to the sole care of the referring specialist or primary care physician once this is felt appropriate by all involved.

The authors argue that the advantages of this model offers are that it recognizes the important role of the primary (also known as "generalist" or "nonspecialist") palliative care clinician, allows increased access to specialist palliative care for those who need it, reinforces existing relationships, increases satisfaction and enhances the skills of all clinicians in palliative care, and potentially contributes to cost control by reducing the number of specialists routinely co-managing cases. On their own, specialist palliative care clinicians will never be able to care for all patients with palliative care needs, and increasing demand is already outpacing capacity. The fragmentation of the healthcare system is well recognized, and the addition of another layer of expert care, such as specialist palliative care, should only be considered when benefits outweigh disadvantages.

2 Defining Levels of Palliative Care Provision

The coordinated care model of Quill and Abernethy fits well with the thinking of the revised definition of palliative care published by the World Health Organization (WHO) in 2002 (Sepúlveda et al. 2002) and of the three-tier framework of the European Association for Palliative Care (EAPC) (Gamondi et al. 2013). The WHO description of palliative care as an "approach" to care and a core component of universal healthcare underscores the importance of weaving palliative care into the fabric of healthcare provision and making palliative care accessible to all that need it. The EAPC provides greater depth to the distinction between generalist and specialist practice by describing three recommended levels of education in palliative care for healthcare professionals (Table 1).

Table 1 Agreed levels of education currently adopted by the EAPC to reflect the scope and focus of professionals involved in the delivery of palliative care

Palliative care approach
A way to integrate palliative care methods and procedures in settings not specialized in palliative care. Should be made available to general practitioners and staff in general hospitals, as well as to nursing services and nursing home staff. May be taught through undergraduate learning or through continuing professional development
General palliative care
Provided by primary care professionals and specialists treating patients with life-threatening diseases who have good basic palliative care skills and knowledge. Should be made available to professionals who are involved more frequently in palliative care, such as oncologists or geriatric specialists, but do not provide palliative care as the main focus of their work. Depending on discipline, may be taught at an undergraduate or postgraduate level or through continuing professional development
Specialist palliative care
Provided in services whose main activity is the provision of palliative care. These services generally care for patients with complex and difficult needs and therefore require a higher level of education, staff, and other resources. Specialist palliative care is provided by specialized services for patients with complex problems not adequately covered by other treatment options. Usually taught at a postgraduate level and reinforced through continuing professional development

Reproduced from Gamondi et al. (2013)

Internationally, several policy and strategy documents recognize the place of these levels of palliative care provision and core competencies; however, variation does exist. In some documents, palliative care approach and general palliative care levels are collapsed into the one category of "generalist palliative care," while other documents provide further subdivisions of three EAPC levels. Notably, these documents do not address the core competencies or training needed by informal carers and volunteers, despite the significant contribution they make toward supporting people with both generalist and specialist palliative care needs.

The different levels should not be regarded as descriptors that value the contributions of one group over another; in fact, the opposite is true. The value of recognizing different levels of palliative care provision is as follows. First, recognition of different levels of competence and service provision emphasizes that many palliative care needs can be met by generalists without the need for referral to specialist services. Second, it can inform the development of palliative care training programs for generalists and specialists. Third, distinctions based on healthcare professionals' skills and training and patient complexity address ambiguity about the nature and scope of generalist and specialist palliative care and help clarify and value respective roles. Finally, defining levels of palliative care and their corresponding core activities facilitate measurement of the extent to which generalists and specialists are, respectively, addressing palliative care needs.

3 Respective Roles and Responsibilities of Generalist and Specialist Palliative Care Practitioners

As previously discussed, the coordinated care model proposed by Quill and Abernethy (2013) acknowledges the skills and expertise of both generalist and specialist practitioners. Indeed, the distinct advantages of supporting primary care providers to deliver palliative care were recently highlighted in a publication by the EAPC Taskforce in Primary Palliative Care (Murray et al. 2015). The Taskforce noted that primary care providers:

- Use their detailed knowledge of patients and families and strong relationships with them to reach all people with life-threatening illnesses and begin providing a palliative care approach immediately following diagnosis with a life-limiting illness.
- Address the various domains of palliative care needs including physical, social, psychological, and spiritual.
- Deliver care directly to patients in all relevant settings including home, clinics, and nursing or care homes.
- Support family caregivers and provide bereavement care.

The role of specialist palliative care providers then is to provide holistic care to patients and families with complex palliative care needs; support complex end-of-life decision-making; provide bereavement care; act as a resource for other healthcare professionals by providing education, training, and support; and demonstrate leadership in advancing the field of palliative care through research, practice, and policy development.

Rather than viewing the roles and responsibilities of generalist and specialist providers as discrete skill sets, some authors have suggested that palliative care input should be divided between generalists and specialists on a continuum (Ryan et al. 2014; Carroll and Quill 2015). "Core" competences are regarded as those attitudes, knowledge, and behaviors that are common to the care provided by all health and social care professionals. Discipline-specific competencies are described in ascending expertise of palliative care practice. There is broad agreement between bodies on what the core competences are that are common to all clinicians (Table 2).

Distinct groups of patients with varying levels of palliative care need may be identified as existing within the population of people with life-limiting or life-threatening conditions. A needs-based approach to palliative care provision advocates that services are provided based on need. For example, people who experience relatively uncomplicated (though potentially troubling) trajectories of illness should be cared for by generalist providers, while people who experience complex palliative care needs will require the input of a specialist palliative care team. Quality palliative care is best realized when strong networks exist between generalist and specialist providers and when clinicians work together to meet the needs of all people.

Table 2 Core competences for generalist and specialist palliative care

European Association for Palliative Care – ten core competencies in palliative care (Gamondi et al. 2013)	National competence framework for palliative care, Health Service Executive, Ireland – six domains of competence (Ryan et al. 2014)
Apply the core constituents of palliative care in the setting where patients and families are based	Principles of palliative care
	Communication
	Optimizing comfort and quality of life
Enhance physical comfort throughout patients' disease trajectories	Care planning and collaborative practice
	Loss, grief, and bereavement
Meet patients' psychological needs	Professional and ethical practice in the context of palliative care
Meet patients' social needs	
Meet patients' spiritual needs	
Respond to the needs of family carers in relation to short-, medium- and long-term patient care goals	
Respond to the challenges of clinical and ethical decision-making in palliative care	
Practice comprehensive care coordination and interdisciplinary teamwork across all settings where palliative care is offered	
Develop interpersonal and communication skills appropriate to palliative care	
Practice self-awareness and undergo continuing professional development	

4 Factors Supporting Collaboration Between Generalist and Specialist Palliative Care Providers

Working in teams is an essential feature of palliative care delivery (Sepúlveda et al. 2002), and the need for partnership working and collaboration between generalist and specialist palliative care providers is at the center of international palliative care policy and guidelines. The emphasis on coordination within palliative care policy as a means for improving access and outcomes is supported by studies reporting the benefits of team working for both patients and healthcare professionals. A systematic review by Gardiner et al. (2012) found that for patients receiving palliative care, these benefits include increased likelihood of dying in most preferred location, improved symptom management, and greater opportunity for patient education. Generalists reported improved confidence in providing palliative care and increasingly positive attitudes toward specialist palliative care providers.

Given the critical role of effective collaboration in ensuring access to palliative care support for all patients living with a life-limiting illness, it is important to understand the factors that promote and sustain working relationships between generalists and specialists. Overall, studies examining the topic have drawn broadly similar conclusions about the factors influencing collaboration across all care settings. These center around three themes: characteristics and views of generalists, the nature of interpersonal and interprofessional relationships and communication, and organizational factors.

Factors related to generalist providers themselves influence the extent to which they engage in collaborative practice. Their preferences for collaboration with specialist palliative care are often shaped by their own perceptions about the necessity or value of team working. Limited knowledge about the nature or scope of palliative care may also serve as a barrier to collaboration. Similarly, professional judgments about specialists' skill set also influence generalists' willingness to collaborate and the types of issues they seek input for. For instance, while generalists widely believe that specialist palliative care services provide a level of support that requires additional training and expertise, some have reported concerns that specialists have limited knowledge about disease-specific issues. Firn et al. (2016) report that these perceived gaps in proficiency directly

impact on generalists' willingness to collaborate with specialists.

The nature of interpersonal and interprofessional relationships between generalists and specialists, and the quality of their communication, also influences partnership working. Good communication is central to collaboration but requires considerable time and effort, while working relationships are being established and often develop through personal interactions between generalists and specialists rather than any type of formal process or procedure (Gardiner et al. 2012). Studies have found that successful collaboration between generalists and specialist providers is often characterized as being built upon respect, trust, and expertise (Walshe et al. 2008; Firn et al. 2016). Specifically, generalists trust that specialist palliative care providers will respect the hierarchy of decision-making by continuing to consult with the referring team around the patient's care. This approach to communication and negotiation ensures that generalists and specialists are both acknowledging and supporting the expertise of the other and sharing decision-making responsibilities. Moreover, without this clear delineation in roles and responsibilities, the working partnership between generalist and specialist palliative care providers can break down (Brueckner et al. 2009).

Organizational factors also impact on collaboration. Often cited is generalists' need for efficiency and ease of access to specialist palliative care services in hospital or the community. Good partnership is fostered through specialist palliative care services being flexible, visible, and available to provide advice and support round-the-clock. With most patients accessing care across several settings, IT infrastructure is also crucial in supporting efficient communication between healthcare professionals.

To date, the factors supporting collaboration tend to be ad hoc and driven by informal interactions rather than formal structures. There is also limited evidence about outcomes associated with or methods for evaluating various formal models of partnership working to guide practice and policy.

5 Specialist and Generalist Palliative Care Practice and Models of Care

A model of care broadly describes a framework that brings together regulatory, organizational, financial, and clinical aspects of service provision to outline best practice in patient care delivery. The concept is an important one because of the link between adoption of best practices (as described in a model of care) and improved patient outcomes. Viewing palliative care through the lens of a model of care demands that stakeholders consider how best health services can best utilize the skills of generalist and specialist palliative care professionals. It offers opportunity to critically appraise areas of commonality, separation, and overlap in generalist and specialist palliative care practice and to ensure that organization of practice is optimally configured to meet the needs of patients and their families.

In the traditional model of medical care, palliative care was only provided when curative or disease-modifying treatment was no longer felt to be appropriate. This is gradually being supplanted by an integrated model where palliative care, when needed, is provided at the same time as curative or life-prolonging treatments. To date, a range of different models of palliative care provision have been developed and implemented to meet the requirements of this paradigm shift. Many reviews have been published that have tried to identify the effectiveness and cost-effectiveness of these different models (Luckett et al. 2014; Kavalieratos et al. 2016; Brereton et al. 2017). The reviews acknowledge that palliative care offers benefits to patients and their families but conclude that the evidence base for effectiveness of individual models of care remains limited by heterogeneity, methodological limitations, poor reporting, and a lack of consensus about outcome measures.

Much of the evidence that has been produced relates to models that predominantly focus on specialist rather than generalist palliative care provision. Moreover, within the models there has been relatively little explicit consideration of the interface between specialist and generalist palliative care and how that might optimally

function. While this may in part be due to ambiguous terminology, methodological challenges, and poor reporting of components of the intervention, it contrasts with a growing focus in the general healthcare literature on the integration of primary and specialty care. Instead, research in palliative care arguably remains largely siloed, considering either generalist or specialist interventions separately and failing to move to a space where consideration of the "whole" might be more advantageous than considering the sum of the parts.

What has been learnt from the studies that have been conducted on models of palliative care? Kavalieratos et al. (2016) conducted a systematic review and meta-analysis of palliative care randomized clinical trials (RCTs). RCTs were included if the intervention comprised at least two of the eight possible domains of palliative care as defined by the National Consensus Project for Quality Palliative Care. Interestingly, interventions addressed a median of five (range two to seven) of eight palliative care components. The 43 randomized clinical trials included data on 12,731 patients (mean age, 67 years) and 2479 caregivers. In the meta-analysis, palliative care was associated with statistically and clinically significant improvements in patient QOL at the 1- to 3-month follow-up and symptom burden at the 1- to 3-month follow-up. Findings for caregiver outcomes were inconsistent. When analyses were limited to trials at low risk of bias ($n = 5$), the association between palliative care and QOL was attenuated but remained statistically significant, whereas the association with symptom burden was not statistically significant. Evidence of associations with other outcomes was mixed.

Due to the diversity and lack of standardization of models studied, it is difficult to classify or group the interventions studied in these reviews. Models of specialist palliative care studied included services provided by unidisciplinary and multidisciplinary teams in hospital (inpatient and outpatient) and community settings. Models of generalist palliative care were similarly conducted across a range of settings, often focusing on communication, advance care planning, or improvements in needs assessment, psychosocial support, and symptom management. Notably, of the five RCTs focused on quality of life at 1- to 3-month follow-up that were judged by Kavalieratos et al. to be at low risk of bias, three comprised a specialist palliative care intervention (Bakitas et al. 2009; Temel et al. 2010; Zimmermann et al. 2014), one was generalist in nature (Rummans et al. 2006), and one comprised both specialist and generalist components (Higginson et al. 2014) (Table 3).

Luckett et al. (2014) adopted a different approach in their rapid review and aimed to identify the elements of effective palliative care models. They concluded that models of palliative care should integrate specialist expertise with primary and community care services and enable transitions across settings, including residential aged care. They considered the following elements to be essential to effective care: case management, shared care, specialist outreach services, managed clinical networks and/or health networks (clinical networks), integrated care, and the use of volunteers. Luckett also encountered the problems of heterogeneity of

Table 3 Generalist and specialist palliative care interventions

Bakitas et al. (2009)	A multicomponent, psychoeducational intervention (Project ENABLE [Educate, Nurture, Advise, Before Life Ends]) conducted by advanced practice nurses with palliative care specialty training consisting of 4-weekly educational sessions and monthly follow-up sessions until death or study completion versus usual care for patients with advanced cancer
Temel et al. (2010)	Early outpatient specialist palliative care for patients with advanced cancer
Zimmermann et al. (2014)	Early hospital, community, or outpatient specialist palliative care for patients with advanced cancer
Rummans et al. (2006)	Structured multidisciplinary intervention comprising eight 90-min sessions over 3 weeks for patients with advanced cancer scheduled to undergo radiotherapy
Higginson et al. (2014)	Short-term, single point of access breathlessness support service integrating specialist palliative care, respiratory medicine, physiotherapy, and occupational therapy

studies; methodological issues; problems mapping between evidence at the outcome levels of the patient, caregiver, provider, and service; and variable findings.

Indeed, the importance of the trials with negative or equivocal findings should not be overlooked in the search for understanding effective components of specialist and generalist practice. Negative studies highlight methodological issues that need to be addressed in future work and help us understand the "active ingredients" in palliative care interventions. For example, in their study of early specialist palliative care among advanced cancer patients, Groenvold et al. (2017) hypothesized that their negative result might be attributable to a failure to provide more specific guidance on the frequency and nature of the input of the specialist palliative care team, a relatively short intervention period, some degree of crossover, and contamination of control groups (as this was not a cluster RCT). Similarly, in Carson et al.'s (2016) RCT of the effect of palliative care-led meetings for families of patients with chronic critical illness, it has been hypothesized that the negative result was attributable to a highly structured study protocol that solely aimed to provide informational support with little regard to what makes this process meaningful to many patients, families, and clinicians: frequent and longitudinal follow-up, close involvement with the primary clinical team, and a focus on relief of physical and psychosocial distress (Malani and Widera 2016).

It is important to recognize that much of the research evidence on specialist and generalist palliative care originates from high-income countries where more is spent on healthcare and research. Generalizability of findings to low- and middle-income countries cannot be assured, and there is a lack of research on models of generalist or specialist care set in these countries. Lowther's et al. (2015) high-quality RCT that studied nurse-led palliative care for HIV-positive patients taking antiretroviral therapy in Kenya is a standout example of what can be achieved outside of high-income countries. It serves as an encouragement for further research to be undertaken to ensure that models of care are fit for each country's purpose.

6 Specialist and Generalist Practice and Integrated Care

"Integrated care" is a complex and still evolving concept. Integration (from the Latin integer, meaning whole, complete, entire) generally means combining parts so that they either work together or form a whole, although its definition in healthcare is somewhat more complex and multidimensional. The technical brief prepared for WHO's Department of Health System Governance and Service Delivery in 2008 (World Health Organization 2008) describes integration as "the organisation and management of health services so that people get the care they need, when they need it, in ways that are user-friendly, achieve the desired results and provide value for money." The purpose of integrated care is to reduce fragmentation of healthcare, duplication of health services, and missed opportunities for appropriate healthcare and instead improve the user experience and outcomes of care.

As previously discussed, the term "integrated palliative care" is commonly used to distinguish between the traditional dichotomous model of provision of palliative care at the end-of-life only and the model where palliative care is provided at the same time as curative or life-prolonging treatments. However, as the range of models of palliative care provision demonstrates, organizations have demonstrated considerable diversity in the structures and processes that they have used to achieve integration. While there is no single agreed conceptual model for health systems integration, arguably efforts to integrate palliative care in the mainstream of health provision would benefit from a more considered application of organizational theory and management science. This would help policy makers, planners, managers, clinicians, and researchers study, promote, and implement integrated palliative care and consider the optimal place and relationship of generalist and specialist palliative care practice in achieving integration with the wider health system.

While a detailed review of integrated care is outside of the scope of this chapter, several key points about integration may be made. Fulop et al.

(2005) describe five types of integration occurring within the system:

1. Organizational integration (where organizations are brought together through legal instruments or agreements such as mergers, collectives, or networks)
2. Functional integration (where back-office and support functions are integrated)
3. Service integration (where different clinical services are integrated at an organizational level such as through multidisciplinary teams)
4. Clinical (professional) integration (where care by professionals and providers to patients is integrated into a single coherent process within and between professionals and their organizations, such as the use of one care plan, shared clinical guidelines and protocols, devolved shared decision-making, etc.)
5. Normative integration (where an ethos of shared organizational and professional values enables trust and collaboration in delivering healthcare within and across organizations)

Levels and breadth of integration have also been described as important dimensions of integration in the literature. Authors variously describe three levels of integration as macro (regulation, policy, and strategic planning), meso (organizational and professional or physician), and micro levels (clinical) (Stevenson Rowan et al. 2007; Curry and Ham 2010). Breadth of integration is described as horizontal or vertical (Shortell et al. 1996). Horizontal integration refers to the combination of two organizations who are at the same level (e.g., two residential care units), whereas vertical integration refers to the combination of organizations who are at different levels (e.g., hospital, nursing home, and home care provider).

The general healthcare literature has used these frameworks of integrated care provision to explore real-life experiences of integration (Lasker and Committee on Medicine and Public Health 1997), categorize collaborations (Martin-Misener and Valaitis 2008) and outcomes (Ramsay et al. 2009), and identify and describe determinants of successful collaboration (Humphries and Curry 2011). For example, Powell Davies et al. (2008) reported on nine types of strategy used to coordinate care within primary healthcare and among primary healthcare, health services, and health-related services (Table 4). The potential application of similar work in generalist and specialist palliative care is clear. Explicit consideration of integrated care frameworks offers opportunity for greater conceptual and methodological clarity in the design and implementation of palliative care interventions and models of care.

Table 4 Types of strategies used to coordinate care. (Adapted from Powell Davies et al. 2008)

Types of strategies used to coordinate care
Patient and provider level
1. Arrangements to improve communication between service providers e.g. case conferencing
2. Using systems to support care coordination e.g. patient held or shared records
3. Structured arrangements for coordinating service provision between providers e.g. joint consultations
4. Providing support for service providers e.g. training
5. Structuring the relationships between service providers and with patients e.g. case management
6. Providing support for patients e.g. education
Organizational level
7. Joint planning, funding, and/or management of a program or service
8. Formal agreements between organizations
System level
9. Changes to funding arrangements

7 Ranking or Rating Systems for Palliative Care

Despite the difficulties inherent in describing and comparing models of specialist and generalist palliative care, several ranking systems have been devised for palliative care systems in Europe and across the world. The best known of these are the Global Atlas of Palliative Care Development at the End of Life (Lynch et al. 2013), the EAPC Taskforce on the Development of Palliative Care in Europe (Martin-Moreno et al. 2008), and the Global Quality of Death Index (The Economist Intelligence Unit 2015). Global categorizations of palliative care development are correlated with

Table 5 Global atlas of palliative care typology (Lynch et al. 2013)

Group 1:
Countries with no known hospice-palliative care activity, i.e., best efforts have been unable to identify any palliative care activity in this group of countries
Group 2:
Countries with capacity-building activity, i.e., there is evidence of wide-ranging initiatives designed to create the organizational, workforce, and policy capacity for hospice-palliative care services to develop. Activities include attendance at, or organization of, key conferences, personnel undertaking external training in palliative care, lobbying of policy makers and health ministries, and an incipient service development, usually building on existing home care programs
Group 3 countries:
(3a) Isolated palliative care provision, i.e., countries characterized by the development of palliative care activism that is patchy in scope and not well-supported, sourcing of funding that is often heavily donor-dependent, limited availability of morphine, and a small number of hospice-palliative care services that are often home-based in nature and limited in relation to the size of the population
(3b) Generalized palliative care provision, i.e., countries characterized by the development of palliative care activism in a number of locations with the growth of local support in those areas, multiple sources of funding, the availability of morphine, a number of hospice-palliative care services from a community of providers that are independent of the healthcare system, and the provision of some training and education initiatives by the hospice organizations
Group 4 countries:
(4a) Countries where hospice-palliative care services are at a stage of preliminary integration into mainstream service provision. This group of countries is characterized by the development of a critical mass of palliative care activism in a number of locations, a variety of palliative care providers and types of services, awareness of palliative care on the part of health professionals and local communities, the availability of morphine and some other strong pain-relieving drugs, limited impact of palliative care upon policy, the provision of a substantial number of training and education initiatives by a range of organizations, and existence of (or at least an interest in the concept of) a national palliative care association
(4b) Countries where hospice-palliative care services are at a stage of advanced integration into mainstream service provision. This group of countries is characterized by the development of a critical mass of palliative care activism in a wide range of locations; comprehensive provision of all types of palliative care by multiple service providers; broad awareness of palliative care on the part of health professionals, local communities, and society in general; unrestricted availability of morphine and most strong pain-relieving drugs; and substantial impact of palliative care upon policy, in particular upon public health

the state of palliative care as a field of specialization in each system, although the relative weight given to specialist and generalist practice varies significantly between systems.

The Global Atlas uses a six-part typology to describe levels of hospice and palliative care development (Table 5). As can be seen from the descriptors, aspects of both generalist and specialist palliative care provision are considered in each typology.

The EAPC Taskforce describes the development of palliative care in the context of processes, structures, policies, and resources that support the delivery of palliative care. Data is gathered from multiple sources including qualitative data by means of the Eurobarometer survey, quantitative data by means of the FACTS Questionnaire, bibliographic review, and interview of key informants. Both generalist and specialist palliative care data are collected, although it is arguable that the focus on specialist palliative care provision is greater than in other rating systems.

The Quality of Death Index is scored on 24 indicators in 4 categories, each with a separate weighting, as follows:

1. Basic end-of-life healthcare environment (20%)
2. Availability of end-of-life care (25%)
3. Cost of end-of-life care (15%)
4. Quality of end-of-life (40%)

Eleven of the Index's 24 indicators are based on quantitative data, such as life expectancy and healthcare spending as a percentage of GDP. Ten of the indicators are qualitative assessments of end-of-life care in individual countries, for example, "Public awareness of end-of-life care," which

is assessed on a scale of 1–5 where 1 equates to "little or no awareness" and 5 to "high awareness." Three of the indicators describe whether something is or is not the case, for example, "Existence of a government-led national palliative care strategy," for which the available answers are Yes, No, and In Progress. Only one indicator (availability of hospices and palliative care services per million population aged 65 and over) refers specifically and solely to specialist palliative care.

Despite the different methodologies, the different systems show broad agreement, with the United Kingdom, Australia, New Zealand, and Ireland ranking highly. The rating systems should be used and interpreted with caution, however, as they are associated with both advantages and disadvantages. As should be clear from the preceding discussions on the evidence base for models of palliative care, the methodology underpinning the scoring systems is far from an exact science. Moreover, despite best efforts, data may be unreliable or unverifiable. While the systems provide some absolute measure of development as well as change over time and can be used to advocate for development in specific countries, they can also prove to be demotivating for some countries where areas of achievement are not given adequate recognition or weighting.

8 Access to Generalist and Specialist Palliative Care

The way in which palliative care is delivered is determined by the nature of patients' and families' needs. The majority can have these addressed by generalists providing a palliative care approach, with referral for specialist input required only for more complex needs. As previously discussed, a growing body of evidence demonstrates that receiving palliative care support is associated with several positive benefits. Nevertheless, access to both generalist and specialist palliative care is less than optimal. Many who would benefit from a palliative care approach are never identified, and referrals to specialist palliative care services are often delayed or poorly managed. Access is also inequitable for those with non-malignant disease. Overall, current evidence suggests that only a minority of those who need specialist palliative care, approximately 14%, ever receives it (Connor and Bermedo 2014). Further to this, projected increases in the number of annual deaths and disease burden indicate that the need for palliative care will continue to grow.

Meeting this demand is a serious challenge for healthcare systems. However, returning to the coordinated palliative care model outlined by Quill and Abernethy, health systems need to ensure that they do not simply focus on ensuring access to specialist palliative care – rather they must also consider issues of access to generalist palliative care. To date, evaluations of access to palliative care have focused primarily on patients' utilization of specialist palliative services. However, if many patients can, and do, have their palliative care needs adequately addressed by generalists, it follows that using specialty as a proxy for measuring access to palliative care systematically underestimates how much palliative care people are receiving. Indeed, future research activities should also seek to define what a palliative care approach is and develop methods for measuring and evaluating its delivery. Such exercises would allow for more informed discussion around how best to respond to the growing need for palliative care.

8.1 Timing the Introduction of Generalist and Specialist Palliative Care

Related to concerns about access to palliative care services is the issue of timing. Uncertainty about the nature or scope of palliative care can make it difficult for generalists to identify patients and families with multiple unmet needs who would benefit from a palliative care approach or specialist palliative care in a timely manner. This late identification is one of the main reasons people do not receive palliative care. Education and training has been cited as crucial for helping generalists develop the skills required to identify and address needs and the confidence to introduce a

palliative care approach or seek specialist input, thus ensuring patients have timely access to the appropriate level of support.

It is worth noting that the literature on introducing palliative care tends to reflect concerns around appropriate timing of referral to specialist services. This development is understandable as referrals to specialist palliative care late in the disease trajectory are common and can have serious consequences for patients, families, and healthcare professionals including perceived poor coordination of care, unexpected death, and lower satisfaction with palliative care services (Gardiner et al. 2012). Hui et al. (2012) found the median interval between referral to specialist palliative care and death in patients with advanced cancer was 42 days. Delays can be significantly longer for patients with a non-malignant disease, as demonstrated by Bakitas et al.'s (2013) chart review of access to specialist services among a cohort of patients with advanced heart failure which reported a median time between consultation and death of only 21 days. These delays in referral to specialist services are often attributed to difficulties with prognostication and predicting disease trajectory, particularly for those with a diagnosis other than cancer.

Several tools have been developed to help generalists identify patients with palliative care needs. Some use prognostic estimates and clinical indicators to gauge when palliative care should be introduced. One example is the Gold Standards Framework Prognostic Indicator Guidance (GSF), a tool originally developed to improve quality of care for patients near the end-of-life. The GSF uses multidimensional criteria to assess need including the "surprise question" (*Would you be surprised if this person dies within the next 6–12 months?*), if they voice preference for comfort care only and clinical indicators relevant to the patient's diagnosis (Department of Health 2008). Alternatively, some tools, such as the Supportive and Palliative Care Indicators Tool (SPICT), focus on helping generalists identify patients who are *at risk* of deterioration or dying (Highet et al. 2014) for palliative care needs assessment and future care planning. The SPICT includes six general indicators suggesting increasing need or deteriorating health status and other indicators of advanced disease, depending on the patient's diagnosis. The SPICT also advises on assessment and review of current and future care needs, including considering referral to specialist palliative care. Like the GSF, the SPICT may be used in all adult patients with life-limiting conditions.

9 Conclusion

It is essential that policy makers, service providers, and service users all recognize that the provision of palliative care is the responsibility of the whole healthcare system and not just specialist providers. Patients with life-limiting or life-threatening illness must be able to engage easily with the level of expertise most appropriate to their needs regardless of care setting or diagnosis. Quality service provision is best realized when generalist and specialists work together in an integrated and coordinated way to respond to, and meet, those needs. However, worldwide, there is significant variation in the level of specialist and generalist palliative care service provision.

The success of generalist and specialist partnerships can be critically affected by lack of clarity and agreement regarding roles and responsibilities. Ideally, models of care should be developed that describe the optimal structures and processes of specialist and generalist practice so that patients and their families experience the best possible outcomes of care. To date, while palliative care has been shown to improve patient and family outcomes, research has largely focused on specific generalist or specialist interventions. As a result, the evidence base is not yet able to describe universal models of comprehensive, evidence-based palliative care that span services and settings. There are methodological and practical challenges to conducting clinical and cost-effectiveness work in palliative care, but these are not insurmountable and should not delay further study. Transferable learning from the fields of integrated care and implementation science may be of help in achieving the goal of designing

whole system approaches to care and in ensuring that palliative care is an integral part of universal healthcare provision.

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Access to Palliative Care

31

Tony Ryan

Contents

Abstract

Access to palliative services is currently an important issue facing policy makers around the globe. Much of this discussion is centerd on the significant challenges facing the developing nations and how health care leaders are seeking to integrate high-quality palliative care. But inequality of access is also apparent within developed health care economies. This chapter addresses some of these challenges as they are experienced by those suffering from nonmalignant conditions. Using two case-studies, the chapter highlights evidence that draws attention to the ways in which people with dementia and those experiencing Chronic Obstructive Pulmonary Disorder (COPD) are often excluded from palliative provision.

1 Introduction

The World Health Organization now regards access to palliative and supportive care at the end of life as a human rights (World Health Organization 2014). While much has happened in policy terms to facilitate the development of such services, particularly in developed nations, the reality for many means that they will experience an end of life where access to palliative care is

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_30

denied (Brennan 2007). Evidence from the UK suggests that every year over 100,000 people who demonstrate high levels of palliative need will die without the benefit of such care, and poor access continues to be experienced by particular groups of patients via persistent inequalities (Dixon et al. 2015). In the past, inequity has been demonstrated as a result of socioeconomic status (Lewis et al. 2011), while others have noted inequality of access to palliative care on the grounds of sexual orientation (Harding et al. 2012) and age (Gardiner et al. 2013). However, a key theme of much of the literature relating to inequality of access to palliative care focuses on the importance of the patient's condition. The experience of cancer patients has for some time, at least within developed healthcare systems, continually demonstrated elevated palliative service usage and improved outcomes for those diagnosed with a form of cancer (Boland and Johnson 2013). In contrast, nonmalignant conditions have been the subject of relatively slow progress and poor access. For example, US citizens living with nonmalignant chronic lung disease are less likely to access palliative services (Brown et al. 2016). Similarly, people suffering from heart failure also demonstrate poor access to palliative care (Gadoud et al. 2013). Readers of this book will be well aware of what we mean when talking about such care, but how this is accessed or indeed denied and what shape or form palliative care takes is not so clear cut. This chapter will explore the literature which centers upon access to palliative care. It will explore what we mean by access via the more contested notion of transition. Furthermore, the chapter will look at inequity of access across the globe and across particular condition groups. Using two case "exemplars," the chapter addresses sources of barriers to access and attempts to provide a way forward in policy and practice fields.

2 Palliative Care: Access to What?

Across the globe, a great variety of forms of palliative care exists. Wiencek and Coyne (2014) point to four models: ambulatory; home-based; hospital-based specialist units; hospital-based specialist services (consultation). A global perspective of the scope and reach of palliative care services suggests that, although patchy, the pervasiveness of such provisions is increasing (Lynch et al. 2013). Add to this the growing potential for palliative and supportive care to be provided in residential and nursing home facilities for older people and a fairly complex web of services and types of provision exists. Measuring access to specialist palliative care services, such as those listed, provides a relatively straightforward means to exploring patterns of service usage across and within populations. In doing so, we are able to observe patterns of service usage, inequalities, and unmet need. But measuring how patients access palliative *regimes* of care is less straightforward. Kaufman (2015) talks of the process of crossing a threshold at the end of life when care turns from a curative form to palliative, readers will also be familiar with wedge and wave models of shifting approaches to the care of patients. The notion of transition has emerged as an important notion in the process of these changes in the emphasis of care and treatment. Two reviews looking at the nature of transition from curative to palliative care have been undertaken in the past (Gardiner et al. 2011; Marsella 2009). Both reviews point to the importance of understanding the nature of transition, partly as a result of the relationship between the introduction of palliative care and outcomes for patients. But addressing transition is important because of the increasing focus upon inequality of access and the attention that this brings to the investigation of barriers to palliative care experiences. Those writing about transition have noted that it is often not clear cut, particularly in the absence of a specific referral or physical admission to a specialist service. In other words, transitions can often occur while patients remain within the same place of care, such as a hospital or ward setting, often under the treatment of the same team of clinicians. This is partly an outcome of more recent approaches to palliative care, which firstly may be undertaken by generalist staff, but secondly as a result of the use of curative approaches which coexist with palliative care. The timing of

transition is of critical concern to those undertaking research in the field, but more importantly to the medical and nursing staff providing care, patients, and their families. One of the key challenges remains the culture and environment of care where transitions are experienced. Kaufman (2015) in her classic ethnography of end of life care on the United States points to this as one of the key challenges in making the transition, and something we will return to later in this chapter. But equally challenging remains the issue of prognostication. As increasingly experience death as a result of noncommunicable disease and long-term chronic conditions, the nature of end of life trajectories has shifted toward protracted and unpredictable clinical states thee ways in which medicine can prognosticate effectively (Murray et al. 2005).

Notwithstanding the problems associated with observing and measuring its prevalence, there remains a great deal of evidence to suggest that there exists inequality in relation to the experience of accessing services and making the transition to palliative and supportive care is problematic for some groups of people. This chapter will use two case exemplars to highlight such inequality.

2.1 Case Exemplar One: Dementia and Failure to Make Transition

There are almost 40 million people living with dementia across the world (Prince et al. 2013). Recent global policy has placed emphasis upon early diagnosis, better information and support, as well as enhanced end-of-life care throughout the condition trajectory. Indeed the improvement of access to palliative care and high quality end of life care has become an important policy objective across the globe. Palliative care and improved end of life experiences for people with dementia is emerging as a critical area of concern and debate, with national dementia strategies across the globe focusing attention upon the issue of access (Nakanishi et al. 2015).

The evidence to support claims that people with dementia do not access palliative and supportive care comes from a range of sources. For a long time, access to hospices was more or less denied to people with dementia, with less than 1% of the hospice population of Europe being diagnosed with a neurological condition (Sampson 2010). This failure to access a key front line palliative care service having implications for referral to other specialist end of life services. Recent research undertaken in the UK would further support these observations. Based upon census research carried out within two large hospitals, identifying the range and prevalence of symptoms which might indicate palliative needs (Gardiner et al. 2013), people with dementia were identified as experiencing heightened levels of physical burden (pain, fatigue, poor function) and psychological burden (anxiety, depression, mood) when compared to other patient groups, such as those with cancer. Despite this heightened degree of burden, people with dementia were less likely to have made the transition to palliative forms of care, especially in the form of a referral to specialist services (Ryan et al. 2013). Furthermore, a number of reviews have highlighted the lack of transition to more palliative forms of care for people with dementia at the end of life, with the continued use of regimes of care which favor an aggressive approach. Paradoxically, it is claimed that throughout their illness people with dementia often receive "*too little*" care, whereas end of life care is often characterized by "*too much*" (Small et al. 2007). A failure to access palliative care for people with dementia has, it might be argued, led to poor quality end of life experiences. In the past, a tendency to rely upon aggressive forms of medical care (feeding tubes for example) have been emphasized, denying people with dementia the opportunity for more palliative approaches at the end of life, with little or no evidence suggesting this form of care contributed to improved outcome (Sampson et al. 2009). More recently evidence from the Netherlands has highlighted similar unequal access to palliative approaches to end of life care. For a long time, the systematic use of antibiotics has been viewed as a means of extending life, often at the cost of quality of life. Hendriks et al. (2015) identified increased prevalence their use among people with dementia, when compared to cancer patients. There is also

continued evidence that enteral tube feeding is more prevalent amongst hospital patients with dementia at the end of life, a practice which might be considered contrary to palliative principles.

2.2 Case Exemplar Two: Chronic Obstructive Pulmonary Disease (COPD)

COPD is the umbrella term given to represent a range of chronic lung disease, including emphysema, chronic bronchitis, and chronic asthma. It is characterized by increasing chronic breathlessness. There are estimated to be around 380 million people living with COPD worldwide (Adeloye et al. 2015). As is the case with dementia, the end of life care experience for people with COPD continues to be blighted by unequal access to palliative services. Furthermore, there is evidence that patients with COPD often fail to make the transition to palliative regimes of care, especially compared to other conditions. A recent major US study highlighted a lack of access to palliative care for patients with COPD after hospitalization (Rush et al. 2017), noting unfavorable comparisons with patients with cancer. Szekendi et al. (2016), also reporting research carried out in the US, observed high levels of unmet palliative care need and identified COPD patients as being less likely to be referred to such services. Furthermore, Ahmadi et al. (2015) identified a reduced proportion of patients with COPD receiving a referral to palliative services (including home-based), increased hospital admission, and few opportunities for end of life discussions.

As is the case in dementia, there is also evidence that, use of specialist services aside, people with COPD also fail to make appropriate transitions to high quality end of life care when compared to other patient groups. The Ahmadi et al. study (2015) is also interesting in this respect. The team was able to collect data on symptoms at the end of life, noting higher levels of uncontrolled breathlessness, nausea, and confusion at the end of life for COPD patients, when compared with cancer patients at a similar point in the disease trajectory. Invasive procedures are also likely to persist within the end stage COPD population, with mechanical ventilation being difficult to withdraw once established and indicating a high level of burden on the patient and family (Hajizadeh et al. 2015). One important element of palliative and end of life care is to have open discussions with those caring for the person. A great deal of the literature within the field of COPD and palliative care relates to this issue, with some evidence that the opportunities for discussion are limited for COPD patients, again when compared to those with cancer (Rocker et al. 2008).

3 Explanations for Inequity of Access

The reasons for this inequality of access for people experiencing dementia and or COPD and reluctance for providers to facilitate transition are now well established and barriers to palliative care for people with dementia are known to take a number of forms.

3.1 Prognostication

Note has already been made within this chapter about the nature of the end of life experience for people suffering from long-term chronic conditions. The implication for transitions to palliative forms of care is centered on the timing of changes in treatment or indeed the decisions to refer to a specialist service. Some argue that the failure to prognosticate effectively is, however, a product of a culture of care which is more readily focused upon life sustaining treatment as opposed to palliative care. Coupled with a rise in the use of life sustaining technologies, prognostication is increasingly delayed (Seymour and Gott 2011). Nonetheless, prognostication is difficult within the context of dementia and several authors have therefore chosen to cite this issue as a particular reason for this failure (Birch and Draper 2008). Typically a person with dementia will live for around 5 years after diagnosis, but this varies and the trajectory of experience is unique to each person. This is made more complex when the

person experiences comorbidities or death as a result of an additional condition (Lee and Chodosh 2009). Similarly, prognostication in the context of COPD is problematic, leading to challenges in transition to palliative forms of care.

Despite the challenges in the field of prognostication in dementia, some attempts have been made to identify markers which might be indicative of the last 6 months of life. Van der Steen et al. (2014) argue that professionals should be able to use clinical judgement alongside such tools to help in the process. Importantly, they add that communication with the family on the issue of prognostication is critical to help in the preparation of shared decisions making. Efforts to develop prognostication tools within the field of COPD have similarly taken place. The PRO-LONG tool uses 11 indicators to assess mortality postdischarge and has shown promise within early field trials (Duenk et al. 2017).

3.2 End of Life or Advance Care Planning Discussions

Open discussion about end of life treatment is thought to enhance decision making and provide preferential regimes of care in the late stage chronic conditions. The most prominent form of discussion is termed Advance Care Planning (ACP), defined by the World Health Organization as: *"planning in advance for decisions that may have to be made prior to incapability or at the end of life. People may choose to do this planning formally, by means of advance directives, or informally, through discussions with family members, friends and health care and social service providers, or a combination of both methods"* (World Health Organization 2004). ACP is felt to improve end of life outcomes for people experiencing a range of conditions (Brinkman-Stoppelenburg et al. 2014). In both dementia and COPD contexts, however, the prevalence of active engagement with ACP is thought to be low (Lovell and Yates 2014) and a number of explanations have been put forward. In the context of dementia, it is thought that the idea of planning for the end of one's life is both actively and passively avoided. A recent review of the qualitative literature on the subject suggests a number of explanations which alongside avoidance of the matter include: lack of support from services; carer burden; living for today; a lack of confidence in professionals being able to deliver choice (Ryan 2017). In the case of COPD, a similar line of exploration has taken place. Patel et al. (2012) note that patients lack an awareness of ACP options, they do not have well established lines of communication with professionals, fear of abandonment, and an assumption that conversations will occur when they are needed. Additionally, the authors note delays in diagnosis and concerns among physicians that initiating ACP will take away the patient's hope.

It is difficult to assess the significance of the absence of ACP on the quality of end of life care or transition to preferred forms of palliative care. Nonetheless some suggestions are provided to help facilitate the ACP process within both a dementia and COPD context. Ryan suggests that the skills within professional groups need to be enhanced so that initiation of future planning conversations may take place (Ryan 2017). Furthermore, the importance of sharing the responsibility of planning is stressed to help lift the burden of responsibility from the individual and family. Patel et al. (2012) also stress the skills involved are complex and subtle, pointing to the importance of appropriate timing of the conversation and relaxed environment. They also highlight the evidence relating to decisions aids as a potential route to improved prevalence of ACP within the COPD population.

3.3 Organizations and Cultural Factors

Kaufman's classic ethnography of US hospitals focuses very much on the environmental and cultural features of institutions and professional groups in their influence on end of life care (Kaufman 2015). This study is important as it helps us to gain insight into the values, concerns, financial, and policy drivers which shape decision making. She notes a great deal, but among these valuable insights, Kaufman highlights the ways in which

discussion about death is delayed, partly as a product of the medical profession's attention to life sustaining treatments and a failure to see it as a possibility. The literature around the failure of people with dementia or COPD to gain access to palliative care via transitions or the accessing of services rings true here. Within both conditions, there is a reluctance to view end of life as a possibility. In a paper which engaged the views of medical and nursing staff about access to palliative care services for people with dementia, the notion of candidacy is used (Ryan et al. 2012). This describes the idea that dementia is not viewed as a cause of death and as such people with the condition are not viewed as candidates for palliative services.

The nature of the exploration of end of life care for people with dementia in the book by Small et al. (2007) chimes also with Kaufman's work. This study focuses on what is called the distinction between the *"life world"* of the person, their sense of self, wishes, and preferences and the *"system world"* a culture of care which denies preference, choice, and autonomy, consequently leading to overuse of technology and life sustaining interventions. Organizational issues have also been identified as a barrier to the accessing of palliative services, particularly in the form of generalist provision in the field of COPD. Hynes et al. (2015) working in acute environments in Ireland draw attention to the episodic nature of hospital care which focus on the short term management of exacerbations. This, they argue, is at odds with a long-term approach to understanding the physical, emotional, and spiritual challenges faced by people with long-term conditions such as COPD. Specifically, they state that rather than a person-centered approach, acute environments address these challenges with a "disease-centered" focus.

3.4 Systems and Resources

Many have noted the problems faced by people with dementia or COPD in relation to access to palliative services or end of life care as a result of systemic failings or resource limitations. Recent research in the United States demonstrates relatively poor access to hospice care for patients diagnosed with COPD and neurodegenerative disorders when compared with cancer patients (Riggs et al. 2016). Problems in gaining access to services such as hospices in the field of COPD are also noted. Vermlyn et al. (2015) describe access problems in the UK as a result of hospices being viewed as a resource for cancer patients. In the USA, the issue of access to hospice care is made more complex by Medicare regulations, with eligibility restricted to those in the last 6 months of life and who forgo curative treatment resourced via Medicare (Part A) funding. Given the problems associated with prognostication for people with COPD or dementia, it is not difficult to see how these access problems may persist. Referral and communication issues of a systemic nature have also been shown to restrict access for particular groups of patients, including those diagnosed with dementia. Illife et al. (2013) have conducted pan-European research to highlight the problems associated with a failure of community-based medical practitioners in identifying people with dementia as candidates for specialist services, noting that in some cases fewer than one in five were recorded on palliative care registers.

Palliative provision outside of specialist services is often undertaken by generalist staff working either in community- or hospital-based settings. For some time now, the challenges in generalist staff being able to provide palliative forms of care have been noted, especially in acute settings. Gott et al. (2012) note in their work in hospitals that resources were often identified as the reason that generalist staff were unable to provide what they saw as high quality palliative care. Specific examples from the field of COPD highlight this issue. During fieldwork, Hynes et al. (2015) note that COPD specialist nurses in Ireland were being expected to carry significantly higher workloads when compare to specialist palliative practitioners within the same organization. Ryan et al. (2012) note that specialist palliative care providers often viewed eligibility for access to hospices as being limited to those diagnosed with cancer. In particular, they report already stretched resources and limited capacity in

dealing with the specific needs of people with dementia as a means of rationing access.

4 Implications for Future Policy and Practice

This chapter has highlighted the inequity which is evident in accessing palliative care for two specific populations of patients: people with dementia and those diagnosed with COPD. This is not to say that inequality does not occur for other patient populations or indeed along other lines, such as socioeconomic or between developed and developing nations. Rather the two case studies used here exemplify condition specific inequality and the sources of inequity. A number of potential explanations have been offered and it now may be pertinent to offer a way forward. Firstly, specific guidance should be made available where problems of access or palliative care practice deficits are identified. This has already occurred in the case of dementia to some extent. The EAPC White Paper on optimal care for older people with dementia has helped to clarify consensus on this issue in a European context (van der Steen et al. 2014). A number of key features were identified, including access to palliative care, promotion of advance care planning, avoidance of overly aggressive approaches at the end of life, and education and training for key health and social care professionals. Guidelines do, however, need to be developed to meet the needs of national populations and embedded within organizational practices and cultures of care. Secondly, a critical perspective around the relative importance placed upon prognostication is required. It is well established that prognostication is challenging within the context of some conditions. But prognostication is only relevant to end of life decision making. Palliation is much broader than end of life care and needs to be embedded within pathways of care from a much earlier time point. Placing less emphasis on prognostication and more on the introduction of the palliative principles of care would allow for the introduction of such approaches in a timely and appropriate manner and would have the benefit of improving end of life experiences. Thirdly, it is clear that established methodology around ACP is failing populations of people who suffer from long-term chronic conditions. Work is required in enabling more informal approaches to ACP to be established, where a focus on relational practices and collective responsibilities are central themes. Health and social care professionals need to be provided with the capacity (skills and resources) to be able to introduce the notion of ACP at a timely manner for all.

5 Conclusion

This chapter has drawn attention to some of the key challenges facing policy makers and practitioners in addressing some of the inequalities in palliative care provision. Using two distinct case studies, the chapter demonstrates that while access to palliative care in developed countries remains relatively unproblematic for some patients, especially those with malignant disorders, the route for others is more fraught. A number of explanations are considered and these have implications for professional groupings, policy makers, organizational leaders, and legislative bodies. Evidence surrounding the issue of inequality in the developed world remains insubstantial compared to those global concerns about access to palliative care for all. If access for all is to be realized and the goal of palliative care as a human right is to be achieved, then there remains a great deal of work to be done.

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Interprofessional Practice in Palliative Care

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Marion Jones and Jill Thistlethwaite

Contents

Abstract

Interprofessional practice informed by and developed through interprofessional education is critical for working within modern healthcare contexts and particularly within healthcare teams. Palliative care is a complex area of healthcare delivery, and interprofessional practice is a way of working together learning from, with, and about other health professionals. This chapter

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_41

explores the terminology used within the interprofessional working and learning contexts. The challenges, opportunities, and barriers to interprofessional practice are explored in relation to what they are and how they can be constructive instead of creating conflict. One model of interprofessional practice is discussed, and the stages health professionals need to work through are outlined. The importance of interprofessional teamwork and collaborative practice is recognized as being critical to develop in settings such as palliative care where the focus is on the patient and their family.

1 Introduction

Palliative care is typically provided by a range of healthcare professionals, frequently with a core multidisciplinary team (MDT) or primary healthcare team (if the patient is being cared for at home). Members of the core team are also likely to collaborate with other health- and social care professionals for specific purposes such as for advice about particular aspects of management, financial issues, or family support. Palliative care is a complex area of health care delivery. It may be ethically challenging and, in our experience, for optimal outcomes requires values-based and patient-centered approaches. In this chapter, we consider the nature of this teamwork and collaborative practice through the lens of interprofessionality. We discuss the definitions of concepts related to interprofessional practice (IPP) and explore the rationale for IPP while acknowledging the challenges. Conflict may arise when there is diversity among team members in relation to personal, professional, and/or organizational values. Such conflicts may be prevented or they may need to be addressed, through a process of negotiation to reach consensus. Indeed conflict may be ultimately constructive if managed well, whereas avoiding conflict at all costs may be deleterious (Tekleab et al. 2009). One model to develop interprofessional practice is outlined and rationalized as being a process of cultural change as well as interprofessional learning and working.

There are multiple definitions being used locally and globally, and this can be confusing. In the following section, we discuss the definitions we use in this chapter.

2 Definitions

2.1 Interprofessional Practice

Interprofessional practice (IPP) implies that boundaries and territories are broken down, and the professionals work together with intent, mutual respect, commitment, and a common objective (Jones 2000). IPP is fostered through interprofessional education (IPE) which is "when two or more professions learn from, with and about each other to improve collaboration and the quality of care" (CAIPE 2002). IPP breaks through the boundaries of role specialization of a discipline. Ideally, IPP should involve shared education and practice opportunities that assist health professionals to work together more effectively with the interests of the clients being the focus from admission to discharge from care or death (though support will carry on for carers and the family). Therefore the word "interprofessional" when applied to practice implies a way of working together above and beyond a group of professionals interacting with the same patient and family.

The interest in interprofessional practice in healthcare has increased, and, over many years, "interprofessional" has become a key word in practice development. In 2009, the World Health Organization's (WHO) global consultation on primary healthcare and the global health agenda listed two objectives as building effective partnerships and fostering interprofessional collaboration (World Health Organization 2009). It has been a focus of the WHO's health plans and is the subject of growing research globally. In addition, there has been the development of worldwide networks devoted to IPE and IPP, for example, in the United Kingdom, Sweden, Canada, Australia, New Zealand, the United States, and more

recently in Sub-Saharan Africa, Japan, India, and South America.

One might talk of a semantic debate with the terms of interprofessional, multiprofessional, multidisciplinary, and interdisciplinary carrying a variety of meanings depending on the perception of the interpreter within a specific context. This reinforces that all perceptions could be thought of as socially constructed. In addition, the prefixes "multi" and "inter" may be considered as value-laden. They focus the interpretation on the ways that team members predominantly interact. Multiprofessional has been defined as two or more professionals working side by side (in parallel), with little interaction, as "multi" suggests "many" (Thistlethwaite 2012a). In contrast, "inter" implies "between," "among," and "mutually," leading to interprofessional approaches (with the global consensus now being to spell the word without the hyphen) with the nuances of cooperation, coordination, and frequent communication.

In order to clarify further the concepts used in practice and the literature, and to distinguish between terms that are often used synonymously, the following additional terms are outlined to clarify how language can be confusing as well as helpful:

Multidisciplinary implies that more than one profession/discipline may be involved in the particular scenario being described, but discipline-specific solutions evolve which denotes that working is primarily in parallel and health professionals only come together when there is a problem to solve.

Interdisciplinary pertains to a situation or group between more than one branch of learning and that members meet to look at areas of common interest and knowledge (Jones 2000). Coyle et al. (2011) believed that when inter- was used, confusion existed from working together to working separately. Boon et al. (2004) tried to overcome this and had seven different team-oriented models ranging from parallel to integrative. The interprofessional approach to patient care involves practitioners from different professional backgrounds delivering services and coordinating care programs to achieve different and often disparate needs. Ideally goals are set collaboratively, including with the patient, through consensual decision-making, and this results in an individualized care plan, which may be delivered by one or more professionals. This level of collaborative practice may be difficult to achieve but does maximize the value of shared expertise.

2.2 Interprofessional

Practicing interprofessionally means crossing occupational boundaries – setting aside our own professional view of healthcare as being the only right one and actively listening to what our colleagues have to say (Jones 2000). Interprofessional practice needs to involve the patient, family, and health professionals in planning the care together with a shared vision and direction, taking into consideration that it is critical to consider the cultural, social, economic, and personal needs and preferences of the patient, carers, and family.

2.3 Interprofessionality

D'Amour and Oandasan (2005, p. 9) defined interprofessionality as "the development of a cohesive practice between professionals from different disciplines." It may also be thought of as being characterized by "the transformation in practice which may result from combining and blending specialist knowledge and expertise" (Brooks and Thistlethwaite 2012, p. 405). Brooks and Thistlethwaite (2012) have asked some critical questions about the transformation in identity that may be associated with working and learning across professional boundaries, such as in the context of palliative care, and the challenges due to the synergy and possible disjunctions between multiple professional identities. The term "interprofessionalism" also appears in the literature and has all the nuances and controversies associated with professionalism (Thistlethwaite et al. 2016). The US-based Interprofessional

Education Collaborative Expert Panel (IPEC) defines "interprofessional professionalism" as a "consistent demonstration of core values evidenced by professionals working together, aspiring to and wisely applying principles of altruism, excellence, caring, ethics, respect, communication, [and] accountability to achieve optimal health and wellness in individuals and communities" (IPEC 2011, p. 17). Interprofessional practice is integral to the health reform changes worldwide, and those involved in this approach to practice have joint goals and break down their professional boundaries to allow for interactive learning between professions to take place (Jones 2000).

Recognizing opportunities rather than identifying barriers is the thinking that is required to move past the traditional ways of working and how the preconceived ideas of professions and professionals influence the culture of teams and the language used. Curriculum structures for continuing education are influenced by staff attitudes, administrative structures, and lack of resources which in turn impact on palliative care and practice (Jones 2000). When health professionals successfully work together from assessment through to intervention, they have a shared goal toward the patient's best interests.

Interprofessional collaboration is the process of developing and maintaining effective interprofessional working relationships with learners, practitioners, patients/clients/families, and communities to enable optimal health outcomes (CIHC 2010).

2.4 Discipline

Grossman and Hooten (1993) talk of the broad aims of a discipline being to specify its proper place in society along with defining the knowledge framework for practice. They expand that by saying a professional discipline must explicate its historical, social, philosophical, and learning traditions in order to understand its connectedness to others in the field of epistemology and to provide a meaningful context for its method of inquiry and its content areas for practice (p. 867).

2.5 Discipline Culture

Each discipline has a specific culture or health profession. Culture means different things to different people and is seen as a set of definitions of reality held in common by a group of individuals who share a distinctive way of life (Strasen 1992). Within this view are the crucial elements of shared values, beliefs, expectations, attitudes, assumptions, norms, and social relevancies which are often not explicit, discussed, or recognized as they are lived and internalized as norms that provide social signposts for behavior (Jones 1993). A health professional's discipline will therefore have shared practices, beliefs, knowledge, language, and resources which are specific to them along with how they influence and relate to other health professionals (Sohier 1992; Jones 1993).

Therefore understanding the professional culture provides direction, interpretation and meaning, energy for action, and the map for "how we do things around here." Culture in the context of interprofessional practice relates to each discipline and what each one brings to a specific team. This in turn could surface the cultural gaps that may be perceived as conflict or just being difficult. This has the potential to influence interprofessional practice and the actual professional development that occurs within the discipline and the team itself. How disciplines influence interprofessional practice is what is important to consider.

3 Barriers to Interprofessional Practice

There are a number of barriers evident that prevent interprofessional relationships developing and include "problematic power dynamics, poor communication patterns, lack of understanding of one's own and others' roles and responsibilities and conflicts due to varied approaches to patient care" (Zwarenstein et al. 2009, p. 2).

Gilbert (2005, p. 90) overviewed the barriers to working and learning interprofessionally and

emphasizes one of the barriers as how "the use of language varies considerably across social groups – the language used by health disciplines is no exception." He goes on to explore how disciplines have developed a culture of communication including gender-related differences which then mix with institutional dialogue and the professional associations' way of working. Complexity reigns and these aspects need to be made very transparent in the development of interprofessional working and learning.

Alongside the use of language, specific health professional barriers with the differences evident inhibit an interprofessional curriculum being developed. Over time a curriculum can change; however to work together to develop interprofessional learning and working is what helps all health professions take ownership of the process. Then there are the scheduling issues both from an individual and institutional perspective including no time to develop interprofessionally, lack of confidence to change, lack of funding and resources to change, and lack of knowledge to name a few.

Health professional regulations are developed in isolation from each other with separate Councils and Boards, and this in itself prevents IPE and IPP being transparent in the competencies required for practice. In some countries, evidence of integration and working with other health professionals is evident in codes of practice. Examples include having the terms integration, team development, interdisciplinary, and occasionally interprofessional.

Therefore institutional barriers can be within legislation, registration, and accreditation processes. However Gilbert (2005, p. 98) recognizes that there "are clearly clinical (or care) settings for which it is highly desirable to have three or more professionals engaged in teaching about that setting," for example, palliative care. Oishi and Murtagh (2014) emphasize that fragmentation of healthcare and delayed referrals to palliative care result in some patients not receiving the palliative care when they need it.

4 Team Development

Despite the importance of team development and interprofessional practice, many health professionals continue to practice and educate disciplines in isolation. The challenge for palliative care health professionals is to examine where and how they value skills in relation to team decision-making, customer service, and quality of care within an interprofessional framework. Interprofessional collaboration is the message being given in all practice settings, and palliative care settings are no exception.

Working effectively together is facilitated by health professionals understanding each other's disciplines, identities, and diversities and how these impact on day-to-day practice to work together (Jones 2000). It is also important to consider that breakdowns in communication can jeopardize the team development and individual practice itself recognizing the person who is disadvantaged is the patient. Interprofessional practice demands collaboration and organizational structures to support it (Walby et al. 1994; Soothill et al. 1995). It is well documented that organizational efficiency is more vulnerable if interprofessional communication is not effective (Henry and LeClair 1987; Farley 1989; Shortell and Kaluzny 1994; Clinton and Scheiwe 1995; Jones 2000). Literature from the 1990s is purposely used to emphasize that interprofessional practice has long been considered as best practice although many areas of practice still struggle with it holding on tightly to only their disciplined ways of working, thinking they will lose their identity (Jones 2000). Instead to work interprofessionally, health professionals need to identify explicitly disciplined ways of learning and in doing so actually strengthen their discipline.

Given the above perspectives, it is important to examine how any diversity of professional discipline may impact on interprofessional practice, along with recognizing that culture encompasses practice, beliefs, knowledge, language, and resources all of which are relevant to health professional practice and the strategic directions in healthcare (Jones 2000). The main consideration

here is the patient and the patient outcome, not the discipline.

Some may ask what is new as there have always been teams in healthcare. However, how the concept of team is interpreted is important for setting the context for interprofessional practice. Each profession in finding its own identity appears to have become territorial in setting the boundaries of what makes it a unique group. This, in turn, can set up power and authority interplay in the process of legitimating the separate entity of the specific profession (Jones 2000).

Alongside this, the leaders of interprofessional practice within a supportive infrastructure provide the context for practice to be strengthened (Jones 2000). Therefore there needs to be a balance between developing the team, each discipline or health profession, and interprofessional learning and working.

As mentioned earlier, Boon et al. (2004) identified a range of team development from parallel to integrative with the process of growing to interprofessional working developing through seven stages. From parallel to consultative teams, Boon et al. believed these were part of the biomedical model of health; whereas the development progressed to collaborative, coordinated, and multidisciplinary, the emphasis increases to patient-centered care models. Finally with the development to interdisciplinary and integrative models, changes occur in philosophical underpinnings, structure, process, and outcomes. The important part of the development was that the practice model chosen depended on the patient needs not the health professionals (Coyle et al. 2011).

5 Types of Teamwork and Collaboration

Interprofessional practice is not solely about "teamwork," and in this section we consider the nature of teamwork, the relationship between teamwork and wider collaborative practice, and the implications for palliative care.

There is an extensive literature on teamwork spanning many disciplines such as business, organization theory, sociology, psychology, and the health professions. For example, "*a team is a set of interpersonal relationships structured to achieve established goals*" (Johnson and Johnson 2006 p. 5, p. 595), while the following adds in values from a business perspective: "*Teamwork represents a set of values that encourage behaviors such as listening and constructively responding to points of view expressed by others, giving others the benefit of the doubt, providing support to those who need it, and recognizing the interests and achievements of others*" (Katzenbach and Smith 1993, p. 15). There is an implication here of a small number of people – the core palliative care team, for example.

A common theme of definitions of teams is of such a small number of people with a common purpose. Indeed, research indicates that optimal team functioning is dependent on common goal settings, together with regular meetings and reflection on performance. For example, a study from the UK found that health professionals, who had identified themselves as working in teams, reported less job satisfaction and more burnout if they did not meet frequently (or at all) to review performance in relation to their goals. There was also a greater probability of patient safety issues (Dawson et al. 2007). Reeves et al. (2010), from their extensive review of the teamwork literature, and through empirical research in healthcare settings, also conclude that for teams to be effective they need to have clear team goals, shared commitment, role clarity, interdependence, and integration between members. Additional attributes of functional healthcare teams include democratic approaches; agreement on ground rules for working together; active participation by all members; mutual role understanding; good communication; the development of joint protocols, training, and work practices; and good performance management (West and Slater 1996; Hammick et al. 2009; Reeves et al. 2010). In addition, emphasizing the need for a workable number of members, teams need to have a single shared work location and regular time to develop team working away from practice (Reeves et al. 2010).

To achieve a common good or aim, a team has to have a specific structure and organization

process in order to present a cooperative accountable outcome. Manion et al. (1996) differentiate between a working group and a team in the responsibility, authority, and accountability of each. In order to accomplish a task as a successful team, it is important to recognize that the different skills, knowledge, and expertise each team member brings needs to be combined to meet the patient needs: this translates into interprofessional working. This should be achieved through an agreed formal decision-making process and a valuing of differences that is seen as a collective strength that develops trust and confidence that results in a highly productive, effective, creative group of people (Ovretveit 1995).

6 Collaborative Practice in Action

In healthcare practice, however, many health and social care professionals are not together in bounded "official" teams even though they may interact at times with the same patients, families, and carers. The palliative care team, whose core membership may include nurses, a palliative care specialist, a cancer specialist, a physiotherapist, and a psychologist, may also work in collaboration with others including social workers, occupational therapists, and pharmacists. There are also likely to be hierarchical lines of authority within each profession together with varying levels of professional autonomy. Multi- rather than interprofessional collaboration may mean that health professionals interact individually with patients, setting their own goals and management plans without consultation with others who are involved – a situation that is not helped if patient records are not shared (even with the patient) (Thistlethwaite 2012a). Collaborative working is a skill that needs to be learnt and involves negotiation and often conflict resolution. As mentioned earlier health and social care professionals work within strict boundaries set by their professional bodies, and this can be frustrating for others who prefer greater flexibility in patient care. Having interprofessional practice within their codes of practice could loosen these boundaries and provide a more integrated approach to care.

While we have given one definition of collaboration, this word is yet another term with multiple meanings. Another useful definition is that of Thomson et al. (2009), formulated following their review of the literature and through interviews with stakeholders:

> Collaboration is a process in which autonomous or semi-autonomous actors interact through formal and informal negotiation, jointly creating rules and structures governing their relationships and ways to act or decide on the issues that brought them together; it is a process involving shared norms and mutually beneficial interactions. (p. 25)

The World Health Organization has stated that there is now sufficient evidence to show that collaborative practice enhances health services and improves health outcomes, particularly for patients with chronic diseases (WHO 2010).

Reeves et al. (2010) have conceptualized interprofessional relationships as a series of widening circles. Their work was based on a critical assessment of published works relating to interprofessional practice in a variety of settings and national contexts. In the smallest circle is interprofessional teamwork defined as "the most 'focused' of health professional practice with high levels of interdependence, integration and shared responsibility" (p. 44). Collaboration, coordination, and networking then ripple out as more people and interactions become involved. Collaboration is therefore envisaged as a looser form of IPP – health professionals work together but with reduced levels of interdependence, integration, and shared responsibility. While a healthcare team may involve three to ten people, collaboration assumes many more than this. Coordination involves a shared identity, but integration and interdependence are much less important, while networking may relate to virtual working with asynchronous meetings across wider distances and many institutions.

This work of Reeves et al. (2010) has been expanded more recently through a further critical review on interprofessional interventions culminating in the development of the InterProfessional Activity Classification Tool (InterPACT) (Xyrichis et al. 2017). New subcategories are

added to the four previously defined, under collaboration, consultative collaboration and collaborative partnerships, and under coordination, coordinated collaboration, delegative coordination, and consultative coordination. Each category and subcategory is categorized by the relative importance of the following six dimensions: (1) shared commitment; (2) shared team identity; (3) clear goals; (4) clear team roles and responsibilities; (5) interdependence between team members; and (6) integration between work practices.

How is this classification useful in relation to palliative care? By categorizing the type of interprofessional work undertaken within any given setting and the health professionals involved, it is hoped that it will be easier to evaluate performance, plan training, and compare research studies into the impact of interprofessional practice. For example, palliative care by the core team directly with involvement of the patient is teamwork with very high levels of each of the six dimensions required. Consultative collaboration, such as when a specialist is required for advice about a particular patient care problem, requires a lower level of interdependence. Networking features "networks" of clinicians who share best practice, clinical guidelines, and innovations in care across a number of organizations with little integration across work practices at the level of individual patients. Orchard et al. (2005) emphasized that the development of an interprofessional culture that supports collaborative practice is critical, and this is supported by Gilbert (2005) as well.

7 Collaborative Decision-Making

Within any MDT, including palliative care teams, members make clinical decisions informed by several factors unique to the health professionals, and the patient and family, involved. Clinical guidelines, professional and organizational rules, and national regulations help provide the infrastructure to any action, but these are interpreted in relation to the views of the clinician and patient preferences that help direct decisions. Such views and values are central to the function of the MDT (Thistlethwaite and Hawksworth 2014).

Adopting a patient-centered approach facilitates the process by which the perspective of the patient is paramount in shared decision-making. Shared decision-making is informed by collective values and the sharing of different views. It is important to ensure that the patient (and carer/family as appropriate) is regarded as part of the team. Thus, a "new" team is formed for every patient (Thistlethwaite and Hawksworth 2014).

The first step in the collaborative decision-making process is to invite and listen to the patient's perspective and experiences. The patient's needs, ideas, concerns, values, and expectations are explored using a biopsychosocial approach without solely focusing on the biomedical or reverse view (Fulford 1989). "The biopsychosocial model enables the physician to extend application of the scientific method to aspects of everyday practice and patient care previously not deemed accessible to a scientific approach" (Engel 1981, p. 102).

Of course adopting a patient-centered approach and eliciting the patient's perspective may be difficult. Impeding factors may include such factors as a professional's concept of their duty of care, organizational values based on efficiency, medical paternalism and professional hierarchies, as well as power imbalances between professional and client (Fulford 1989). The team needs to bear these factors in mind and their influence on professional decisions. The team needs to reflect, analyze, and challenge members' views within an ethos of trust and respect.

8 Dysfunctional Teams

Coming back to considering practice at the level of the palliative care team, challenges arise when teams become dysfunctional. A common problem is that team members start to work as a group of individuals with each team member identifying more with their own profession and their own professional colleagues than with their team members from other professions. Some teams manage to avoid conflict, yet working through conflict

rather than burying and ignoring it can make a team stronger and more productive. Alternatively there is the indecisive team. Prioritization of tasks becomes difficult, perhaps when workload increases or leadership changes.

Lencioni (2002) identified five common characteristics of dysfunctional teams: absence of trust, fear of conflict, lack of commitment, avoidance of accountability, and inattention to results. Trust between team members is imperative: trust is required for people to be able to work together and implies a certain level of vulnerability. Trust may be lost for many reasons: personal experience with an individual or members of a particular profession, lack of confidentiality in relation to team or personal conversations, dislike between team members, etc. Lack of trust may also be due to team members not fully understanding each other's roles and responsibilities, what each has been trained to do and is competent at doing. Regular team meetings and discussion of values, patient cases, near misses, and significant events are necessary to build and maintain trust (Thistlethwaite 2012a). Self-awareness is required to diagnose that the team is dysfunctioning and needs help. Team members always need to remind themselves that the focus is on improving quality of life for the patient and their families.

9 Team Conflict

Dysfunction may lead to conflict within the team, while unacknowledged and unattended conflict may lead to dysfunction. Conflict, however, does not necessarily have to be a negative experience with a negative outcome. Conflict has been described as occurring when "behaviour is intended to obstruct the achievement of some other person's goals" (NHS Institution for Innovation and Improvement 2010, p. 297). It is a feature of human life and thus of healthcare. It may take place in teams, between teams, between teams and their organization, and, indeed, between patients and health professionals. One of the core underpinnings of working in palliative care is that health professionals will focus on total patient care. Like a family, teams do have conflict at times and is probably inevitable. However the key to resolution is that it will be effectively managed. Conflict in itself can be a positive and healthy process in that there will always be differences, and the diversity can become a strength of a high functioning team. Competencies required for interprofessional practice include those relating to conflict resolution, through awareness, negotiation, and compromise (see, e.g., CIHC 2010; IPEC 2011).

Reasons why conflict occurs include poor and miscommunication, personal dislikes, lack of understanding of roles and responsibilities of team members, poor leadership, hierarchies within the health system, diverse values, maldistribution of workload, etc. Within an interprofessional practice framework conflict may also arise from leadership (principally if medical) restricting healthcare delivery to a predominantly medical model. Brown et al. (2011) found three main sources of team conflict – role boundary issues, lack of understanding of scope of practice, and accountability. True interprofessional practice is based on full participation by all health and social care professionals and the patient: teams need to put aside traditional authority relationships and adopt an egalitarian philosophy (Shaw 1990).

To help prevent conflict, teams need to share their feelings and values regularly and feel safe to do so. There should be frequent updates about individual's roles and responsibilities and the boundaries of their professional scope. It is helpful to agree guidelines for dealing with conflict. Good leaders monitor the psychological safety of the team and its members: psychological safety constitutes a shared belief that the team is safe for interpersonal risk taking (Edmondson 1999).

Orchard et al. (2005) offer a model for "Creating a culture for Collaborative Practice" and emphasize the importance of managing power imbalances between professions when developing power sharing in collaborative practice. In this model, Orchard et al. (2005) identify the main barriers to working with, from, and about health professionals are organizational structures, power imbalances, and role socialization. Gilbert (2005)

reinforces the barriers to collaborative practice in that he identifies institutional and professional barriers hinder progress, whereas Orchard et al. (2005, p. 4) stress that "organisations need to shift from their rigid bureaucratic structures to facilitate health professionals providing patient centred care." The World Health Organization (2010) agrees with these influences in that the barriers are seen as opportunities to change the institutional structures, collaborative practice teams, and a power with culture in that over time collaborative practice strengthens and transforms the education and health systems.

10 Interprofessional Education

In order to develop this further interprofessional education is required for all the palliative care team members so they work together with a common vision as well as recognizing the differences each brings to care. Historically health professional education was developed in silos keeping each profession separate in its education and in many areas this is unchnaged. Interprofessional education (IPE) is informed by educational, psychological, and sociological theories for its rationale and delivery, including but not limited to sociocultural and activity theory, social identity theory, situated learning, and organizational change (Thistlethwaite 2012b). It involves integration and shared learning throughout the continuum of professional education, training, and practice. Interprofessional education needs to be both at undergraduate and postgraduate levels as well as onward into continuing professional development (CPD) or in this case continuing interprofessional development (CIPD). Effective interprofessional education (IPE) enables effective collaborative practice, and effective collaborative practice strengthens health (and social care) systems and improves health outcomes (WHO 2010, p. 5). Interprofessional collaboration in palliative care is an opportune context for the team working together to "learn from, with, and about" each other for optimal patient care (CAIPE 2002) and well-planned, committed work for patients.

The opportunity for interprofessional working and learning and decision-making extends beyond interprofessional learning in palliative care and end of life care. Therefore to share some models that can assist in the development of interprofessional collaboration will follow.

CIPD should be based on adult learning principles and the identification of specific interprofessional learning outcomes of relevance for all participants (Thistlethwaite 2015). It may be delivered through seminars, short courses, and certificate programs that give different health professionals the opportunity to develop teamworking and collaborative skills together through case study analysis, role-play, storytelling, and perhaps problem-based learning to name a few strategies.

In order to create change and transform the systems, Orchard et al. (2005) identified four phases of change including sensitization, exploration, intervention, and evaluation (Fig. 1).

Sensitization identifies the barriers; exploration clarifies and values the roles; and throughout the implementation trusting relationships develop through power sharing within teams and valuing each other's roles. As this development process

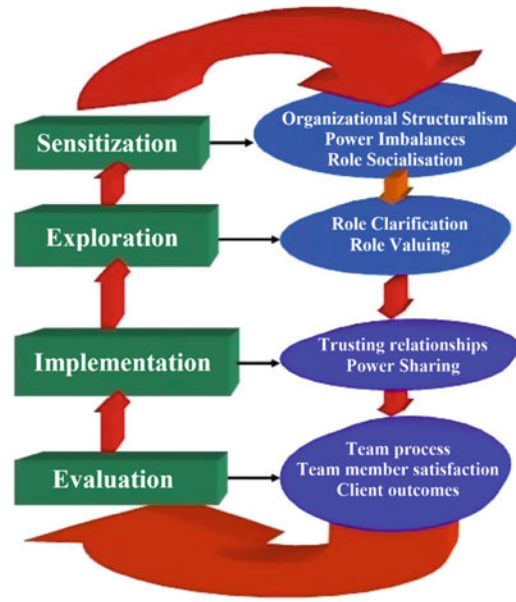

Fig. 1 Change process during team development. (With permission from the authors)

evolves and becomes the way of working, evaluation (4th phase) is undertaken with the team including the patient.

However opportunities for teams to work together once clarification of roles is transparent involve diversity being valued and power sharing occurring. It's moving through the four phases along with valuing, trusting, and respecting each other's role through working together for the best outcome for the patient and family – thus developing a cultural change to interprofessional working which includes a shared vision. Gilbert (2005) summarizes this well by saying "we not only need to build a culture of interprofessional education collaboration but at the same time as we build that culture, we need to be able to access a wide range of resources that can build new knowledge, new skills, respect and esteem for all collaborating partners along with the development of trust" (p. 102).

Consideration for transforming the barriers needs to include the structure of the organization along with the power imbalances and clarification of roles along with developing trust. The total process is shown in Fig. 2.

Ho et al. (2015) found that EOC (end-of-care) discussions with patients and families are challenging and that there are "additional ethical, emotional and practical concerns compared to other forms of healthcare decisions" (p. 798). The barriers of discomfort with death and dying, role responsibility, and uniprofessional working impact further on the health professional working outside a team. There needs to be a move from uniprofessionalism to interprofessionalism (Jones et al. 2015). Orchard et al. (2005) is one model that can guide that change. Given the global workplace crisis, the WHO supports collaborative practice (WHO 2010). Ho et al. (p. 801) emphasize "modern health care is increasingly interprofessional, and patients with complex situations may spend more time" with the team of health professionals.

11 Conclusion: Moving Forward

Understanding each other's profession, crossing the boundaries, valuing the diversity that is uncovered, and learning to practice together bring a collegiality that is interprofessional practice. Careful planning and working together are needed to build successful interprofessional practice. So decide on the team's work, a team development that works for the organization within which it sits, and work together to learn from each other as you work with each other, having learned about each other's profession. Interprofessional practice

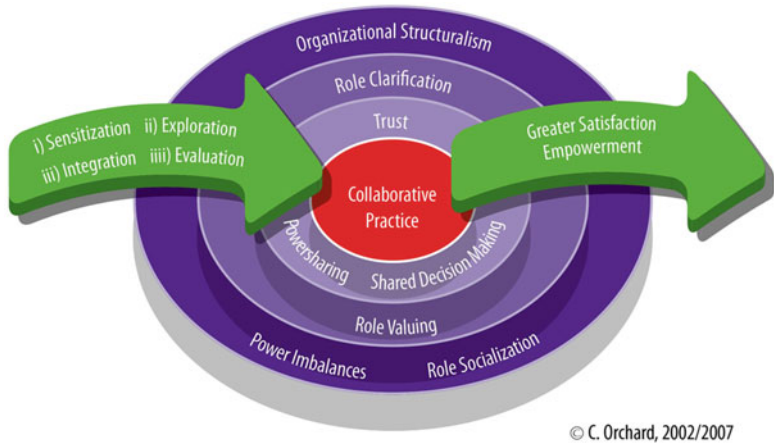

Fig. 2 Conceptual model for patient-centered collaborative interdisciplinary practice. (Figure from an Open Access article distributed under the terms of the Creative Commons Attribution License, http://creativecommons.org/licenses/by/4.0/, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited

needs palliative care teams to work together, meet challenges, and overcome any barriers to patient care.

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Nursing and Palliative Care

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Contents

Abstract

Nursing is integral to meeting the growing demand for palliative care which is being driven by population aging and the increasing burden of chronic, noncommunicable disease. Palliative nursing and nursing in general share many of the same principles and practices. Both are committed to addressing the holistic domains of health (physical, psychological, emotional, cultural, social, practical, spiritual, and informational aspects of a person's health and well-being) (Fitch, Hosp Q 3(4):39–46, 1999). This chapter provides an overview of the role of nursing in the context of contemporary interdisciplinary specialist and primary palliative care, key constructs underpinning palliative nursing, the core competencies of specialist and primary palliative care nursing, and how these competencies can be applied to provide best evidence-based person-centered palliative care, regardless of the care setting.

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1 Introduction

Nursing care is central to all hospice and/or palliative care ("palliative care") service delivery and is underpinned by the World Health Organization definition of palliative care (World Health Organization 2003). Having emerged from its informal religious roots, palliative nursing has evolved into a dynamic discipline that works with other interdisciplinary team members to improve care outcomes for people living with and dying from

R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_43

progressive illness and their families. Palliative nursing, along with palliative care, has evolved rapidly since the late 1970s and has largely been driven by a social movement designed to improve the care of people dying from cancer (Phillips et al. 2015). Dame Cicely Saunders (1918–2005), a nurse, social worker, and physician, responded to this need and established St Christopher's Hospice in North London, where care was focused on the physical, psychological, and spiritual needs of dying patients (Pace and Lunsford 2011). This holistic care model was rapidly translated to other high income countries such as Canada and Australia, while the uptake of palliative care in the United States of America occurred much later, partially in response to the landmark "SUPPORT study" (Connors et al. 1995). This large randomized controlled trial conducted at five US teaching hospitals lent considerable support to the need to improve palliative care in the world's largest economy. The subsequent release of the Institute of Medicine's "Approaching death: improving care at the end-of-life" (Institute of Medicine 1997) strengthened this call to action. Emerging from these developments has been the establishment of specialist palliative care nursing and recognition of the increasing importance of primary palliative care (Box 1) (Quill and Abernethy 2013).

The purpose of this chapter is to provide an overview of the role of nursing in the context of contemporary interdisciplinary palliative care.

Box 1 Key Definitions

Nurses – Regulated health professionals who work across all care settings (acute care, aged care, primary care) and in doing so provide care for people with palliative care needs and their families. These nurses provide primary palliative care.

Palliative nurses – Nurses who work specifically in the care of people with palliative care needs and their families. These nurses might work in specialist inpatient services (e.g. hospices, palliative care units) or in a consultative role working alongside nursing and interdisciplinary colleagues. These nurses provide specialist palliative care.

Palliative care – The definition provided by the World Health Organization has been adopted for this chapter: http://www.who.int/cancer/palliative/definition/en/. This definition refers to people who are affected by a life-limiting illness and advocates for the nursing role (generalist and specialist) to enable those affected to live as well as possible with their complex healthcare needs managed as well as possible.

1.1 Key Constructs Underpinning Palliative Care Nursing

Palliative care demands a skilled interdisciplinary response, with nurses playing a central role. Several constructs underpin contemporary palliative care nursing practice, including domains of nursing practice, evidence-based practice, person-centered care, and a population-based approach to palliative care. Each is essential to providing best palliative care, at the right time, every time, as detailed below.

1.1.1 Evidence-Based Practice

The notion that health service evaluation must be guided by scientific evidence, not clinical impression, was first suggested in the 1970s (Rosenberg and Donald 1995). Since then, evidence-based healthcare has become a guiding force in clinical practice and gradually embedded across various disciplines, including nursing. Evidence-based nursing care extends beyond mere reliance on research evidence, with nurses required to concurrently assess the risks, benefits, costs, inconveniences, and patient preferences in relation to proposed care (Scott and McSherry 2009). In the palliative care setting, these considerations are even more crucial due to the complex interplay of a patient's

vulnerability, diagnosis, prognosis, goals of care (Owens 2009), and a rapidly evolving evidence base (Tieman et al. 2008).

In order to exercise astute clinical judgment, nurses need prerequisite capabilities to successfully integrate evidence with their clinical expertise and patient preference(s) (Scott and McSherry 2009). Despite having positive attitudes toward evidence-based practice (Mehrdad et al. 2012; Stokke et al. 2014), recent research suggests that many nurses minimally engage in providing evidence-based care (Stokke et al. 2014). Keeping abreast of new evidence is challenging (Phillips 2015), which has led to the development of various publicly available websites, including: CareSearch (www.caresearch.com.au); Cochrane Library; Joanna Briggs Institute; and eviQ, which all host specialized evidence-based resources relevant to palliative care.

Having located the evidence, the next challenge is to critically appraise this in a rigorous way. At a minimum, all nurses need to be able to evaluate a study's methodological strengths and weaknesses before carefully considering its results, relevance, and applicability to their own practice. Critical appraisal tools such as those electronically hosted in the Critical Appraisal Skills Program (CASP) and Joanna Briggs Institute website provide nurses with a framework to systematically analyze research evidence for their trustworthiness and relevance.

Notwithstanding, the step up from "best evidence" to "best practice" requires concerted system level efforts, and nurses have ample opportunities to integrate best evidence to practice in day-to-day decision-making and care delivery. As nurses continue to shape palliative care practice through their diverse roles, from providing bedside care in an institutional setting to working as advanced nurse practitioners, every nurse needs to consider how they can integrate and promote evidence-based care into all healthcare decisions.

1.1.2 Ethical Behavior and Consumer Rights

The responsibility of providing palliative nursing care to vulnerable patients is often associated with ethical challenges that need to be addressed judiciously. An understanding of beneficence, non-maleficence, autonomy, and justice (Webb 2005) helps nurses uphold high standards of ethical conduct while addressing the unique issues pertaining to a patient's end-of-life care needs. Some of the common ethical issues that nurses' encounter are determining competency to consent, advocacy, and withholding and/or withdrawing treatment. Determining a patient's competency to consent is critical to striking a balance between respecting their autonomy to making informed decisions and protecting them if they are unable to do so.

When a patient lacks the competence to make a decision about treatment, substitute decision makers must be sought. Nurses have a responsibility to ensure that competent patients are provided with relevant information to assist them in making informed choices about the goals of care, proposed treatments, and burdens and benefits of participating in clinical trials (Anyfantakis and Symvoulakis 2011). Vulnerable palliative patients may be easily persuaded to make choices that they would not normally make. In such situations, nurses have a responsibility to act as patients' advocates ensuring that the patient's voice is heard and their choices are respected (Webb 2005). As the discipline that spends the most time with patients, nurses are best placed to advocate for the patient's preference and goals of care, symptom management, and cultural and spiritual needs (Earp et al. 2008). Advocacy in palliative care is not limited to speaking up "on behalf" of the patient but also involves providing patients with the support and information they require to speak for themselves regardless of their level of dependency (Webb 2005). The strengths of the nurse-patient relationship provide nurses with unique access to the perspectives, preferences, wishes, and concerns of the patient living with and dying from progressive illness.

Nurses play a central role in ensuring that the patient's voice is heard, especially when decisions about forgoing and/or starting a medical treatment are made (Albers et al. 2014). Careful consideration of the benefits versus the burden of proposed treatment and its impact on the patient's quality of life ought to inform all decision-making processes.

While physicians are more often responsible for such decision-making, the involvement of nurses in this process is essential (Albers et al. 2014). It is also crucial for nurses to be able to differentiate between withholding and withdrawing treatment, and provision of effective symptom relief and euthanasia. While the former is carried out with an intent to minimize treatment burden and improve patient's quality of life, the latter is intended to end a patient's life (New South Wales Department of Health 2005). Nurses may receive requests from families asking for "something" to bring an end to the suffering of their loved ones in the last days of their life. Such requests demand the utmost care to identify why such a request is being made at this time and to determine alternative actions that could address the patient's and/or family's concerns (Caresearch 2017).

1.1.3 Person-Centered Care

Person-centered care is a fundamental component of effective palliative care and underscores the importance of interdisciplinary care for people living with and dying from progressive illness. There are many definitions of person-centered care; however, two are of specific relevance to palliative care nursing, namely: (1) dimensions of patient-centered care as articulated by the Picker Institute (Picker Institute Europe 2017) and (2) constructs articulated in a person-centered practice framework developed by McCormack and McCance (2017). The Picker Institute identified eight characteristics of care that are most important to patients and their families (Barry and Edgman-Levitan 2012) and has since detailed these as the principles of person-centered care, namely: (1) fast access to reliable healthcare advice; (2) effective treatment delivered by trusted professionals; (3) continuity of care and smooth transitions; (4) involvement of, and support for, family and carers; (5) clear, comprehensible information, and support for self-care; (6) involvement in decisions and respect for patient's preferences; (7) emotional support, empathy, and respect; and (8) attention to physical and environmental needs (Picker Institute Europe 2017). In the McCormack person-centered practice framework, four constructs are considered essential for the provision of person-centered nursing care: (1) prerequisites and/or nursing attributes; (2) care environment and/or context of care; (3) person-centered processes of care; and (4) person-centered outcomes (Fig. 1) (McCormack and McCance 2017).

Nurses are in a unique position to both lead and innovate in relation to provision of person-centered care especially as they are the only health professional available 24 hours a day in most care settings. This exposure to patients and families provides nurses with a unique opportunity to establish and develop therapeutic relationships that address the principles of person-centered care. Understanding how to achieve person-centered care is fundamentally important for all nurses but particularly for those providing palliative care given the complexity of patient and family needs. Indeed, a synthesis of a large body of research conducted over the past 25 years has identified the elements of care inpatients and their families considered to be most important at the end-of-life (Fig. 2) (Virdun et al. 2015, 2017). These areas of importance align with the principles and constructs of person-centered care. It is these elements of importance that ought to inform the provision of optimal person-centered palliative nursing.

1.1.4 A Population-Based Model of Palliative Nursing

The demand for palliative nursing continues to grow in response to changing epidemiology, population aging, the recognition of the value of early palliative care, and the need to extend timely palliative care to populations beyond cancer (Morrison et al. 2011; Temel et al. 2010). Meeting this increased demand will be challenging for specialist palliative care services, especially, if people with palliative care needs are to have access to a comprehensive and holistic service. There is now recognition of the importance of developing interdisciplinary population-based models that are designed to improve access to palliative care in accordance with need (Luckett et al. 2014).

A population-based approach to palliative care service planning focuses on strengthening the delivery of palliative care provided by the patient's usual care team ("primary palliative care") in the acute care, community, and aged care settings (Quill and Abernethy 2013).

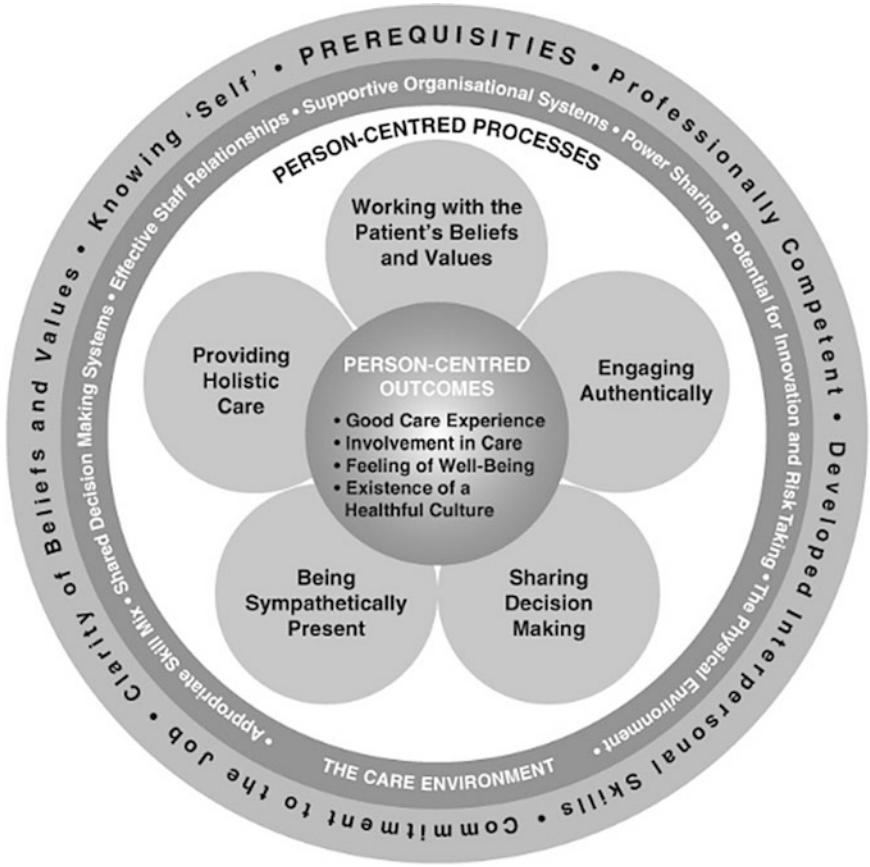

Fig. 1 The person-centered practice framework (McCormack and McCance 2017, p. 63) (Source: Permission obtained to use the figure)

Adopting a population-based approach helps to facilitate a responsive and inclusive method of addressing the particular geographical, social and cultural needs of people with a progressive illness (Palliative Care Competence Framework Steering Group 2014). It helps to ensure that palliative care is more accessible for Aboriginal-first nation peoples, socially disadvantaged people, people living with nonmalignant illness, and people living in rural and remote areas, all of whom often have more limited access to palliative care (Palliative Care Competence Framework Steering Group 2014). For example, a population-based model of care is key to improving the provision of palliative care to older people in nursing homes who have unmet palliative care needs. In this care setting, the primary palliative care ought to be provided by the older person's usual care team (care assistants, registered nurses, and general practitioner) and be augmented with specialist palliative care input and active patient and primary care engagement (Candy et al. 2011; Hall et al. 2011; Davies et al. 2011). Implementing this type of model would do much to address poor symptom control, unnecessary hospitalizations, suboptimal communication, inadequate advance care planning, and families who are dissatisfied with palliative care (Phillips et al. 2006).

Comprehensive interdisciplinary specialist palliative care services are central to operationalizing a population-based model of care. Providing direct care and/or consultative services in the tertiary, secondary and/or primary care settings, these specialist palliative care services (including specialist nurses) are ideally placed to provide local leadership, training, mentorship,

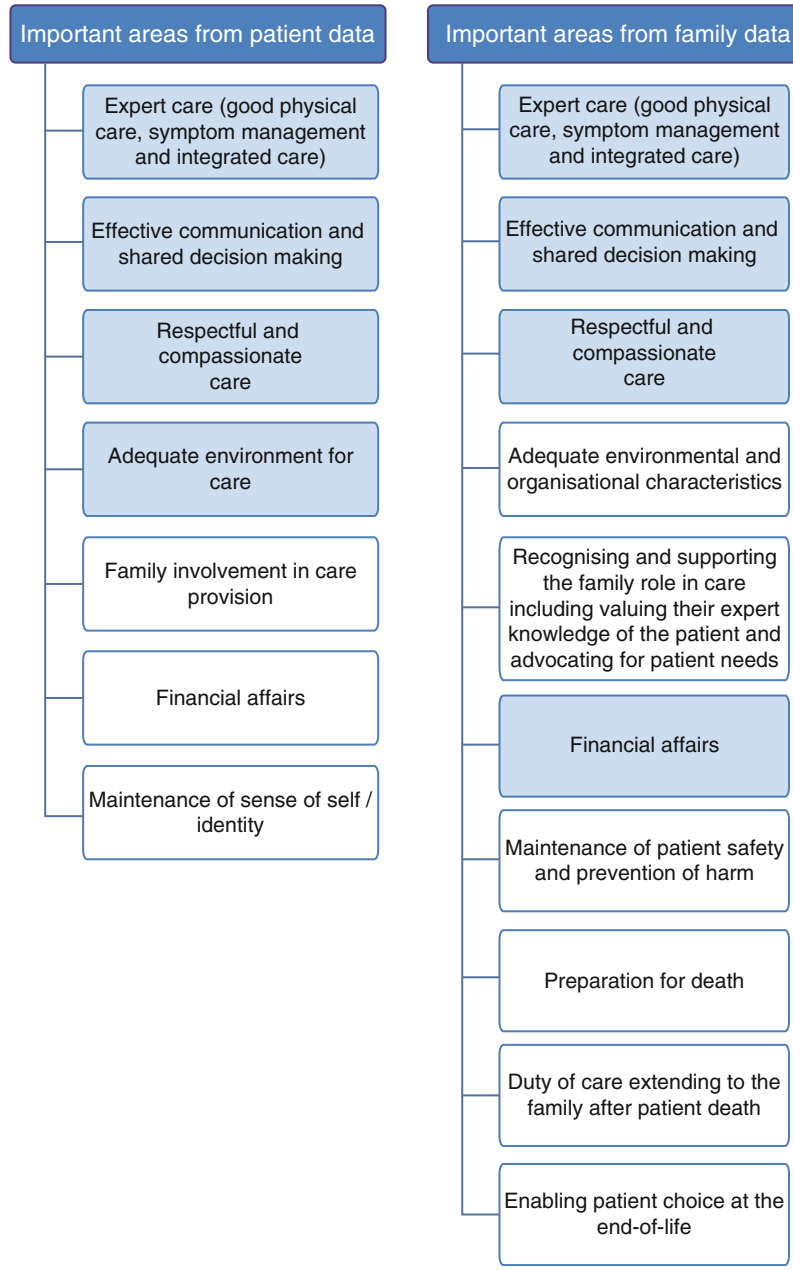

Fig. 2 Area of importance for optimal end-of-life care in hospitals: patient and family perspectives (Virdun et al. 2015)

and supervision to support the delivery of primary palliative care by other health professionals and to undertake research and/or quality initiatives (García-Pérez et al. 2009; Higginson and Evans 2010). Implementing a population-based approach requires that all nurses, regardless of specialty training, are able to provide primary palliative care to the patients and families they service. It also requires specialist palliative nurses to operate alongside nurses providing primary palliative care. Furthermore, a commitment to building collaborative care partnerships and the palliative care capabilities within the broader interdisciplinary care team is vital. By making better use of scarce resources, specialist palliative nursing is then reserved for patients and families with the most complex needs (Palliative Care Australia 2005).

1.1.5 Domains of Nursing Practice

Regardless of the care setting or population, all nurses are required to practice in accordance with the relevant legislation affecting nursing practice in healthcare. Nurses function within several key domains of practice, and while these may vary across countries and/or jurisdictions, they largely focus on (1) critical thinking and analysis; (2) engagement in therapeutic and professional relationships; (3) maintenance of the capability to practice; (4) comprehensive assessments; (5) development of a plan for nursing practice; (6) provision of safe, appropriate, and responsive quality nursing practice; and (7) evaluation of outcomes to inform nursing practice (Nursing and Midwifery Board of Australia 2016). In Australia, these standards are conceptualized as a matrix, with interrelated Standards 1–3 forming the y-axis, while Standards 4–7 describe the dimensions of practice and form the x-axis. Each standard has criteria that specify how that standard is demonstrated within the context of each registered nurse's practices (Nursing and Midwifery Board of Australia 2016).

Nurses are also required to operate within a professional and ethical nursing framework. Practicing within an evidence-based framework, participating in ongoing professional development, and systematically developing the capabilities of others are considered core competencies necessary for critical thinking and analysis. The provision of coordinated and effective care requires nurses to have the capabilities to conduct a comprehensive and systematic nursing assessment, plan care in consultation with other members of the interdisciplinary team and in accordance with patient preference, implement comprehensive safe and effective evidence-based nursing care, and evaluate the care. Establishing and/or maintaining therapeutic relationships as well as appropriately concluding them and collaborating with other members of the interdisciplinary team underpins all collaborative and therapeutic practices (Nursing and Midwifery Board of Australia 2016). The competency standards for registered nurses are the foundation upon which specialist competencies are built.

1.1.6 Palliative Care Competencies

Preparing the nursing workforce to operate within a population-based model requires consideration of the competencies required to fulfill the different levels of specialization and defined scope of practice. While there is considerable debate about the most appropriate definitions and methods of assessments, nursing competencies are generally considered to represent a dynamic combination of knowledge (basic or specialized), skills (assessment, communication, critical thinking, time management, customer services, technical skills, and teaching), and abilities (caring, character, and professional presentation) which contribute to understanding (Aranda and Yates 2009). In preparing the nursing workforce to provide palliative care, it is important to consider the competencies required for each of the four levels of nursing practice across the six domains of palliative care, namely: (1) principles of palliative care; (2) communication; (3) optimizing comfort and quality of life; (4) care planning and collaborative practice; (5) loss, grief, and bereavement; and (6) professional ethical practice in the context of palliative care (Palliative Care Competence Framework Steering Group 2014). The European Association for Palliative Care has identified the following ten core interdisciplinary palliative care competencies considered necessary for optimizing patient and family outcomes (European Association for Palliative Care 2013) (Box 2).

Box 2 Ten Core Interdisciplinary Palliative Care Competencies (European Association for Palliative Care 2013)

1. Apply the core constituents of palliative care in the setting where patients and families are based.
2. Enhance physical comfort throughout patient's disease trajectory.
3. Meet patient psychological needs.
4. Meet patient social needs.
5. Meet patient spiritual needs.
6. Respond to the needs of family carers in relationship to short, medium, and long-term patient care goals.

(*continued*)

Box 2 (continued)

7. Respond to the challenges of clinical and ethical decision-making in palliative care.
8. Practice comprehensive care coordination and interdisciplinary teamwork across all settings where palliative care is offered.
9. Develop interpersonal and communication skills appropriate to palliative care.
10. Practice self-awareness and undergo continuing professional development.

As the provision of high-quality palliative care is an essential responsibility of the whole healthcare system, many countries, jurisdictions, and/or professional bodies have developed palliative care competency frameworks (Palliative Care Competence Framework Steering Group 2014; Aranda and Yates 2009; Palliative Care Nurses New Zealand 2014). Competencies have been variously defined but generally refer to ". . .a cluster of related knowledge, skills and attitudes that affects a major part of one's role (a role or responsibility) that correlates with performance on the job, that can be measured against well–accepted standards, and that can be improved by training and development" (Parry 1996).

Recognition of the different levels of palliative care nursing specialization is central to developing a competency framework, with four different levels of palliative care nursing specialization evident across the healthcare system, including primary palliative care nurses ("all"), palliative care nurses' champions ("many"), specialist palliative care nurses ("some"), and palliative care advanced practice or nurse practitioners ("few") (Table 1) (Palliative Care Competence Framework Steering Group 2014; Aranda and Yates 2009; Palliative Care Nurses New Zealand 2014).

The palliative care nursing capabilities required for each of these four levels increases in intensity as the role becomes more focused on the specialty. At a minimum, all nurses require the capabilities to provide basic pain and symptom management, including managing anxiety and depression, and initiating conversations about prognosis, suffering, and goals of care and patient preferences, especially around resuscitation status (Quill and Abernethy 2013). Specialist palliative care nurses are required to have more advanced skills and the capabilities to manage refractory pain and other symptoms, including complex depression anxiety and existential distress; and assist with resolving goals of care, treatment, and/or family conflicts as they arise (Palliative Care Australia 2005). Palliative care nurse practitioners have a broader scope of practice and operate in accordance with the values, guidelines, and principles set out by their governing regulatory and professional bodies (Aranda and Yates 2009). All nurses will need to continue to learn throughout their professional life as new evidence emerges within this field.

As developing a sustainable nursing workforce capable of providing high-quality care requires a targeted response, several countries have established national professional development frameworks for cancer and/or palliative care nursing (Palliative Care Competence Framework Steering Group 2014; Aranda and Yates 2009; Palliative Care Nurses New Zealand 2014). Underpinned by a population-based approach, these professional development frameworks define nursing's contribution to palliative care and highlight the contribution all nurses make, irrespective of their role (Palliative Care Nurses New Zealand 2014). As previously described, four broad levels of palliative care nursing practice have been identified (Refer Table 1) to reflect the different levels of competencies required of nurses working in different contexts (Palliative Care Nurses New Zealand 2014). The level of palliative care competencies required at each of the four levels of practice reflects the number of palliative patients cared for by nurses and is best conceptualized as the "all, many, some, and few" competency framework as depicted in Fig. 3 (Aranda and Yates 2009; Palliative Care Nurses New Zealand 2014). Within each of the four levels, nurses will be functioning at differing levels of competencies from beginning through to advanced levels. This progression is reflected

Table 1 Levels of palliative care specialization (Palliative Care Competence Framework Steering Group 2014; Aranda and Yates 2009)

Level of specialization	Guiding principles
Level I – *ALL* Primary palliative nurses	Palliative care principles or a palliative approach needs to be practiced by all nurses working in the acute, community, or nursing home settings. Many people with progressive life-limiting illnesses will have their care needs met comprehensively by their usual healthcare team and not require referral to specialist palliative care units or personnel
Level II – *MANY* Palliative nurses champions	As an intermediate level, a proportion of individuals and families will benefit from the expertise of local palliative nursing champions who, though not engaged full time in palliative care, have undertaken additional palliative care training (i.e., graduate certificate and/or diploma levels) and/or intensive palliative care clinical internships and training. With this training and their networks, they are able to act as a palliative care resource within their organization. Many of these nurses will work in cancer, renal and/or respiratory care, intensive care, acute care, domiciliary care, and/or aged care
Level III – *SOME* Specialist palliative nurses	Specialist palliative nurses are focused entirely on the provision of palliative care. These nurses are involved in the care of patients and families with more complex and demanding palliative care needs. As a consequence these nurses require higher level palliative care training at the masters level in order to develop the competencies and specialist skills required for managing complex problems
Level IV - *FEW* Palliative care nurse practitioners/ advance practice nurses	Palliative care nurse practitioners or advanced practice nurses are able to work as independent nurses and in many countries have prescribing rights

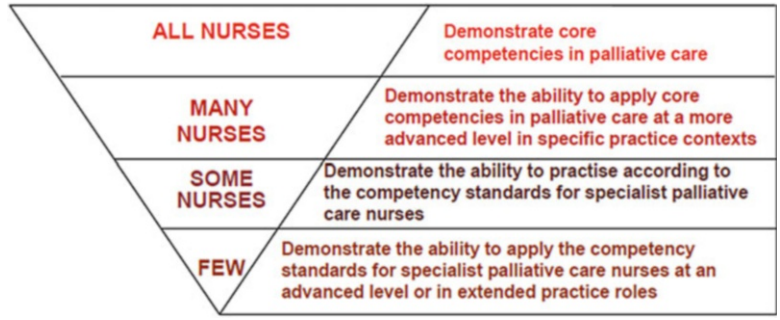

Fig. 3 A professional development model for palliative care nurses (Palliative Care Nurses New Zealand 2014, p. 6)

in their capacity to integrate theory, practice, and experience (Palliative Care Nurses New Zealand 2014). Increasing degrees of autonomy in judgment and interventions is evident as nurses become more specialized (Palliative Care Nurses New Zealand 2014).

1.1.7 Certification and Credentialing

In addition to the competency framework, some organizations have moved to introduce certification and/or credentialing processes. Certification is generally undertaken by professional bodies (i.e., Palliative Care Nurses Australia) on behalf of its members. Certification processes are designed to publicly acknowledge the achievements of nurses working in specialized areas against a predefined set of requirements (Aranda and Yates 2009). A major limitation of most certification processes is they lack the detail necessary to guide employers as to whether a particular nurse can function effectively in all areas of practice (Aranda and Yates 2009), whereas credentialing is a more comprehensive process that is normally undertaken by an employing organization. Credentialing clearly documents the scope of practice of a particular nurse in a specific practice setting and is often locally defined (Aranda and Yates 2009).

Table 2 Applying palliative care competencies to ensure the provision of person-centered palliative nursing (McCormack and McCance 2017)

Person-centered care (McCormack and McCance 2017)	Translation to palliative nursing	Opportunities for improvement/innovation
1. Prerequisites		
Professionally competent	Relevant registration requirements confirmed Implementation of palliative care nursing competencies for "all, many, some, and few" nurses Annual appraisal of competencies and identified areas for growth Ability to think critically, problem solve, predict outcomes, and use judgment and wisdom to devise optimal palliative care interventions and evaluation of care	Validation of competency frameworks for palliative nursing and competency indicators for each level of palliative care nursing Aligning nurses' continuing professional development (CPD) opportunities with their required competencies
Developed interpersonal skills	Interpersonal communication capabilities (managing workplace conflict, challenging conversations) clearly defined and measured in accordance with level of competencies Builds therapeutic relationship with patients and families Develops interpersonal and communication skills appropriate to palliative care	Partnering with universities and/or communication experts to build nurse's interpersonal skills Integrates communication into CPD opportunities Evaluates patient and family experience in relation to care received to drive improvement efforts
Commitment to the job	Rewards commitment with professional development and advancement opportunities Acts as a resource to others in the interdisciplinary team	Organizational efforts to value, develop, and reward excellence in care provision accessible to staff Evaluation and/or research of what fosters commitment to one's role to drive organizational strategies for staff development and retention
Clarity of beliefs and values	Shares a common philosophy of care Alignment of organization and individual beliefs and values Acts in accordance with national, international, legal frameworks and patient's wishes and values	Creates a values-driven workplace Development of and linkage to accessible CPD opportunities to provide information about legal frameworks with particular reference to advance care planning, directives, effective palliative care, and euthanasia to support staff understanding about the clear differences between palliative care and euthanasia
Knowing "self"	Engages with clinical supervision to support development of self-awareness and how this may impact on palliative care Practices self-awareness and undergoes CPD Implements self-care strategies to prevent burnout Recognizes early sign of burn out and seeks appropriate help	Builds the evidence on effective self-care and sustainability strategies for palliative care Identifies ways to strengthen resilience and prevent burnout Validates clinical supervision models to understand best practices Develops tools for nurses to use for self-care, based within emerging technologies Ensures integration of learning about strategies to prevent burnout and maintain health within undergraduate and postgraduate education
2. The care environment		
Appropriate skill mix	Provides the correct nursing and interdisciplinary skill mix requirements for optimal palliative care	Develops and tests innovative models of care Researches the unique contributions made by nursing within palliative care provision to enhance understanding of such roles in both

(*continued*)

Table 2 (continued)

Person-centered care (McCormack and McCance 2017)	Translation to palliative nursing	Opportunities for improvement/innovation
	Balanced skill mix to optimize patient outcomes	primary and specialist roles Identifies optimal skill mix models to drive policy support for best care across all settings (aged care, acute care, primary care). Such work could inform structural quality indicators for service commissioners to align with
Shared decision-making systems	Enables patients and families to participate, in accordance with their wishes, in consultations, case conferences, bedside handovers, articulation of goals and plans for care Supports patients and families to participate in daily planning sessions for their care to enable changes in priorities to be identified, over time Champion nurses' unique position to advocate for the patient and family voice in care planning and provision	Considers the role of emerging technologies to assist in shared decision-making Develops and tests new models that deliver integrated and coordinated care Evaluates patient and family experience in relation to shared decision-making
Effective staff relationships	Supports and fosters collaborative interdisciplinary relationships and effective communication Supports and mentors new graduates or staff new to a clinical area Palliative nurses actively support colleagues providing primary palliative care	Develops new models to promote interdisciplinary collaboration both within the specialist and primary palliative care teams Develops, utilizes, and evaluates explicit supports for new graduate staff and staff new to a clinical area which align with the constructs of a person-centered practice framework Evaluates current practice to identify areas for improvement
Supportive organizational systems	Creates an environment that actively implements the existing evidence and supports the delivery of best evidence-based nursing care Values and rewards the provision of excellent person-centered care at all times	Enables regular staff feedback in relation to supports provided and improvements required to allow optimal person-centered care Evident organizational support for identification and management of key areas for improvement Evident no blame culture – respect for staff reporting concern so as change can occur
Power sharing	Actively engage patients and families in organizational and patient level decision-making processes Understand and respect practice and disciplinary boundaries	Prioritizes consumer involvement (patients and their families) in organizational decision-making processes Considers use of technological feedback systems for staff to use in reviewing working relationships
Potential for innovation and risk-taking	Implements the existing palliative nursing evidence base Critically considers all aspects of care, questions appropriately, and fosters opportunities to develop new evidence Engages consumers in all change initiatives and/or new developments Displays agility in professional practice to	Builds the palliative nursing evidence base Develops and test new models of care and non-pharmacological strategies to improve care outcomes Seeks philanthropic funding to build palliative nursing research Specialist palliative care nurses to lead in the

(*continued*)

Table 2 (continued)

Person-centered care (McCormack and McCance 2017)	Translation to palliative nursing	Opportunities for improvement/innovation
	enable creative care options (based within the evidence) for people with complex care needs	adoption of new evidence for people with chronic and complex healthcare needs
The physical environment	Consider the needs of people living with and dying from progressive illness within each care environment Identify areas within each environment that can be improved and where possible, do so (e.g., visiting hours, supported parking fees, privacy for families) Work with each patient to understand their needs as these vary with each individual (e.g., single room, home setting, remote locations)	Self-assess a care environment to identify areas for improvement, some of which can be fixed much more easily than others Work with consumers to understand their areas of importance in relation to the care environment Consider partnerships with designers and architects to assist in altering clinical environments to enable best palliative care
3. Person-centered processes		
Providing holistic care	Provides optimal palliative care at all times, in accordance with patient wishes and preferences and best available evidence Applies the core constituents of palliative care in the setting where patients and families are based Enhances physical comfort throughout the patient's disease trajectory Meets patient psychological, social, and spiritual needs	Builds the evidence base to support palliative nursing interventions that, in conjunction with interdisciplinary care, drive optimal palliative care
Working with the patient's beliefs and values	Conscious and respectful of the patient's boundaries in terms of cultural taboos, values, and choices Ensuring the translation of unique patient's beliefs and values to the interdisciplinary team to inform care Provision of creative solutions where needed to enable person-centered care, irrespective of care environment (e.g., Enabling spiritual practices to occur; working to enable identified goals be achieved; considering opportunities to allow pets to visit)	Creates agile and adaptable organizational systems that accommodate the patient's beliefs and values Works closely with consumers to understand what aspects of care need improving in relation to care provision, organizational practices, or physical environment
Engaging authentically	Effectively engages patients and their families, clinicians providing primary palliative care, and other members of the interdisciplinary team	Creation of networked palliative care models Effective use of technology to optimize engagement Assessment of patient and family experience in relation to this aspect of care to drive improvement efforts
Shared decision-making	Optimizes patient and family engagement in decision-making Ensures patient and family information accurately translates into the care plan Understands when and how to refer for expert specialist advice	Researches patient and family requirements for shared decision-making in palliative care – What level of "shared" is of most support? Investigates the impacts of effective shared decision-making for families in relation to their bereavement needs Considers, designs, and evaluates educational needs for health professionals in relation to enabling effective shared decision-making
Being sympathetically present	Responds appropriately to the needs of patients and families and other members of the interdisciplinary palliative care team	Evaluates this aspect of care experience for patients and their families to highlight areas for improvement

(*continued*)

Table 2 (continued)

Person-centered care (McCormack and McCance 2017)	Translation to palliative nursing	Opportunities for improvement/innovation
	Recognizes the uniqueness and value of each patient and works to maximize their coping abilities Understands the meaning and impact of life-limiting illnesses on patients and their families Adheres to evidence-based guidelines for breaking bad news	Works with universities to create simulated opportunities for skill development for students at both undergraduate and postgraduate levels
4. Person-centered outcomes		
Good care experience	Utilizes patient reported outcome measures to drive practice assessment and change	Develops and tests novel approaches for understanding real-time patient and family experience Embeds real-time experience data into systems that drive opportunities for improvement and uture research
Involvement in care	Actively involves patients and their family in care planning and delivery Supports patients to receive palliative care in their setting of choice Enables patients to manage their personal affairs Actively promotes comprehensive care coordination	Develops mechanisms to regularly assess patient and family experience in relation to this aspect of care Considers novel technologies that enable real-time feedback for care teams in relation to patient and family experiences of care delivery
Feeling of well-being	Values the patient and works to provide a positive care experience Acknowledges patient's emotions and provides sensitive support Prevents suffering and unnecessary distress Promotes patients' and families' coping mechanisms Understands patients' and families' social context and how this may impact on their palliative care experiences Paces the provision of information according to patient preferences and cognitive capacity Identifies complex bereavement needs and refers accordingly Prioritizes work environments that are supportive and staff feel valued for their work and positive about their role	Develops and tests novel approaches for understanding patient and family experience in relation to this aspect of care Enhances the evidence base informing how to work and foster patients' and families' coping mechanisms Works with available evidence in relation to bereavement assessment and care to implement where possible and/or identify new research questions Considers unique population needs and allows consumers to drive service design in accordance with these
Existence of a healthful culture	Responds to the challenges of clinical and ethical decision-making Supports colleagues throughout emotionally challenging work Positively responds to opportunities for change and improvement Utilizes supportive and empowering leadership approaches based in mutual respect for colleagues and a willingness to continually work for excellence in care delivery	Considers novel technologies to support interdisciplinary staff feedback in relation to this aspect of organizational culture Clear management support for a positive organizational culture based in respect for staff and a shared vision for care delivery Development of CPD resources to shape understanding about leadership and change management

1.2 Policy and Practice

Operationalizing a population-based approach to palliative care requires consideration of the competencies required by all nurses working within the healthcare system and strategies to ensure the provision of best evidence-based person-centered care. Integrating the person-centered practice framework to palliative nursing in accordance with the EAPC's ten core palliative care competencies allows for the identification of systems, education, clinical service delivery, and research improvements and/or innovation opportunities to improve care outcomes for patients and their families with palliative care needs (Table 2). All such areas have implications for global palliative care nursing policy and practice.

1.3 Conclusions

Nurses globally are central to addressing the palliative care needs of people living with a progressive life-limiting illness and their families. In partnership with other members of the interdisciplinary team, nurses are responsive to palliative populations' needs within the context of the governing values, guidelines, and principles set out by the relevant regulatory and professional nursing bodies' and governments' priorities. The adoption of a population-based approach to planning offers opportunities to increase the access patients and families have to timely and best evidence-based palliative nursing care. Continuing to evolve and integrate new evidence into practice while building palliative care nurses' capabilities within their scope of practice will ensure that more patients have access to optimal palliative care. In order to improve outcomes for populations with palliative care needs, nurses need to develop new knowledge in partnership with their practice, education, and research colleagues.

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Integrated Palliative Care: Clinical, Organizational, and Health System Perspectives

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_31

Abstract

This chapter explores current literature and initiatives in the field of integrated palliative care. The chapter starts with an exploration of the concept of integrated palliative care, followed by practice examples across Europe, models from the literature, and examples from guidelines. After this, barriers and opportunities for integrated palliative care are investigated. Finally, proceedings from the World Health Organization are highlighted to picture an international perspective. We conclude that integrated care has often been considered and discussed from the perspective of better integrated healthcare delivery, which is needed and valuable. But efforts for better integration of palliative care should move beyond a better organization of medical care and need to be rigorously designed from the perspective of the suffering patient in the last phase of life, and their families.

1 Introduction

Increasing numbers of people are living with, and dying from, advanced stages of cancer and chronic diseases. In the Western world, cancer is regarded as a most important disease, and many efforts are taken to improve survival. The burden of dying with cancer is greater in resource-poor regions of the world because more people are diagnosed late, with metastatic disease (Fadhil et al. 2017). Although a lot of research and attention was – and will be – invested in finding better treatments and strategies for these diseases, it is also clear that not every patient can be cured. Therefore, optimal care and efforts to improve the quality of a patient's remaining life are valuable. This is where palliative care comes to the fore. Although the demand and the need for palliative care are expected to increase in the coming years, many countries still struggle to deliver sufficient care for palliative patients and to ensure that palliative care is given adequate prominence in their health policies, health systems, and healthcare. The ideal is often that a very ill patient dies in a comfortable place, free of pain and other symptoms, surrounded by a caring and loving family. The inconvenient truth is that too many patients still experience hospital transfers in the last phase of life, suffer from pain and distressing symptoms, are surrounded by stressed and overburdened family members, and eventually die at a place that was not their initial preference.

The purpose of this chapter is to explore if and how better integration of palliative care can resolve or at least ameliorate these problems.

This chapter therefore starts with an exploration of integrated care based on a published definition and shows some clinical practice examples from a European project to illustrate the topic. Secondly, recent investigations in the field of integrated palliative care will be highlighted, revealing models and topics that may be relevant to better integrate palliative care. Thirdly, the state of the art of palliative care integration in professional guidelines will be explored. Fourthly, policy strategies will be introduced and the mapping of integrated palliative care will be discussed, including barriers and opportunities. Finally, next steps to progress integrated palliative care will be identified and discussed.

2 A Description of Integrated Palliative Care

Integrated care mostly focuses on giving the right care, at the right time, by the right caregiver. When translated into the field of palliative care, this involves questions like: "what is appropriate palliative care at a given moment in the trajectory of a patient with advanced illness?", "what is the right moment to start or enhance palliative care?", and "which informal and professional caregivers are involved at what moment and how do they interact?"

In the context of a European Commission-funded project on integrated supportive palliative care (http://www.insup-c.eu), a working definition for integrated palliative care has been agreed that reads as follows:

> Integrated palliative care involves bringing together administrative, organisational, clinical and service aspects in order to realise continuity of care between all actors involved in the care network of patients receiving palliative care. It aims to achieve quality of life and a well-supported dying process for the patient and the family in collaboration with all the caregivers, paid and unpaid. (Van der Eerden et al. 2014)

To investigate integration in the context of palliative care, the model proposed by Valentijn et al. (2013), originally developed for primary care, may be helpful. In its essence, the model distinguishes six elements of integration, namely, clinical integration, professional integration, organizational integration, system integration, functional integration, and normative integration. Furthermore, these elements of integration have a role at a microlevel, a mesolevel, and a macrolevel (Table 1).

When considering integrated palliative care, several of these elements resonate. Examples of *clinical integration*, with a focus on person-centered care, are improving a patient's quality of life and prevention and relief of suffering. But also the multidimensional investigation of physical, social, and spiritual problems in palliative care reflects an important element of clinical integration. The call for early applicable palliative care could be considered an example of *professional integration*, where professionals from several disciplines work together in a multidisciplinary team to provide timely palliative care. *Organizational integration*, referring to organizational relationships to deliver comprehensive services, could emerge in developing a support system to help patients and their families live as actively as possible, by arranging a package of social care, home care, and volunteering. *System integration* can refer to the financial healthcare structures that support or not support palliative care development, the presence of healthcare plans for

Table 1 Aspects of integrated care. (Based on Valentijn et al. 2013)

	Microlevel	Mesolevel	Macrolevel
Description of integrated care elements	*Clinical integration*: refers to the coordination of person-focused care in a single process across time, place, and discipline	*Professional integration*: refers to interprofessional partnerships (competences, roles, responsibilities) to deliver a comprehensive continuum of care to a defined population *Organizational integration*: refers to organizational relationships like contracting and strategic alliances, network, including governance mechanisms to deliver comprehensive services	*System integration*: refers to a tailor-made combination of structures, processes, and techniques to fit the needs of people and populations
	Normative integration (all levels): refers to a common frame of reference with shared values, culture, and goals to ensure coherency *Functional integration* (all levels): refers to supportive functions and activities (e.g., financial, management, and information) structured around the primary care process		

palliative care, but also the financial and medical sources and education available for palliative care at a country and at a regional level. Normative integration of palliative care can be traced back in the WHO definition when it is said that palliative care affirms life and regards dying as a normal process and intends neither to hasten nor postpone death. Finally, *functional* integration considers supportive functions and activities with a management, financial, and informational background, needed to align the work of care professionals. It is important for any palliative care service to have appropriate management, possibilities for (digital) information sharing, and financial resources to pay staff. As will be seen in the next paragraph, palliative care services sometimes struggle with this.

3 Five Examples of the Organization of Integrated Palliative Care Across Europe

In 2010, the European Association for Palliative Care (EAPC), in its white paper on standards and norms, introduced a graded system of palliative care services (Radbruch and Payne 2010). They make a distinction between a palliative care approach, general palliative care, and specialist palliative care. General palliative care is provided by all kinds of healthcare professionals like, for example, oncologists and geriatric specialists, whose primary focus is not palliative care but who have a profound knowledge and experience with death and dying in their practices. In addition, specialized services like palliative care units, inpatient hospices, or hospice at home teams are available for patients with complex palliative care needs, based on a multidisciplinary team approach. A palliative care approach requires, for example, that basic principles of palliative care are integrated in the education of physicians, nurses, and other related professions. Considering this theoretical model, it is of interest to see how palliative care is organized in practice, in particular what examples of integrated palliative care can be found.

Recently, a European project about integrated palliative care (InsupC) investigated 22 promising initiatives in 5 European countries, namely, the Netherlands, Hungary, Belgium, England, and Germany. The project has been described in a free e-book (Hasselaar and Payne 2016), where the below offered case descriptions can be found in more detail. Initiatives were eligible to be included when:

- The initiative was an established local palliative care collaboration.
- The collaboration contained at least two different organizations.
- A hospital could be part of that collaboration.
- Collaborating healthcare professionals provided direct patient care.
- The collaboration had a multidisciplinary background.
- The collaboration aimed to provide palliative care for one or more target groups (cancer/advanced COPD/chronic heart failure).

Integrated palliative care initiatives selected for participation in the InsupC study mainly involved hospital- or hospice-based services in conjunction with home care services. Although initiatives were selected based on accepting referrals of patients with cancer, COPD, and heart failure, the majority of included initiatives mainly treated patients with cancer. Table 2 and Fig. 1 show the InsupC research design and the

Table 2 Number of included patients in European InsupC study

	Belgium	Germany	Hungary	The Netherlands	UK	Total
Number of patients included	14	34	42	31	35	156
Cancer	*11*	*30*	*14*	*22*	*18*	*95*
CHF	*0*	*0*	*11*	*3*	*10*	*24*
COPD	*3*	*3*	*17*	*6*	*7*	*36*
Number of family caregivers included	14	9	30	22	13	88
Number of IPC initiatives included	3	4	5	5	5	22

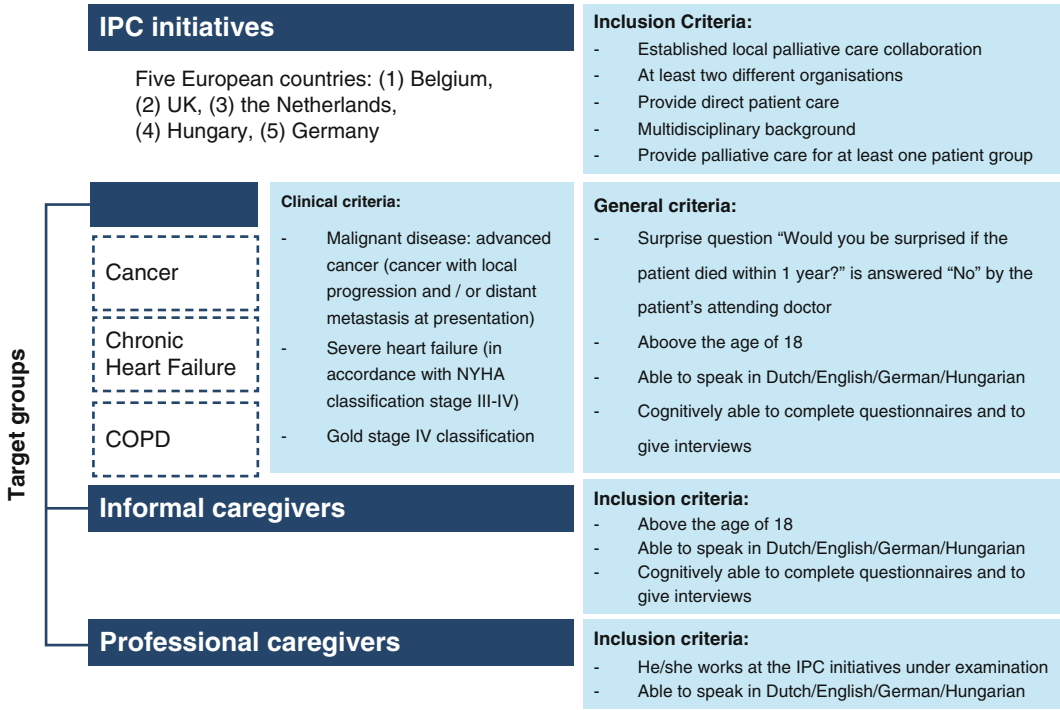

Fig. 1 Inclusion criteria for the InsupC study

inclusion of patients ($n = 156$) and informal caregivers ($n = 88$) within the InsupC project. Semi-structured interviews were performed with patients and with their informal caregivers. In addition, group interviews were held with professional caregivers at each initiative.

From all selected initiatives, five examples were further selected and described (Hasselaar and Payne 2016). Below, short descriptions of these five initiatives in five European countries are given in order to get a better understanding of integrated palliative care but also to see how inspiring initiatives work toward better integration.

3.1 A Palliative Care Pathway at Home in Belgium

In Belgium, a regional home care initiative called "White Yellow Cross" was investigated that has developed a care pathway to enable patients to stay at home until death. When a patient meets predefined palliative care criteria, the pathway becomes activated, nurses consult with the GP, and systematic pain and symptom monitoring is started. Specialist palliative care nurses act as case managers for the palliative patients. Strong relationships have been developed with the general practitioners and local hospitals in order to support patient transfers and to treat patients at home as well as possible. A specialist palliative care team (Pallion) is available when needed. This enables the initiative to offer family care and medical supplies alongside nursing care. Information is exchanged via an electronic system, including pain and symptom monitoring. After a patient has died, evaluation meetings among involved professional caregivers take place. Aftercare is part of the pathway, and once a year a memorial ceremony is organized to remember deceased patients. Improvement opportunities were identified including that palliative care is often limited to terminal care, that there are too few specialized nurses, and that electronic information exchange with hospitals is virtually nonexistent.

3.2 A One-Stop Integrated Palliative Care Facility in Germany

Germany offers an example of a one-stop integrated palliative care facility in Tübingen. The "Tübinger" project started in 1994 as a fundraising project and offers different options for palliative patients, like inpatient care, outpatient care, and palliative care in home settings. It has a specialized unit with ten beds served by a multidisciplinary team also including psychological and social support as well as art and music therapy. There is a specialized palliative home care team (SAPV team) consisting of physicians, a coordinator, and nurses, all trained in palliative care. This SAPV team also collaborates with two other regional hospitals, general practitioners, home care services, other professionals involved in palliative care, and pharmacies. The majority of referrals were initiated by general practitioners or self-referrals. About one third of admissions came from hospital. Upon referral, a first visit takes place, and, if the patient meets the inclusion criteria, a care plan will be developed. Although treatment at earlier stages of disease (early integration) is possible, this is often not compensated by health insurers. Charitable funding is still possible through the initial fundraising group, which enables the initiative to offer extra services, for example, a car for the home care team. In the "Tübinger" project, hospital and home care work closely together to offer palliative care, for example, palliative care professionals are often simultaneously employed. This enables a single point of reference and caregiver continuity for patients and family. Using a cloud-based system, information within the team is easily spread. The fact that the initiative had already existed for 25 years fostered acceptance of coordination and participation in local care networks. In three quarters of patients who preferred to die at home, their wish could be realized. Still, there is a predominance of advanced cancer patients; reimbursement can be cumbersome, in particular, when it comes to early integration; and continuity of care in transfers between hospital and home sometimes remains vulnerable.

3.3 Integrated Inpatient and Outpatient Palliative Care in Hungary

In Hungary, there is a general lack of well-trained care personnel in the field of palliative medicine and care. Inpatient hospice services are unevenly distributed across the country and concentrated in a few urban areas. Access to hospices is mostly limited to advanced cancer patients. A promising example of well-integrated palliative care can be found in Pécs, located in the South of Hungary. The clinical center of Pécs is one of the largest healthcare providers in Hungary and part of Pécs University. It hosts academic staff for research and education in palliative care together with a clinical consultation team (started 2013), an outpatient clinic (started 2012), and inpatient beds on the oncology ward (started 2016). There are close connections with the hospice (inpatient and at home; founded in 2004), partly sharing the same employees. Altogether, the palliative care network includes palliative care consultants, general practitioners, nurses, physiotherapy, psychology, and social work. The problems reported were lack of qualified staff, mainly physicians and nurses with many professionals only part-time working in palliative care. Furthermore, there is lack of funding and understanding of services, leading to late and limited use of hospice care. Currently, IT systems for patient documentation are fragmented, hampering transfer of information.

3.4 A Network Approach in the Netherlands

The Netherlands has a geographical coverage of regional networks for palliative care established in the early 2000s. The exemplary initiative involves a network connecting advanced cancer care in primary and secondary care in Schiedam (close to Rotterdam). The initiative started from a regional hospital with the goal to provide continuity of palliative care for patients with cancer, regardless of where they are. As patients often moved between care settings, a network was needed to connect these care settings and to

optimize collaboration. Therefore, the oncology unit started weekly multidisciplinary meetings as a part of the regional palliative care network "Nieuwe Waterweg Noord," covering four medium-sized towns. This network is supported by the comprehensive cancer center in Rotterdam. What makes this initiative exemplary is the way they succeed to create a seamless web of care around a single patient in need of palliative care and his/her family.

The multidisciplinary meetings consist of the hospital staff, a nursing home physician also palliative care consultant, a network coordinator also representing home care and palliative care units, and general practitioners by invitation. Caregivers however stay employed at their own organizations. Collaborations have been built with other care providers like mental healthcare, general practitioners, family care support, home care, volunteers. Every participant can list patients to the meeting and inpatients as well as outpatients can be discussed. Workplans are written after each meeting and spread to involved caregivers. Altogether the initiative succeeds in connecting primary and secondary care within a well-functioning regional network, not at least due to the presence of a coordinating nurse as a linchpin function. The network would benefit from better involvement of general practitioners, for example, in attending the weekly meetings, and better electronic information exchange like video conferencing or transmural electronic patient records. Finally the daily running of the network depends on a few highly committed professionals and is mainly dedicated to advanced cancer patients.

3.5 A Hospice Without Walls in England

One final example concerns a hospice at home in a rural area in West Cumbria, in the North of England. This initiative was established in 1987 when there was a need for specialist palliative care, but funds were lacking to establish a hospice building. Alternatively, an approach was chosen where patients were supported at their usual place of care, regardless whether this is their home, a hospital, or a nursing home. This service works alongside the National Health Service (NHS) in a "service level agreement" and delivers services from a town center building. It accepts referrals from patients with all life-limiting diseases, like cancer, COPD, and chronic heart failure. It receives one quarter of its funding from the NHS and the rest through public donations. It offers home nursing, a lymphedema service, family and bereavement support provided by trained volunteers, one-to-one support, and complementary therapies. There is no inpatient unit, but the service collaborates with local community hospitals, nursing homes, social work, and NHS-funded general practitioners and palliative care nurse specialists. There is an important place for volunteers in a variety of roles, from administrative tasks to massage therapy and bereavement support. Collaborations are built via weekly multidisciplinary meetings, one meeting covers current patients receiving care, and one meeting covers patients with complex palliative care needs. Due to the rural area, caregivers work in rather small teams, and emphasis is put on well-developed interprofessional relationships. Improvement opportunities involve an electronic system for information sharing which is planned, funding is uncertain and highly dependent on local donations, due to rural location staff can be difficult to recruit, and there is still a challenge to integrate healthcare and social care.

3.6 Patient and Informal Carer Interviews

In the analysis of the InsupC patient and family caregiver interviews, it was considered how relational, informational, and management continuity were considered important aspects of *functional integration* (Den Herder-van der Eerden et al. 2017). Experiencing close relationships with their palliative caregivers was considered important in all countries, in particular, that professionals were not only interested in the disease progress but also considered the patient as a person. Although general practitioners were generally considered important actors in the network of

the patient, some complaints were made about a lack of GP involvement. For patients in the last phase of life, not only continuity of care but also continuity of carer is important. Retelling their stories to different professional caregivers was therefore considered frustrating and decreased trust. However it appeared that information continuity became very vulnerable when healthcare providers didn't share and transfer information well. Management continuity became blurred when healthcare professionals worked in a fragmented fashion and lost sight at the patient as a whole person. In the study this was often related to hospital settings or hospital-home transfers. Collaborative team approaches were considered pivotal to facilitate relational, informational, and management continuity.

3.7 Current Challenges

It is of interest to see that across European countries, initiatives increasingly start to pay attention to the integration of their services in the local and national healthcare system. This often results in the building of networks between regional healthcare providers. Palliative care teams frequently exist of professionals of several organizations who work together in a multidisciplinary setting. It also happens that palliative care professionals have a labor contract in several organizations, for example, working as a GP and working in a hospice at home environment or working as a medical specialist in a hospital and in a palliative care consultation team. In particular connections between primary and secondary care are sought after but also are experienced as a challenge. This is partly due to the fact that electronic sharing of information outside the specialized palliative care team is mostly lacking, for example, an electronic patient record that can be shared between professionals from different organizations. Paper documentation and informal communication channels like mobile phones are often used but limit a structural and systematic approach to information exchange and joint action.

An important observation is that integration of palliative care earlier in the disease trajectory and beyond cancer is often not well supported by current healthcare culture and policies and difficult to implement. For example, reimbursement is often directed at terminal care with an expected life expectancy of less than 6 months, patient referrals come in late, advance palliative care planning may therefore be difficult, and services are mostly originating from (and still highly linked to) advanced cancer care.

Despite these challenges, interesting developments are currently ongoing. Inpatient palliative care providers recognize the value of integration and facilitate regional palliative care networks, connecting a diversity of service providers that deliver generalist palliative care. And at the same time, there seems a wider recognition that specialized palliative care should become available where the patient is, including his/her home. The UK hospice at home, for example, although partly born out of a lack of budget to build a hospice, proved to be very supportive in treating patients at home. The Dutch developed a network approach to support this, the Belgians have a primary care pathway, the Germans developed a one-stop shop, and in Hungary they established a hospice at home connected to a hospital consultation team. However, the long-term success of these initiatives requires that collaborations and reimbursement structures in primary care are supportive to palliative care, which is not always the case, for example, when indication and reimbursement for patients are limited to end-of-life care in the last months. Vulnerability exists where initiatives hinge upon the involvement and drive of a few dedicated professional care professionals but may be overcome when federal regulations support the building of teams. In the end, integration also should define roles and make space for generalist as well as specialist palliative care.

4 A Synthesis of Five Models of Palliative Care Integration

In an example of professional integration, the WHO definition states that palliative care "is applicable early in the course of illness, in

conjunction with other therapies that are intended to prolong life." In previous years, an increasing number of papers have been published showing the positive effects of this "early palliative care integration" with efforts to identify and assess patients earlier in the disease trajectory. In addition, end-of-life care pathways have been developed and investigated together with primary care initiatives. In this section, some recent developments from the literature will be shown.

4.1 Early Integration in a Hospital Setting

One important example of clinical integration in a hospital setting is early integration, which has been increasingly investigated after a landmark RCT study by Temel et al. (2010), showing that newly diagnosed metastatic non-small cell lung cancer patients assigned to an early palliative care visit had a better quality of life and less depressed mood after 12 weeks. In addition they used less aggressive care and reported a longer survival, compared to those receiving normal US oncology treatment. A secondary qualitative analysis of the medical records of 20 patients revealed that key elements of the early ambulatory palliative care visits (compared to standard oncology visits) included addressing of symptoms and coping with relatively more attention to psychosocial care. Furthermore, building of relationships, better illness understanding, and prognostic awareness were important ingredients of these visits (Yoong et al. 2013).

In 2014, Zimmermann et al. published a cluster RCT involving 461 advanced cancer patients with a limited prognosis (6–24 months) in 24 medical oncology clinics, investigating palliative care team involvement at least once a month. Although the primary outcome of quality of life at 3 months did not statistically improve in the intervention group, it did improve at 4 months, which was considered a promising finding. Studies like these (for example Bakitas et al. 2015) will probably be more in-depth discussed in another chapter of this book, but for this chapter it is interesting to consider the possible working mechanism for early integration from the perspective of the so-called CMO approach based on *context*, *mechanism*, and *outcome* (Busetto et al. 2017). Based on the aforementioned literature exploration, it can be illustrated how the CMO approach can apply to early palliative care (Fig. 2).

Early integration in a hospital setting is often achieved by means of outpatient palliative care consultation, directed toward advanced cancer patients. In this setting, promising results have been achieved in terms of better quality of life, less depressed mood, less aggressive care, and in some studies even improved survival. Studies in this field are ongoing, and the results increasingly find their way to practice.

Based on the emerging evidence for the early integration of palliative care in oncology, the American Society of Clinical Oncology (ASCO), in a recent update (Ferrell et al. 2017:120), formulated as a key recommendation that: *"•Patients with advanced cancer, inpatients and outpatients, should receive dedicated palliative care services early in the disease course and concurrent with*

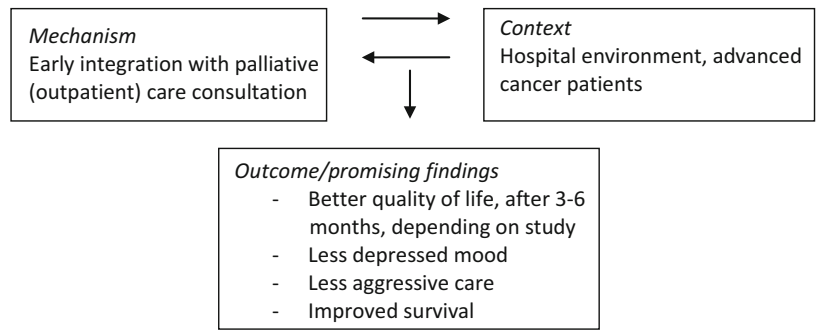

Fig. 2 Context, mechanism, and outcome for the early integration of palliative care

active treatment. Referring patients to interdisciplinary palliative care teams is optimal, and services may complement existing programs. Providers may refer caregivers of patients with early or advanced cancer to palliative care services."

4.2 Integrated End-of-Life Care in Hospitals: The Amber Care Bundle

Amber stands for assessment, management, best practice, engagement, and uncertain recovery. The Amber care bundle is focused on hospital patients whose recovery is uncertain and who are at the risk of dying the next 1–2 months (see www.ambercarebundle.org). It offers a systematic approach to help staff to realize when to start talking with patients and family members about the treatment and the care they prefer when their disease progresses. It combines identification questions, four clinical interventions, and monitoring of patients.

A recent qualitative study among 20 healthcare professionals based at 3 tertiary NHS hospitals in London investigated its potential use in labeling of patients, changing care delivery, and influencing the behavior of involved individuals and teams (Bristowe et al. 2018). Adequate exposure, training, and implementation were considered important preconditions for success. In another study from this group, patients ($n = 19$) were interviewed, and a survey was performed. It was shown that patients with the Amber care bundle had an effect of increased conversation about prognosis between professionals and patients, although the information received seemed not always easy for patients to understand (Bristowe et al. 2015). A retrospective chart review among 149 patients in 5 hospital wards showed that the Amber care bundle is more often applied in cancer patients and that patients received the Amber care bundle on average 10 days after admission, for a median period of 9 days (Carey et al. 2015). Despite positive initial experiences, more rigorous research is required to establish its efficacy in larger samples (see also Currow and Higginson 2013).

4.3 Integrated End-of-Life Care Pathways

A much debated example of an attempt to integrate palliative care in the last days of life, not limited to cancer patients, is the multidisciplinary care pathway for the dying. Although some positive evaluations have been available (Veerbeek et al. 2008), evidence underlying such pathways has been considered limited (Chan et al. 2016). Recently however, a large cluster randomized trial in acute geriatric wards in ten Flemish hospitals was published. Hospitals were randomly assigned to the CAREful intervention, a "care guide for the last days of life, training, supportive documentation, and an implementation guide" (Beernaert et al. 2017). Positive outcomes were found for nurse-assessed comfort of the dying, but not for family-assessed comfort of the dying or symptom improvement.

This is a promising conclusion in the light that a few years earlier, a well-known care pathway for the dying, namely, the Liverpool Care Pathway (LCP), became heavily criticized. One important conclusion from an independent review in 2013 reads that the Liverpool pathway seemed to work well in settings where it was operated by well-trained, well-resourced, and sensitive clinical teams. But when used without much attention, as a tick box exercise, it runs the risk of not showing enough respect to patients (Neuberger 2013). Due to the political concerns raised, the Liverpool Care Pathway became phased out in England. In other places however where the experiences were more positive, like the Netherlands and Flanders, care pathways for the dying are still being implemented. However, the aforementioned experience shows that care pathways should not only be studied in an experimental setting but require a well-thought implementation trajectory before large-scale introduction takes place.

4.4 Integrated Palliative Care for Non-cancer Patients

The aforementioned approaches of integrated palliative care focused on a hospital environment,

mostly related to cancer. Another approach however was taken by Higginson et al. (2014) who studied the effect of a breathlessness service integrating palliative care, respiratory medicine, physiotherapy, and occupational therapy. In a single blinded randomized trial, the service improved breathlessness mastery (the primary outcome) together with survival after 6 months in the intervention group.

In addition, this group also investigated the integration of palliative care as a complementary service for multiple sclerosis treatment in a randomized phase II trial (Higginson et al. 2009). They found lower mean service costs in the first 12 weeks of follow-up. In a related paper, they also reported an improvement in five key symptoms, although the main outcome measures "palliative outcome scale" (POS) and "the multiple sclerosis impact scale" remained unchanged (Edmonds et al. 2010). The experiments give rise to further thinking about the integration of palliative care and home care.

Bone et al. (2016) developed a model of short-term integrated palliative and supportive care for frail older people in community settings, based on the perspectives of older people, carers, and other stakeholders. Their model is designed for people with nonmalignant conditions living at home. The model involves ongoing general practitioner and community nursing team support and integrated working with specialist palliative care services, for example, visits, holistic assessment, single point of contact for general practitioner, and skilled workers for patient/carers. Potential benefits, according to the respondents, involve improved symptom management, improved carer well-being, and reduced hospital admission. This model however needs more empirical research.

4.5 Gold Standard Framework (GSF) in UK Primary Care

The UK Gold Standard Framework, originally developed to improve palliative care in primary care, became an important driver to integrate palliative care in the community setting as well (Clifford et al. 2016). The GSF is considered a quality improvement program with the aim to enhance proactive care at the end of life. It uses a three-step approach based on early identification, better assessment of clinical and personal needs, and focused planning and coordination. Goals are to improve quality of care, to improve coordination of involved care teams, and to reduce hospitalization. Patients considered to be in the last year of life are identified and registered in a GP-based palliative care register in order to improve care coordination. A survey among 6495 primary care practices in the UK showed that GSF uptake was achieved in about 60% of practices (Hughes et al. 2010).

Notwithstanding this, a primary care audit in 2009 showed that of all dying patients in the investigated 502 primary care practices, only 27% were identified in an end-of-life care register, suggesting a significant space for improvement. However, the identified patients seem to have received better end-of-life care (Omega report 2009). Besides, a finding of limited identification but better outcomes in identified patients was also reflected in a Dutch primary care study (Thoonsen et al. 2015). Lessons learned from the GSF program were formulated as follows (Clifford et al. 2016):

- Although many primary care practices reported using the foundation level of GSF, the uptake was still patchy and variable. A new accreditation program for GSF may stimulate better implementation.
- It is considered important that the GSF does not replace local practices and initiatives. There is no "one size fits all," and local primary care practices are stimulated to develop at their own pace, and the overarching framework needs to give opportunities for this.
- Local champions are important together with whole team commitment. Despite busy practices, it is possible to implement the GSF and to improve end-of-life care, not only for cancer patients but also for other target groups like frail elderly people.

The underlying principles of GSF have been adopted in other initiatives like PaTz (Palliatieve Thuiszorg) in the Netherlands. This initiative

attracted national attention and is increasingly implemented in home care (van der Plas et al. 2014). In 2016, almost 100 groups were reported all over the Netherlands. Altogether initiatives like the Gold Standard Framework seem a promising way to integrate palliative care in primary care, although the actual percentage of identified palliative patients in GP practices seems still limited.

4.6 Synthesis

Examples I–III (early integration, Amber care bundle, care pathways) mostly address a micro-level where clinical integration is aimed for in a specific setting. The described examples for non-cancer (example IV) however are more related toward the community, connecting a variety of disciplines like physiotherapy and occupational care. The Gold Standard Framework is a program based in primary care but also has the ability to unite key players involved in the care at home, as happens in the Dutch PaTz project. These models (non-cancer models; GSF) move beyond a clinical perspective and also approach integration from an organizational (meso)perspective, even with elements of a macro – program-based – perspective.

Benefits of integrated palliative care have been shown in cancer care, but there is less evidence of initiatives in other conditions (Siouta et al. 2016a). There is increasing evidence of early integration in hospital-based cancer care. However, integration of palliative care across different sites and settings is much less well developed and may vary by country. In the UK, for example, the Liverpool Care Pathway, one of end-of-life care pathways, was heavily criticized for its poor implementation and has now been discontinued (DoH 2013). However there may be beneficial aspects of structured care pathways as were shown in a rigorous evaluation in Flanders in geriatric care (Beernaert et al. 2017). The Amber care bundle has demonstrated initial promising outcomes and is currently the focus of a large clinical trial. There is accumulating clinical trial evidence on the benefits of structured integrated care in palliative care for those with breathlessness and MLS (Higginson et al. 2009, 2014), but not much research has been done in this area. So far, the Gold Standard Framework seems the most widely implemented initiative in primary care and in nursing homes, although its evidence base and application is rather limited to the UK and needs further rigorous research.

To conclude Siouta et al. (2016b) searched the literature to investigate the evidence from empirical models of integrated palliative care. They recommended the following elements for a successful integration of palliative care:

- Focus of intervention: The focus of intervention will be placed on symptom treatment, consulting of patients/family and training of the personnel.
- Setting: The design of the framework is such that it can be applied to every care setting.
- Timing of intervention: The intervention can be initiated throughout the disease trajectory either concurrently or in the end of life.
- Composition of team: The framework requires a multidisciplinary team with members that are trained in the delivery of PC. This team can consist of GPs, physician specialists, nurses and specialist nurses, psychologists, social workers, and administrative assistants.
- Collaboration strategy: The collaboration strategy, which refers to the ways that the represented disciplines cooperate and assess emerging issues, should be based on the involvement of the multidisciplinary team and its meetings and the utilization of protocols.

The next section will consider the integration of palliative care within professional guidelines more in-depth.

5 Palliative Care Integration: Lessons Learned from Five Professional Guidelines

Van Beek et al. (2016) investigated the integration of palliative care in 60 cancer guidelines and 14 pathways, originating from 6 languages. Relevant

items were categorized using 11 criteria for integrating palliative care in guidelines as proposed by Emanuel et al. (2004). They found that four out of five cancer guidelines advocated a multidimensional assessment and about three out of five mentioned palliative care interventions to reduce suffering and the involvement of a palliative care team. In less than half of the cases, cancer guidelines paid attention to care during the last hours, to advance care planning, to bereavement care, and to (referral) criteria for palliative care involvement. Based on an assessment of five good examples, van Beek et al. made recommendations for integrated care criteria in guidelines (Table 3). However, they also admit that implementation of these criteria in current guidelines can be cumbersome.

Considering the integration of palliative care in guidelines for heart failure (HF) and chronic obstructive pulmonary disease (COPD), a review has been carried out by Siouta et al. (2016a). They investigated European guidelines published between 1995 and 2013 and included 17 guidelines and 2 pathways in their review. Applying the Emmanuel criteria as mentioned above, they concluded that almost all documents addressed suffering reducing interventions, and most (15/19) paid attention to illness prognosis and limitations. About two third of guidelines/pathways mentioned a holistic approach, a palliative care involvement, assessment of the patients' goals of care, and advance care planning. Only few texts included grief and bereavement. The authors conclude that there is a growing awareness but that many areas still need improvement. Although there is no space to discuss all guidelines related to palliative care in non-cancer, it is worthwhile to mention that palliative care in dementia is also emerging, for example in a recent white paper (van der Steen et al. 2014). The Delphi procedure underlying this white paper mentioned the following domains of importance: person-centered care, communication, and shared decision-making, optimal treatment of symptoms and providing comfort, setting care goals and advance planning, continuity of care, psychosocial and spiritual support, family care and involvement, education of the healthcare team, societal and ethical issues, and prognostication and timely recognition of dying. Quite a few recommendations reflect the abovementioned Emmanuel criteria for integrated palliative care. Despite promising examples on the horizon however, a lot of work still needs to be done to fully integrate palliative care into disease guidelines.

6 Five Policy Strategies and Their Value for Integrated Palliative Care

In this section, some current attempts and proposals to map the development of integrated palliative care will be briefly discussed. One approach clarifies barriers and opportunities for integrated palliative care and will be discussed more in detail because this will demonstrate the current state of the art of integration of palliative care. The section closes with a description of WHO strategies about integrated care.

6.1 Indicators for Integrated Palliative Care

Hui et al. (2015), in collaboration with the European Society for Medical Oncology (ESMO), conducted a Delphi survey to establish indicators for the integration of oncology and palliative care programs in hospitals with more than 100 beds. After 3 rounds, they identified a list of 13 major indicators among which:

- Presence of an inpatient consultation team
- Presence of an outpatient palliative care clinic
- Presence of an interdisciplinary palliative care team
- Place of death consistent with patient preference
- Combined palliative care and oncology educational activities

A reply from Verna et al. (2016) however pointed to the necessity of not only drawing program criteria for big hospitals but also to develop sustainable indicators for integrated –

Table 3 Emmanuel criteria for integrated palliative care based on five good examples

Criterion	Recommendations based on cancer guidelines
1. Discussion of illness limitations and prognosis	The guidelines/pathways agree that this can be realized through open and honest communication with patient and family, based on their needs and preferences, and enabling shared decision-making. One pathway also suggests the employment of the surprise question or the Palliative Performance Scale can be used as triggers for initiating such discussions
2. Recommendations for conducting a whole patient assessment including the patient's physical, social, psychological, and spiritual issues, their family, and community setting	There is a unanimous consensus on the utilization of a combined physical, psychological, social, and spiritual assessment
3. Recommendations for when to make these assessments (e.g., at baseline and periodically thereafter)	Assessment should take place early in the disease trajectory. Further, it is recommended that holistic assessment should occur "at any time of day or night" for physical and psychological support and as long as possible for patient's social participation. Also, its realization should vary depending on changes in the disease or on the appearance of new symptoms and based on application of, e.g., a "distress thermometer"
4. Recommendations on when palliative care should be integrated	Three strategies are identified: (i) the use of the surprise question, (ii) the evaluation of the patient's and the family's needs, and (iii) illness stage – disease-/cancer-related prognostic indicators (e.g., like the indicators mentioned in the Gold Standard Framework)
5. Assessment of the patient's goals for care	All the guidelines/pathways agree that this assessment should be based on the continuous communication between the patient and the PC specialists to identify patient goals
6. Continuous goal adjustment as the illness and the person's disease progresses	It is suggested that PC specialists regularly consult the patient and adjust goals accordingly
7. Palliative care interventions to reduce suffering as needed	The guidelines/pathways elaborate on the use of appropriate medication and strategies aimed in reducing both physical and psychological suffering
8. Advance care planning	Decision-making should be based on patient's wishes and preferences. One pathway proposes the identification of the ACP via the use of three models (covenant model, contract model, or DNR code)
9. Recommendation of involving a palliative care team (interdisciplinary team, palliative care consultation, or other palliative care services)	All of the guidelines/pathways strongly recommend the involvement or formation of a multidisciplinary PC team (consisting of physicians, nurses and other health professionals, psychologists, mental health counselors, social workers, spiritual counselors)
10. Recommendations on care during the last hours of living	The following steps are recommended: identification of the dying phase, communication, support based on patients and family's needs and wishes, and symptom control
11. Recommendations on grief and bereavement care	The main proposed strategy involves the immediate and ongoing bereavement, emotional and spiritual support appropriate to the family's needs and preferences

Based on Van Beek et al. (2016). Incorporated guidelines: Ayestáran MA. 2008. Guía de práctica clínical sobre cuidados paliativos Clinical practice guidelines on palliative care (Spain); Muszbek K. 2013. Practice and opportunities of the Hungarian hospice care provided at home. (Hungary); Van den Eynden B et al. 2012. Zorgpad palliatieve zorg eerstelijn Vlaanderen (Belgium); Royal College of General Practitioners and Royal College of Nursing. 2012. Matters of life and death: helping people to live well until they die. General practice guidance for implementing the RCGP/RCN end of life care patient charter; National Institute for Health and Care Excellence. 2011. CMG42 End of life care for adults

community-based – palliative care, in particular in countries who have less resources for implementation. This is also reflected in the report of a German working group that reported best practice recommendations for the integration of palliative care and oncology (Berendt et al. 2016). After three rounds, high agreement was reached for having an organizationally and spatially independent palliative care unit ($\geq$6 beds), a mobile multiprofessional specialized palliative

care team, and cooperation with community-based palliative care.

In 2016, Ewert et al. published a taxonomy for integrated palliative care initiatives, based on a consensus meeting with expert, including the following categories:

- Background of disease
- Type of initiative (pathway, model, guideline)
- Sector (inpatient, home care)
- Time frame of intervention (early integration, concurrent, end-of-life care)
- Coordination strategy (network, protocol, team, case manager)
- Primary contact point (palliative care, team, other)

This taxonomy is designed as a tool to identify and describe integrated palliative care, rather than to measure it. It offers insight in the various ways integration of palliative care can take shape but is not restricted to hospital care.

This short investigation shows that indicators to describe palliative care integration have been developed but not widely implemented. More work is needed in this field.

6.2 Barriers and Opportunities for Palliative Care Integration

An investigation from a public health perspective has been performed by Centeno et al. (2017) who used the EAPC Atlas to draft a picture of palliative care integration in Europe. The EAPC Atlas is based on the views of national palliative care associations in Europe about the current state and development of palliative care in their countries. These perspectives are presented in graphics to illustrate palliative care development across Europe and other parts of the world. Drawing from the palliative care Atlas database, it was considered which indicators – through the eyes of European national associations – were barriers and opportunities to the further development of integrated palliative care. The following figure shows the barriers identified (Fig. 3).

It is of interest to see that one third of the identified barriers fall within the policy dimension, about regional regulation and coordination. The integration of palliative care within non-cancer that appeared an important issue in the aforementioned analysis of promising examples is also listed here. Secondly, the most frequently mentioned barriers concerned the lack of basic training in palliative care in courses and curricula, followed by limited options for formal certification or subspecialization within the field of palliative care and medicine. A third group of barriers was related to the integration of palliative care services like human resources, coordination of services, and maturity of the discipline including the availability of multidisciplinary care.

Interestingly (Fig. 4), many of the aforementioned barriers are also considered opportunities, for example, the expansion of basic training for palliative care and the inclusion of palliative care at universities. Expert training and certification are also considered major opportunities. In the field of policy-making, the regulatory framework has been mentioned by many experts. This refers, for example, to changes in the law favoring palliative care and the development of palliative care strategies and programs. In the context of the previous analysis of inspiring practices, changes in policy strategy like, for example, restricted palliative care reimbursement for advanced cancer may be a solution for better integration toward non-cancer and integration earlier in the disease trajectory. This may also have a positive influence on service development like business plans and resources and the integration of palliative care in professional guidelines which was also discussed earlier in this chapter. Remarkably, research is also mentioned as an opportunity, in particular, by Belgium, Iceland, and the UK. In their study, Centeno et al. (2017) also pointed out that countries with more mature palliative care service availability more often report barriers and opportunities in the area of integrated palliative care, probably related to increasing expectations of palliative care development. Contrary, in countries with less palliative care development, basic palliative care provision seems to be the highest concern.

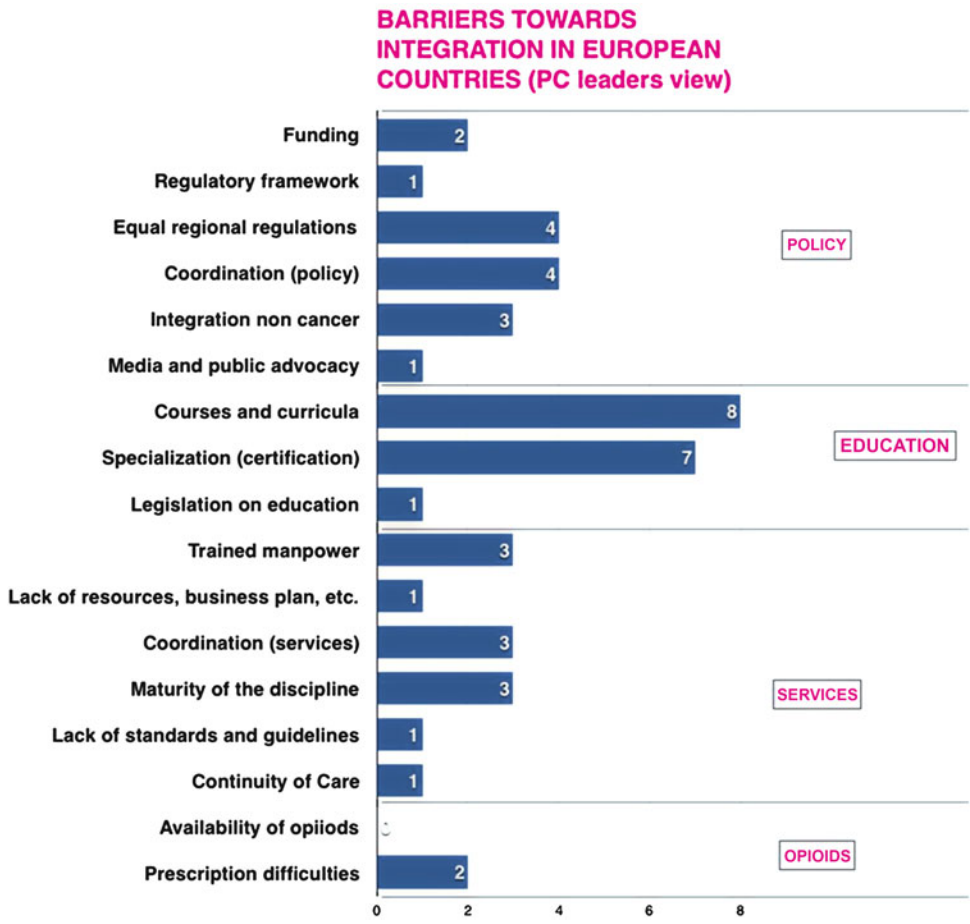

Fig. 3 Barriers toward integration of palliative care in European countries. Figure developed by the Atlantes group, Navarra, Spain (Prof. Centeno, published with permission). The European palliative care atlas is based on the WHO European region involving 53 countries whose national palliative associations nominated an expert to answer the Atlas questionnaire. In this figure only answers to specific questions about palliative care integration are listed

6.3 Policy Initiatives from the World Health Organization

In 2016, the World Health Organization (2016) launched a new framework on integrated people-centered health services based on a vision that all people have equal access to quality health services in a way that meets their life course needs. According to the WHO, integrated care involves five strategies which can be described as follows:

1. *Engaging and empowering people and communities.* Patients and families need to be active participants in care that is delivered in an equal and reciprocal relationship, in order to achieve better clinical outcomes. It is also about communities to organize themselves and to make changes in living environments, in particular, toward the underserved, and to provide place and training for informal care.
2. *Strengthening governance and accountability.* This involves involvement in policy formulation and decision-making but also evaluation and societal accountability. Enhancing welfare requires a stewardship role for governments and participatory involvement of communities.
3. *Reorienting the model of care.* This involves a reorientation toward life course needs of

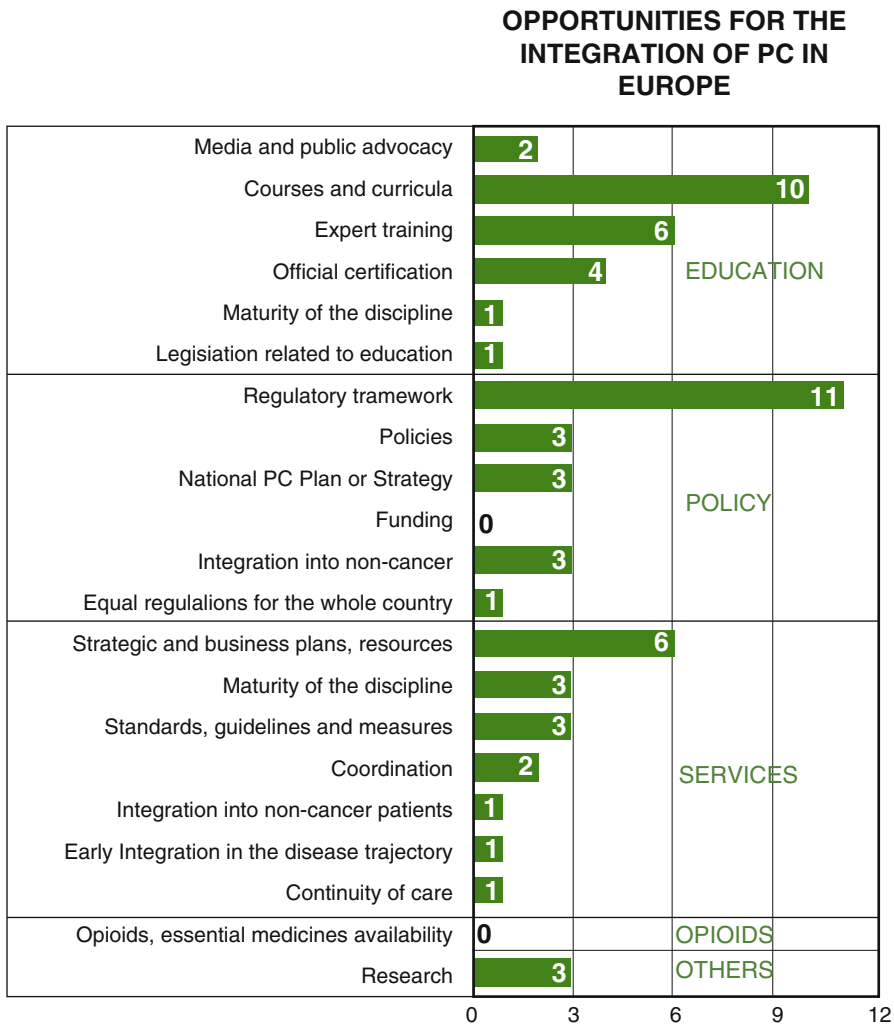

Fig. 4 Opportunities for the integration of palliative care in Europe. Figure developed by the Atlantes group, Navarra, Spain. (Prof. Centeno, published with permission). The European palliative care atlas is based on the WHO European region involving 53 countries whose national palliative care associations nominated an expert to answer the Atlas questionnaire. In this figure only answers to specific questions about palliative care integration are listed

populations. Furthermore a shift from inpatient care to outpatient and ambulatory care, based on a publicly available primary care to reach the entire population. It calls for multiprofessional teams and family- and community-oriented care models where modern technologies and mHealths are embedded.

4. *Coordinating services within and across sectors.* Services should be organized around the needs and demands of people. This requires integration across health settings. It involves intersectoral alignment and harmonizing of processes and information, not necessarily the merging of institutions. It is centered around care for individuals but also coordination of health programs and providers to bridge administrative, informational, and funding gaps. Finally, it involves multiple sectors like healthcare, social care, labor, and housing.
5. *Creating an enabling environment.* In order to make transformation happen, the involved stakeholders need to be brought together

which requires collaborative leadership where improvements in information and knowledge development, regulatory frameworks, and funding incentives take place.

Although it would be interesting to examine to what extent (inter)national palliative care plans and programs use these five strategies, this chapter can only briefly examine one initiative, namely, the WHO resolution on palliative care.

6.4 The WHO Resolution on Palliative Care

In 2014, the World Health Assembly approved a resolution called "strengthening of palliative care as a component of comprehensive care throughout the life course" aiming to integrate palliative care policies in healthcare systems and healthcare education. Soon after this agreement, a Technical Advisory Group for palliative care was installed. In 2017, an accompanying book was released by the Technical Advisory Group in 2017, emphasizing that palliative care should be implemented as a comprehensive and integral part of the care for patients with advanced and life-limiting diseases. Short- and long-term actions have been formulated, among which the involvement of health ministries at a country level, WHO agencies, policies for resource-poor countries, ethics, the relation toward complex and chronic care, a community perspective, and leadership empowerment (Gómez-Battiste and Connor 2017). WHO demonstration projects for palliative care, among others the Catalonian public health program, are described, and the expansion of palliative care to non-cancer patients is stressed.

Altogether there seems to be a momentum to foster the implementation and integration of palliative care in health systems, where several initiatives could reinforce each other. The book as released by the WHO could guide an implementation program to better integrate palliative care, making use of the five WHO policy strategies for integrated care. This implementation program could be monitored by an indicator set based on already existing platforms for palliative care mapping like the Atlas project including the support of the EAPC (European Association for Palliative Care) and the IAHPC (International Association for Hospice and Palliative Care). Such a supportive joint collaboration could support the further implementation of the WHO palliative care resolution toward better palliative care integration.

7 Summary and Conclusion

This chapter started with a definition of integrated palliative care and a brief exploration of several elements of integrated care in relation to palliative care (clinical, professional, organizational, functional, normative, health system integration). Examples from five European countries were described and discussed. Here, functional integration in terms of relational, informational, and management continuity appeared to be vulnerable. Furthermore, based on the literature, five models supporting integrated palliative care were discussed mostly at a clinical or a mesolevel, namely, early integration, the Amber care bundle, care pathways for the dying, integration in multiple sclerosis and a breathlessness service, and the Gold Standard Framework in primary care. In previous years, most research and evidence generation about integration has been directed at early integration for hospital-based cancer care. Promising models outside cancer and in community settings could be identified but often need more rigorous investigation and development. Considering the integration of palliative care in professional guidelines, recommendations were summarized based on an analysis of five promising guidelines. Studies investigating a broader analysis of guidelines however showed that full integration still leaves a world to win. Finally a macrolevel policy approach was taken by discussing current initiatives to map integrated palliative care with indicators. In addition, the newly launched integrated care framework of WHO was summarized together with the WHO resolution for palliative care.

Integrated care has often been considered and discussed from the perspective of better integrated

healthcare delivery, which is needed and valuable. However, coming at the end of this chapter, it should be acknowledged that real integration goes beyond health service delivery. In the 1960s, Cicely Saunders coined the concept of "total pain" to show that patients cannot be reduced just to their physical problems but that social and life views need to be incorporated as well. Integrated palliative care is in its essence about whole patient care in the last phase of life. The welfare of the patient in this last phase is not only dependent upon the medical services he or she receives but also includes the social environment, the housing, the support, and well-being of family members and informal caregivers. In this respect, it is interesting to refer to the concept of a new public health approach for palliative care, which is based on engaging communities (Sallnow et al. 2016). Efforts for better integration of palliative care should move beyond a better organization of medical care and need to be rigorously designed from the perspective of the suffering patient in the last phase of life. This means that the whole living environment of the patient needs to be taken as a starting point, including family care, social care, place of living, health education and (il)literacy, and healthcare arrangements.

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Rehabilitation in Palliative Care

35

Rebecca Tiberini, Karen Turner, and Helena Talbot-Rice

Palliative rehabilitation is 'the transformation of the dying into the living... the restoration of a patient to a person'. *(Doyle et al. 2004)*

Principles in the Context of Life-Limiting Illness, Practices for the Interdisciplinary Team, and the Specialist Contribution of Physiotherapy and Occupational Therapy

Contents

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_34

Abstract

In the context of palliative care, rehabilitation aims to improve quality of life for people living with life-limiting illness by enabling them to be as active and productive as possible with minimum dependence on others, regardless of their life expectancy (NICE. Guidance on cancer services: improving supportive and palliative care for adults with cancer. The manual. National Institute for Clinical Excellence, London, 2004). Palliative rehabilitation helps enable people to participate as fully as possible in all aspects of their daily lives. It represents an important route for people to fulfill meaningful goals, maintain dignity and adapt constructively to the uncertainty and loss that is often intrinsic in the lived experience of advancing illness. In its simplest sense, palliative rehabilitation is about enabling people to live fully until they die (Tiberini and Richardson, Rehabilitative palliative care: enabling people to live fully until they die. A challenge for the 21st century. Hospice, 2015. ISBN:978-1-871978-91-9). Rehabilitation in palliative care combines the specialist contribution of physiotherapists and occupational therapists together with the interdisciplinary practice of "rehabilitative palliative care."

1 Introduction

The interface between rehabilitation and palliative care is not a new concept, with principles of rehabilitation evident as central themes in Dame Cicely Saunders' philosophy and vision:

> The work of all the professional team is to enable the dying person to live until he dies, at his own maximal potential, performing to the limit of his physical and mental capacity with control and independence whenever possible. Dame Cicely Saunders

However, the contribution of rehabilitation to modern palliative care provision is gaining importance in the context of today's society where personal autonomy is paramount. People are increasingly expressing the importance of choice

and independence as major components of dignity in advancing illness and old age. These values underpin the concepts of "rehabilitative palliative care," an important paradigm shift endorsed by Hospice UK to respond to the challenges facing palliative care provision in the twenty-first century.

Rehabilitative palliative care calls for all members of the interdisciplinary team to adopt and actively embed rehabilitative practices and an enabling culture in their delivery of palliative care (Tiberini and Richardson 2015). It draws on the expertise and specialist rehabilitation contribution of physiotherapists and occupational therapists (Box 1) but recognizes that it is crucial to engage the whole team in a rehabilitative approach to best address the multiple needs of the patient living with advanced, complex, and progressive illness (Tookman 2011).

Box 1: Specialist Rehabilitation Contribution of Physiotherapists and Occupational Therapists

- Specialists in palliative rehabilitation.
- Trained in both rehabilitation and palliative care theory and practice.
- Provide expert holistic assessment and personalized rehabilitation interventions.
- Advocate for patients' independence, autonomy, and choice irrespective of prognosis.
- Core members of the interdisciplinary palliative care team (NICE Guidance on Cancer Services 2004).
- Lead the wider team in adopting and implementing rehabilitative palliative care.

This chapter will present the conceptual constructs informing rehabilitation in palliative care and the evidence base for its importance, acceptability, and impact. We will introduce key principles and interdisciplinary practices of "rehabilitative palliative care," in which enabling patients to fulfill their personal goals and priorities is "everybody's business," and explore the specialist rehabilitation contribution of physiotherapists and occupational therapists. A case scenario, Ali, runs through the chapter to illuminate the clinical application of rehabilitation concepts into practice.

2 The Interface Between Rehabilitation and Palliative Care: Are They Compatible?

Rehabilitation can be a misunderstood concept when described in terms of life-limiting illness. At first impression, the term "palliative rehabilitation" may appear contradictory as it brings together two somewhat paradoxical concepts – that of *rehabilitation*, frequently associated with recovery, and *palliative care,* frequently associated with dying (Leslie et al. 2014). This reductionist view of both concepts has contributed to a misperception that active rehabilitation is at odds with palliative care provision, with an ensuing reluctance on behalf of some healthcare professionals to integrate the two, inadvertently depriving patients of opportunities for enhanced quality of life (Platt-Johnson 2007). However, upon closer inspection, the domains of rehabilitation and palliative care are compatible and complementary and share common characteristics, ethos, and values (Fig. 1).

Both rehabilitation and palliative care are holistic, multidisciplinary, person-centered specialisms which place the patient and their family at the heart of the treatment paradigm to ensure the collaborative team input is tailored to best support their needs. Combined, rehabilitative palliative care has the potential to enhance the quality of life for both patients and families, where the sum of these two complementary approaches is greater than the individual parts. Rehabilitative palliative care transcends diagnosis, prognosis, and location of provision and should be viewed as the shared responsibility of all working in this field (Table 1) (Fig. 2).

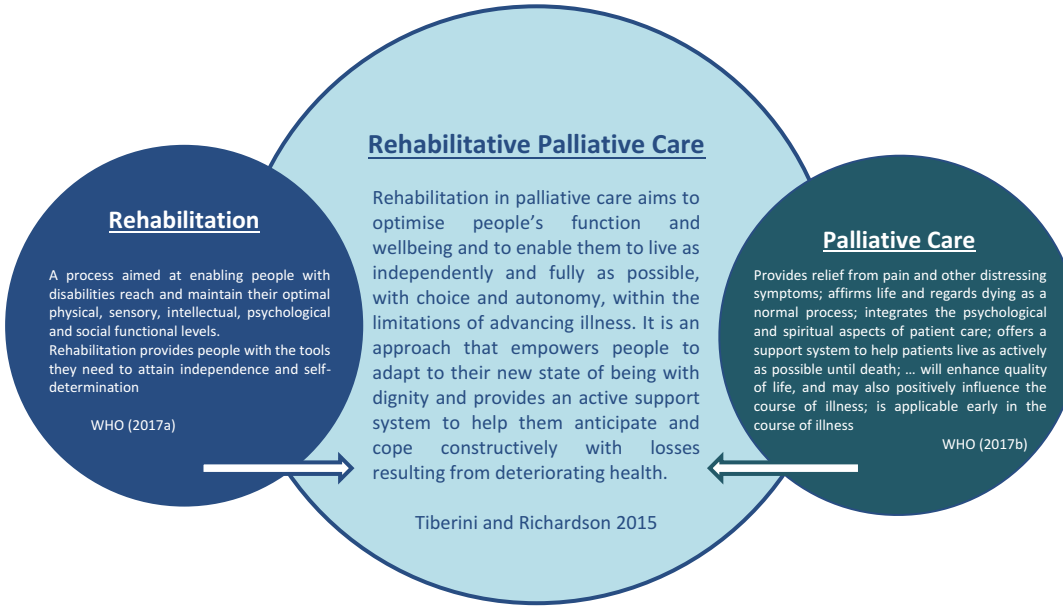


Fig. 1 Rehabilitative palliative care

Table 1 What is rehabilitative palliative care?

Rehabilitative palliative care *is*	**Rehabilitative palliative care *is not***
Person-centered: focusing support to best meet people's goals and personal priorities	Focused on and driven by the allied health professional agenda but led by patients' priorities
An effective integration of rehabilitation and palliative care to actively enhance people's quality of life irrespective of diagnosis or prognosis	The clash of two contradictory and opposing treatment paradigms
Interdisciplinary and multiprofessional: all members of the palliative care team actively contribute to rehabilitative palliative care A collaboration between patients, relatives, and carers and the multidisciplinary team	The sole domain of allied health professionals (AHPs): physiotherapists, occupational therapists, dietitians, speech and language therapists, rehabilitation assistants
About optimizing people's ability to function in the widest sense including moving around, eating and enjoying food, communicating with others, managing activities of daily living, and participating in meaningful activities	About promoting false hope that someone will recover or return to a previous level of function when this is unrealistic Just about mobility and walking
About adopting an enabling approach to provide patients and their relatives or carers with enough support and empowering them to manage on their own	About being less caring but promotes adopting an enabling approach to the way in which we provide care and having a greater focus on support
A way to give people greater independence, autonomy, choice, and dignity	About moving away from the ethos and values of palliative care but enhancing these through shared characteristics of rehabilitation
About living with dying	About ignoring dying or pretending it isn't happening
Everybody's business	

Tiberini and Richardson (2015)

Rehabilitation Case Study: Introducing Ali

Ali is a 74-year-old gentleman who lives at home on his own after his wife died 3 years ago. He is a retired teacher and has two children and five grandchildren who he sees regularly.

Ali has stage 3 lung cancer and has recently undergone chemotherapy. He has a history of COPD and osteoarthritis in both knees.

Ali has been referred to outpatient hospice services because of:

- Increasing breathlessness and fatigue
- Difficulty managing with his normal activities of daily living

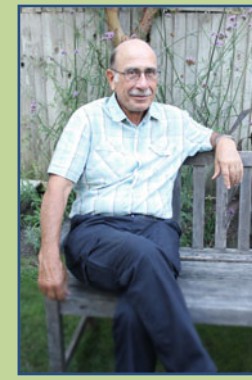


Fig. 2 Introducing Ali – a rehabilitative case study

3 Why Is Rehabilitation in Palliative Care Important?

3.1 Rehabilitative Palliative Care Actively Supports Priorities of Patients with Advanced Illness to Live Life Fully Until They Die

3.1.1 Maintaining Normality of Daily Life

Despite a diagnosis of advanced illness, patients' priorities consistently reflect the importance of maintaining continuity of daily life and living a normal life for as long as possible (Carter et al. 2004; La Cour et al. 2009; Johnston 2010; Reeve et al. 2010). Research has shown that, for patients and their carers, maintaining normality was the most important priority for patients alongside preparing for death. Maintaining normality of daily life is valuable for patients to preserve their dignity when they are losing independence and control in so many areas (La Cour et al. 2009; Johnston 2010). Through actively living a daily life and maintaining routines, patients strive to maintain an overall sense of well-being in the face of terminal illness, but most importantly, they work to maintain a strong sense of who they are and what is important to them.

3.1.2 Maintaining Independence and Choice

Physical function and independence are high priorities for patients living with advanced illness as they represent important routes to maintaining autonomy, control, and dignity (Carter et al. 2004; Cotterell 2008; Waterworth and Jorgensen 2010; Baile et al. 2011; Strohbuecker et al. 2011). While people living with advanced illness identify practical issues of daily living – including maintaining function, the ability to care for oneself, and the ability to do what one wants – as specific issues that are important to them (Carter et al. 2004; Baile et al. 2011), their overarching priorities relate to having a sense of control and choice in life (Cotterell 2008; Waterworth and Jorgensen 2010; Strohbuecker et al. 2011). Independence in the wider sense concerns attaining the right to be free of the influence and control of others (Cotterell 2008). From this perspective, independence, while linked with physical function, is not inherently determined by a person's ability to function. A person with advanced illness may experience a loss of physical functioning which necessitates assistance from others to fulfill tasks of daily living. However, this support can be delivered in a way that enables them to maintain their independence and control their own lives

Fig. 3 Patient's Priorities – 'what matters to you?' not 'what's the matter with you?'

(Cotterell 2008) preserving their sense of dignity and inherent worth (Chochinov et al. 2002) (Fig. 3).

3.2 Rehabilitation in Palliative Care Is Feasible, Acceptable, and Effective for Patients with Life-Limiting Illness

A growing body of robust evidence supports the feasibility, acceptability, and effectiveness of rehabilitation interventions for patients with advanced disease including cancer (Oldervoll et al. 2011; Henke et al. 2014; Jensen et al. 2014; Mayo et al. 2014; van den Dungen et al. 2014); respiratory (Sachs and Weinberg 2009; McCarthy et al. 2015), cardiac (Taylor et al. 2014), and neurological disease (Trend et al. 2002; Khan et al. 2007); and dementia (Pitkälä et al. 2013).

Randomized control trials of rehabilitation in palliative cancer populations have demonstrated improvements in patients' strength, fatigue, physical functioning, Activities of Daily Living (ADL) functioning, social functioning, independence and quality of life (Oldervoll et al. 2011; Henke et al. 2014; Mayo et al. 2014) – wide ranging effects which are also found in real-world clinic settings (Talbot Rice et al. 2014). Gains in physical function are particularly impressive when considered alongside the tendency for function to deteriorate with advancing disease. This demonstrates the potential for rehabilitation to not only prevent or delay deterioration in function but for some patients to actively *improve* their functional status with regard to physical independence, irrespective of advanced disease.

Qualitative research illustrates how rehabilitative approaches can be transformative in empowering patients living with advanced disease to regain a sense of normalcy and control in their lives (Malcolm et al. 2016; Turner et al. 2016).

3.3 Rehabilitation Offers Solutions to Respond to the Changing Needs of Populations Requiring Palliative Care

The global society is aging. In 2010, an estimated 524 million people were aged 65 or over – 8% of the world's population. This number is rapidly increasing and projected to triple by 2050, to 1.5 billion people representing 18% of the world's population (WHO Global Health and Aging 2011). A consequence of increasing age is that longevity frequently becomes compromised through a picture of progressive disability and/or frailty. As treatments continue to improve and

survival for most diseases increases, typical dying trajectories are evolving and converging toward one of chronic illness. While this model is amenable to longer-term control, with a slower progression toward death, it is characterized by increased disability preceding death (Gill et al. 2010).

Disability and frailty can have significant detrimental impacts on a person's ability to undertake normal activities of daily living and are associated with negative patient outcomes including reduced independence and autonomy, decreased participation in meaningful activities, depression, and poorer quality of life. However, both disability and frailty are dynamic states that can be made better or worse.

There is a robust body of evidence that supports the effectiveness of rehabilitation in the prevention and reduction of disability and frailty in people living with advancing illness and/or old age (Crocker et al. 2013).

3.4 Rehabilitation Can Contribute Economic Efficiencies in Palliative Care Service Provision

Reducing the levels of disability arising from disease and health-related conditions is one important key to holding down escalating health and social care costs. Functional disability and reduced independence with ADLs are significantly associated with both hospital stay and need for long-term care which, in the UK, are the primary determinants of cost in the last year of life (Kelley et al. 2012; Portegijs et al. 2012; Georghiou and Bardsley 2014). It has been shown that severe disability and functional decline are significantly associated with increased hospital days in patients in the last year of life (Kelley et al. 2012). Similarly, failure of older patients to regain function in the three months following a hospital admission is recognized as a significant predictor of their being institutionalized within the next twelve months, irrespective of the person's pre-admission ADL impairment (Portegijs et al. 2012).

Considered from an economic perspective, the relationship between rehabilitation and cost savings is simple: the longer people can remain independently mobile and capable of self-care, the lower their use of hospital services and the lower the costs for long-term care to families and societies (WHO Global Health and Aging 2011). Timely access to rehabilitation services has the potential to prevent or slow functional decline, avoid unnecessary hospital admissions, reduce length of hospital stay, help patients counteract the loss of function following hospital admission, and reduce or delay the need for institutionalization (Kelley et al. 2012; Portegijs et al. 2012).

At a population level, small improvements in an individual's functioning can translate into considerable cost savings, demonstrating the economic value of rehabilitation in palliative care (Tiberini and Richardson 2015).

4 "Rehabilitative Palliative Care": Rehabilitation as Core Business for the Interdisciplinary Team

Rehabilitative palliative care is an evolving approach to palliative care where all members of the interdisciplinary team have an active role to play in supporting patients to live fully until they die through integrating rehabilitation, enablement, self-management, and self-care into the holistic model of palliative care provision (Box 2).

Box 2: Rehabilitative Palliative Care Definition

Rehabilitative palliative care is a paradigm which integrates rehabilitation, enablement, self-management, and self-care into the holistic model of palliative care. It is an interdisciplinary approach in which **all members of the team**, including nurses, doctors, psychosocial practitioners, and allied health professionals, work collaboratively with the patient, their relatives, and carers to support them to achieve their personal goals and priorities. Rehabilitative palliative care aims to optimize people's function and well-being and to enable them to live as independently and fully as possible, with choice and autonomy, within the limitations of advancing illness.

(*continued*)

Box 2: (continued)

It is an approach that empowers people to adapt to their new state of being with dignity and provides an active support system to help them anticipate and cope constructively with losses resulting from deteriorating health.

Rehabilitative palliative care supports people to live fully until they die (Tiberini and Richardson 2015).

To realize this approach in practice requires attention to the culture of how we conceptualize and deliver palliative care to:

- Focus our support on the experience of living rather than dying.
- Place patients' personal priorities and goals at the core of any support we provide.
- Work collaboratively to fulfil these through the conscious, active commitment of all members of the interdisciplinary team to adopt these rehabilitative approaches in their daily practice.

A rehabilitative palliative care culture holds two paradigms in balance, embracing concepts of *enablement* alongside *care* (Box 3). Together, these complementary approaches create a spectrum of support, ranging from supportive self-management through to total care which allows palliative care teams to better tailor their input to patients with differing levels of need and to individual patients as their needs change over time. Importantly, a balance of enablement and care ensures we offer just the right amount of support, at the right time, in the right way.

Box 3: Rehabilitative Palliative Care Embraces "Enablement" Alongside "Care"

These paradigms are complementary: enablement is caring and nurturing while actively seeking to preserve people's choice, participation, and autonomy. Care delivery underpinned by these same values can be enabling (Wosahlo 2014).

4.1 Four Key Practices of Rehabilitative Palliative Care

At the heart of rehabilitative palliative care are four key practices: person-centered goal setting, focus on function, supported self-management, and enablement (Box 4).

Box 4: Four Key Practices of Rehabilitative Palliative Care

1. **Person-Centered Goal Setting:** to work in partnership with patients to actively identify their priorities and tailoring our interdisciplinary support to address these
2. **Focus on Function:** to ensure all members of the interdisciplinary team consider the impact of symptoms on a person's ability to function, proactively recognize change in patients' function, and take appropriate actions to optimize their physical potential
3. **Supported Self-Management:** to enable patients to "take charge" – through a consistent interdisciplinary approach which encourages patients (and families) to play an active role in managing their health and well-being, and the effects of their illness, *themselves*.
4. **Enablement:** to empower patients to have maximum choice and control over their own lives – through all members of the interdisciplinary team actively creating opportunities for patients to choose what they want to do, to undertake what they can themselves, and to provide just the right amount of support to meet their individual needs and preferences (Tiberini and Richardson 2015).

4.1.1 Person-Centered Goal Setting

NICE guidance for best practice recommends that patients should "receive an active and planned approach ... involving assessment, goal setting, care planning and evaluation" as an intrinsic part

of palliative care provision. While goal setting is recognized as an important component of palliative care, professionals have a tendency to focus on problems and symptoms, which represent something that we can fix or manage, whereas patients focus on what they want to "do" (Boa et al. 2014). The implication for those working in palliative care is that by failing to explicitly ascertain patients' goals and priorities, teams may be providing "professional-centered" care based around what we can influence or what we perceive to be important to the patient. To provide truly "person-centered" palliative care that is tailored to each patient's personal priorities, an essential starting point is establishing what is most important for that person. Goal setting around these priorities provides a meaningful focus for collaborative action planning between the patient, family, and the whole interdisciplinary team which places the patient actively at the center of their care. It also provides a unifying framework for different professions within the interdisciplinary team to contribute their unique expertise – including symptom control, rehabilitation, psychological, social, and spiritual support – to collectively best support the patient to achieve their goals (Fig. 4).

Reframing interdisciplinary palliative care practice with greater collaborative focus on patients' personal goals has potential to help patients:

- Feel listened to and that their priorities are paramount.

Fig. 4 Person-centered Goal Setting

- Have a more linked up experience of care and support across the interdisciplinary team.
- Find focus and meaning in life.
- Increase motivation and effort to achieve what is important to them.
- Develop resilience and coping – enabling reframing of goals as illness progresses and mourning for unachievable goals as an important aspect of adapting to illness.
- Live actively while dying.

Person-centered goal setting is not about creating an environment of false hope. While goals should be realistic, research suggests the process of setting goals and working toward them is more important than achieving them and that this can be constructive in helping patients understand, and come to terms with, what is manageable and what is not (Boa et al. 2014).

Rehabilitation Checklist for Person-Centred Goal Setting

- Ask patients:
  'What is important for you to achieve in the next few . . . weeks/months?
  'What are your best hopes for . . . this admission/ the next week while?' Boa et al. (2014)
- Make patients' goals the center of all interdisciplinary support – embedding them in the structure of patient notes, ward rounds and team meetings
- Celebrate patients' achievements
- Work in partnership with patients to reframe their goals if their circumstances change and the goal is no longer a priority or no longer realistic

4.1.2 Focus on Function (Beyond Symptoms)

Maintaining function is a high priority for patients with advanced illness as it represents an important gateway to preserving independence and autonomy and participating in meaningful activities that add quality to life. As such, "maximising patients' independence and minimising experiences of dependency should be a priority for those working with people who have life-limiting conditions" (Cotterell 2008).

Function requires greater attention in older populations who are at increased risk of functional decline and frailty. For this group, small deteriorations in function can have a disproportionate impact on capacity for independent living. It is easier to maintain function than it is to regain function once it has been lost. Proactive assessment and identification of factors that may compromise function is key to allow for strategies to prevent avoidable deterioration, e.g., deconditioning arising from inactivity, to be put in place. Functional assessment is also essential to proactively recognize patients' needs for specialist rehabilitation input and ensure appropriate early referral to allied health professionals. (Fig. 5)

Symptoms can be a profound source of discomfort and distress in their own right; however, frequently, the magnitude of patients' experience can only be fully appreciated when symptoms are contextualized within the realm of function. Function is frequently compromised by symptoms and is extrinsically linked to a host of wider losses, which if not properly assessed and addressed can become significant sources of distress for patients and families (Chochinov et al. 2002).

While palliative care defines itself through early identification and impeccable assessment, research suggests that functional concerns of palliative patients are not well identified. Patients' primary concerns were found to relate to loss of function, the future and caring for themselves; however, these were not recognized as priorities by assessing palliative care clinicians (Baile et al. 2011).

Systematic, routine assessment of function by all members of the interdisciplinary team, as a core part of the holistic palliative care assessment, is essential to proactively identify functional concerns and ensure these are adequately addressed. This is important at all stages of symptom control, to ensure that intervention is not ended prematurely at the point where a patient's symptoms are well controlled at rest, but rather, symptom management aspires to have symptoms well controlled when patients are operating at their maximal level of functioning.

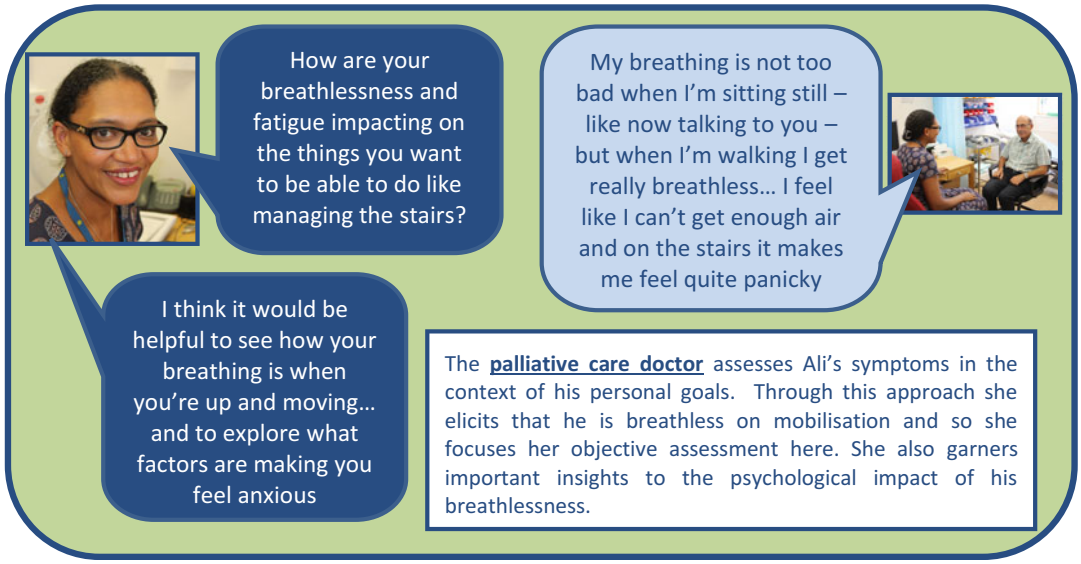


Fig. 5 Focus on Function Beyond Symptoms

Rehabilitation Checklist for Focus on Function Beyond Symptoms

- Incorporate functional assessment as a routine aspect of all holistic palliative care assessments by all team members.
- Proactively screen for functional difficulties by asking patients: Are you having any difficulty with moving around or managing your day-to-day activities?
- Consider the impact that symptoms are having on a patient's ability to function and go beyond symptom control at rest to optimize symptom control when a patient is functioning to their best potential.
- Refer to physiotherapy and occupational therapy early when function difficulties are recognized so patients can benefit from specialist assessment and rehabilitation.

4.1.3 Supported Self-Management

For people living with advanced illness "taking charge" represents a central priority. The right to exercise choice and control, even when extremely ill, is important to patients and is often related to preserving their dignity and maintaining normality. Self-management is about supporting people to take responsibility for their own health and well-being and is closely related to, and often used interchangeably with, self-care. Collectively, these terms aim to empower patients to play an active role in managing their illness and the effects of their illness, *themselves* (Johnston 2010).

In the context of palliative care, supported self-management and self-care do not necessarily mean remaining entirely self-maintaining or fully functional; instead, it involves "maintaining one's usual practices of self-care; those things that are important and unique to oneself in maintaining one's sense of self" and "being given the means to master or deal with problems, rather than relinquish them to others" (Corner 2002). Supported self-management is about redressing the power relationship between health professionals and people (patients) to put the person and their family back in charge.

Rehabilitation Checklist for Supported Self-Management

- Seek to identify what a patient is managing well independently and positively reinforce their self-efficacy.
- Encourage patients to assertively express their needs and wishes and work in

(*continued*)

partnership with them to co-create solutions and coping plans.
- Support and encourage patients to use non-pharmacological symptom management approaches to self-manage their symptoms.
- Support patients to undertake the elements of self-care they can manage themselves which are important to maintaining their sense of self.
- Enable patients to practice positive risk taking to fulfill their goals.

4.1.4 Enablement

Patients living with advanced illness describe priorities of maintaining normality of daily life, physical functioning, and independence and express a clear desire to be supported to manage their health with choice and control right up until they die. Enablement in healthcare is a therapeutic paradigm or process which aims to "recognise, support and emphasise the patient's capacity to have control over her or his health and life" (Hudson et al. 2011).

In the context of palliative care, where realities and losses associated with progressive, advancing illness can erode a sense of control, the practice of enablement can help actively restore the experience of perceived control and self-efficacy for both patients and families. It has been suggested, however, that "considerable paternalism" exists in palliative care (Randall and Downie 2006). Rather than enabling patients to carry out activities they are able to, we can sometimes "over-care" inadvertently disempowering patients by doing these activities for them. By integrating enablement as a core dimension of holistic palliative care provision, all members of the interdisciplinary team can better ensure that care is actively tailored to recognize and support individual patient's capacities and preferences.

Enablement actively supports patient independence and participation; however, this is always led by patients' capacity and willingness to engage. In situations where patients make an informed decision to decline to participate, e.g., in daily care even if they have the capacity to do so, an enablement approach recognizes and respects the patient's choice. A defining characteristic of "enabling care" is that all patients are consistently offered the opportunity to make the choice for (or against) independence and participation in the first place (Fig. 6).

An enablement approach lies at the heart of rehabilitative palliative care (Box 5). It is the route to realizing patients' priorities of normality and functional independence and the bridge between caring and fostering autonomy necessary to be alongside patients as they experience functional losses. Inherent to enablement is the distinction between autonomy and independence. This recognizes that while a person's independence may reduce due to advancing illness, their autonomy to make decisions about what they do and how they are supported can be preserved.

Box 5: How to Adopt an Enablement Approach to Your Practice

- Work in partnership with patients to identify their *person-centered goals and priorities.*
- Start from the underpinning assumption that a person would like to choose if they want or need support.
- Shift your focus to offering *support* to a *person* (rather than the default of providing care to a patient).
- Ensure any support or care you provide is led by people's priorities, goals, and preferences (as opposed to a professional need to "care for" or "fix" patients problems to make everything better).
- Begin by checking what support or assistance a person would like and how they would like this (before making assumptions and automatically providing it).
- Provide support which involves "being alongside" or "doing with" the person (rather than a default of "doing for") whenever possible.
- Practice *enablement* by empowering people to play an active role in their support and care whenever possible – even small acts of participation such as washing

(*continued*)

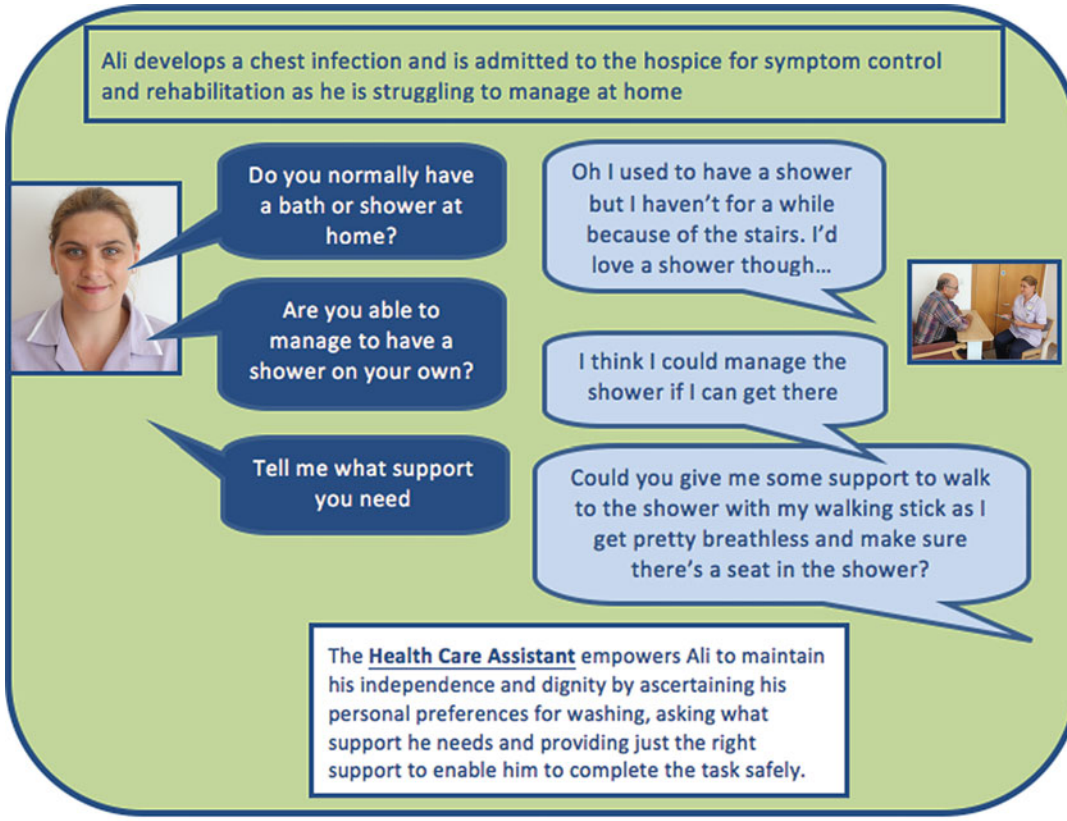


Fig. 6 Enablement and Supported Self-management

Box 5: (continued)

one's own face or genitals can make a big difference to a person's dignity.

- *Focus on function:* by always considering symptom control in the context of a person's function.
- Consciously create opportunities for patients to play an active role in *supported self-management* of their condition and well-being.
- Always work to promote choice and foster autonomy.
- Be conscious that you don't unintentionally "over-care" for patients which may diminish their function, independence, autonomy, and dignity.
- Respect when people make an informed decision not to participate, even if they have the capacity do so – this recognizes that they are exercising personal choice.

5 The Specialist Contribution of Physiotherapy and Occupational Therapy to Rehabilitation in Palliative Care

For physiotherapists and occupational therapists, rehabilitation lies at the heart of their approach to palliative care. With dominant values of "enabling function and independence" underpinning their professional practice, physiotherapists and occupational therapists focus in on what is most

important to people and what they need to be able to do to achieve this. Drawing on holistic assessment skills, physiotherapists and occupational therapists identify physical impairments alongside psychological, social, and environmental factors impacting on a person's ability to function and cocreate a rehabilitation plan in partnership with the patient to address these.

Physiotherapists and occupational therapists are experts in the delivery of rehabilitation interventions and have an important role to play in leading the interdisciplinary team in the practice of rehabilitative palliative care, where all team members adopt an enabling approach to their clinical practice (Boxes 6 and 7).

5.1 Capacity, Needs, and Wishes

To ensure rehabilitation initiatives are tailored to both individual and changing needs of palliative care patients, physiotherapists and occupational therapists have a working knowledge of the relationship between capacity, needs, and wishes (Fig. 7).

Capacity is a person's ability to do things. **Needs** are the things that day-to-day functioning depends on – such as eating, washing, and dressing. **Wishes** are the things like hobbies or leisure pursuits some of which a person can survive without but which ultimately can bring value, purpose, meaning, and quality to life. In an unimpaired state (1), a person will have capacity to meet all of their day-to-day functional needs (they will be "self-caring"). Although some wishes will be unattainable, e.g., running fast for a bus or completing a marathon, most wishes can be met. But a reduction in capacity (2) through illness or treatment may limit participation in more demanding wishes and prevent participation in hobbies or leisure pursuits. As capacity deteriorates further (3), more wishes cannot be met, and some needs are beyond their ability. This is when independence decreases and dependence on others increases, signaling the need for assistance and help.

At its core, rehabilitation in palliative care is about enabling a person's capacity to remain at its maximum potential and allowing someone to be the best that they can be – fulfilling their needs and wishes independently whenever possible – despite advancing illness. It is to support living in the face of life-threatening illness and deterioration and to adapt constructively as capacity diminishes.

5.1.1 Aims of Rehabilitation in Palliative Care

Specialist rehabilitation provided by physiotherapists and occupational therapists is focused around the following aims:

1. **To minimise the effects of advancing disease or its treatment on people's function**

   Life-limiting illnesses including cancer, respiratory diseases, heart failure, and

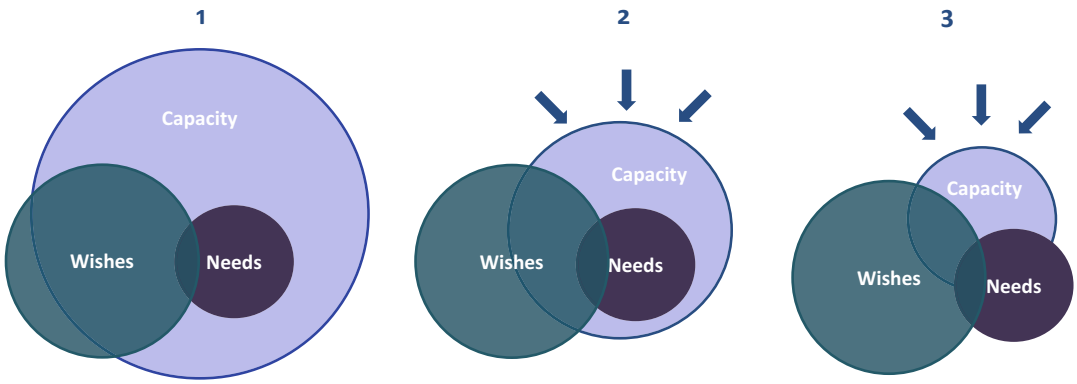


Fig. 7 The Relationship between Capacity, Needs and Wishes in Advancing Illness (Adapted with kind permission of Matthew Maddocks)

neurological conditions can cause disability and impairment. This can be from the disease itself or from the treatment of the disease (e.g., steroids causing proximal myopathy or radiotherapy causing fatigue). Rehabilitation aims to minimize these effects.

2. **To maintain and support people's independence**

   For people facing a life-limiting illness, one of the biggest reported fears is of *being a burden* on family or friends (Waterworth and Jorgensen 2010). Maintaining independence and supporting people to be able to do as much as they can for themselves is paramount. Rehabilitation always aims to promote independence as much as possible, encouraging a person to do as much as they can for themselves.

3. **To empower people to cope effectively with symptoms and associated distress**

   Evidence is increasingly proving the effectiveness of non-pharmacological symptom management to enable people with advancing illness to understand, manage, and live well alongside symptoms of breathlessness, fatigue, pain, and insomnia (Javier and Montagnini 2011). Rehabilitative approaches go hand in hand with appropriate pharmacological interventions and have an important role in increasing people's self-efficacy to cope with symptoms and minimize associated distress, especially earlier on in the pathway.

4. **To enable people to participate in meaningful activity**

   Paramount to good palliative rehabilitation is the ability to support a person's maintenance of their role, identity, and sense of self through participation in activities that are important or meaningful to them. Through creative approaches, this is frequently possible irrespective of their disabilities, symptoms, or prognosis. An example would be to enable a person who loves to cook to access their kitchen and participate in meal preparation despite being in a wheelchair.

5. **To provide expert education and open communication**

   Education and open communication are central to effective rehabilitation provision to both elicit engagement in the rehabilitation process and as a means of empowering patients, families, and carers to fully understand their condition. This may include tailoring education and advice to help people consider risks and limitations and make informed choices in line with their personal values, priorities, goals, and wishes. For example, working alongside a person with a spinal cord compression and resulting paralysis involves educating both the patient and their family. It is essential that they understand what spinal compression is, why it occurs, the impact on their function, and potential for recovery and this information needs to be communicated in an open, sensitive, way to enable them to consider the practical and emotional impact that loss of function will have on their lives.

5.1.2 Specialist Palliative Rehabilitation Interventions

With these aims in mind, the core interventions of specialist palliative rehabilitation are presented below alongside the evidence for acceptability, feasibility, and effectiveness.

5.2 Exercise and Activity

Exercise and activity are critical interventions for maintaining and, where possible, improving patients' physical functioning and independence. They are interrelated in that, for some patients with diminishing capacity, participation in functional activities that support their mobility will represent their dominant and most appropriate form of exercise.

A core focus of any rehabilitation assessment undertaken by an occupational therapist or physiotherapist will be to determine a patient's level of mobility. Mobility is the capability to move or be supported to move, and it is best understood as a spectrum: ranging from being able to move oneself in bed by rolling over or bridging right through to being able to climb stairs or run (Fig. 8). A person's level of mobility is qualified by their use of mobility aids (Fig. 9) and the

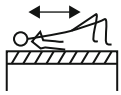
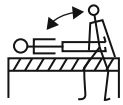
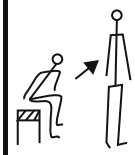
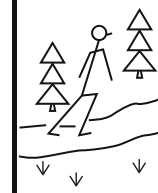
Bed Mobility	Lying to Sitting	Sitting to Standing	Transfers	Walking	Stairs	Outdoor Mobility
						
The ability to move oneself on the bed includes rolling and bridging to move up and down the bed on one's back	The ability to move oneself form a horizontal lying position to upright sitting	The ability to move oneself from sitting to standing	The ability to move oneself between locations such as from a bed to a chair or from a wheelchair to a toilet	The ability to walk	The ability to climb and descend a flight of stairs	The ability to walk around outside

Fig. 8 Mobility as a Spectrum

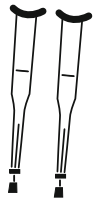
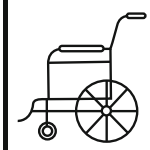
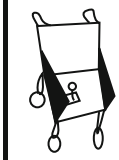
Walking Stick	Crutches	Walking Frame		Wheelchair		
		Zimmer	Rollator	Manual		Electric
				Self Propelled	Attendant Propelled	
						

Fig. 9 Walking Aids

degree of support they require from another person to undertake a task, which may involve assistance, supervision, or no support in the case of independence (Table 2).

Mobility levels will differ from person to person, but it is important to note that a patient who is not able to get out of bed without assistance could gain as much achievement from being able to roll over and change position independently as another patient does from being able to climb the stairs to get to their bedroom. Importantly, mobility levels are changeable and in most cases can be improved through rehabilitation interventions. This can be achieved either directly by rehabilitating a person's impairments such as strength, balance, or breathlessness or indirectly through the provision of aids or environmental adaptations.

Exercise, activity, and mobility go hand in hand. At a very basic level, the phrase is true "if you don't use it, you lose it." So at the heart of specialist, palliative rehabilitation must come the offering of exercise-based interventions. Tailored

Table 2 Levels of support for mobilization

Independent	Supervision	Assistance of one person	Assistance of two people	Assistance of hoist
The ability to move oneself without the assistance of a person One can be independent even if they use a walking aid	The ability to move without hands on manual assistance but requiring supervision to ensure safety – for example, when balance or cognition is compromised	The ability to move with physical hands on assistance of one other person	The ability to move with physical hands on assistance of two other people	When a person cannot be safely supported through the assistance of two people, a hoist is required to assist movement

exercise prescription frequently falls under the professional expertise of the physiotherapist (Fig. 10).

The feasibility and acceptability of exercise to patients with advanced disease are now well established. Studies offering a range of exercise rehabilitation interventions to patients with advanced stage cancer unanimously found it was feasible for this population to participate in exercise rehabilitation, including aerobic, endurance, and resistance training (Oldervoll et al. 2011; Henke et al. 2014; Jensen et al. 2014; Mayo et al. 2014; van den Dungen et al. 2014). A large retrospective analysis of 572 terminally ill cancer patients found that physical exercise (alongside breathlessness management and relaxation strategies) was acceptable to over 90% of patients (Jensen et al. 2014), while the majority of patients with advanced cancer consider themselves physically capable of undertaking some form of exercise and over two-thirds feel prepared to undertake a program (Maddocks et al. 2011).

This strong and growing body of evidence supports the view that rehabilitative interventions are effective in improving strength, fatigue, physical functioning, ADL functioning, social functioning, independence and quality of life in palliative populations (Oldervoll et al. 2011; Henke et al. 2014; Jensen et al. 2014; Mayo et al. 2014; van den Dungen et al. 2014).

Exercise interventions for patients with respiratory or cardiovascular disease are also well established, with randomized controlled trial evidence supporting the effectiveness of pulmonary and cardiac rehabilitation programs. Large Cochrane Collaboration systematic reviews show that pulmonary rehabilitation for patients with COPD (65 trials with 3822 participants) can relieve breathlessness and fatigue; improve physical function, emotional function and feeling of control; and reduce the frequency of hospital admissions regardless of disease severity (McCarthy et al. 2015). Similarly strong evidence exists for cardiac rehabilitation, which, for patients with heart failure (33 trials with 4740 participants), reduces hospital admissions and improves quality of life, irrespective of the degree of heart failure (includes NY Heart Failure Association Class IV) (Taylor et al. 2014).

Several small qualitative studies in the UK have explored the patient-reported impact of participating in exercise on their quality of life. Turner found that in addition to perceived physical and emotional improvements in their well-being, patients felt that engaging in exercise classes gave them a sense of meaning whereby they reclaimed control though active, positive involvement in their own health, greater choice, the opportunity to prolong independence, and confidence and hope to face the future (Turner et al. 2016).

> . . . I am actually doing something to keep well. That feels really good in the situation where cancer makes you feel very powerless because it's out of your control. I can get to the gym, I can walk, I can make my heart rate increase, I can strengthen my limbs as much as I'm able. That control is very good for someone who feels they have so little control...

Fig. 10 The role of the Specialist Palliative Care Physiotherapist

Malcolm's findings reinforced the importance of rehabilitation as a means of enhancing a sense of normalcy, where patients had greater independence and ownership of their health (Malcolm et al. 2016).

> ... it means that I'm able to just be, just feel like I'm normal, feel like things are normal for me.
>
> I think it helps you to ... just get on with being and helping yourself... all of it is leading up to you making that decision for yourself to sort of keep healthy.

Box 6: The Specialist Contribution of Palliative Care Physiotherapists

Physiotherapists work as autonomous practitioners offering specialist, evidence-based assessment, diagnosis, treatment interventions, and guidance. They optimize patients' quality of life by maintaining and improving physical function to attain the

(*continued*)

Box 6: (continued)
highest level of independence possible in advanced illness through:

- **Robust clinical reasoning skills** underpinned by knowledge of anatomy and physiology of advanced illnesses including oncological, respiratory, cardiac, and neurological conditions and multiple comorbidities associated with aging
- **Specialist skills in holistic assessment:** Utilizing both subjective and physical assessment, including respiratory, neurological, musculoskeletal, lymphedema, and functional assessments, to systematically identify factors impacting on a patient's ability to function and make clinical diagnoses
- **Palliative rehabilitation:** Specialized interventions and guidance to optimize a person's mobility and functioning by analyzing, treating, and managing impairments, including muscle weakness, fatigue, balance, breathlessness, pain, lymphedema, and anxiety, to work in partnership with patients to achieve their personal goals
- **Advanced communication skills** to help patients and their families proactively plan for the future, anticipate potential functional changes, avert functional crises, and adapt constructively to the spectrum of losses related to functional decline in advancing illness
- **Non-pharmacological symptom management** of breathlessness, fatigue, pain, lymphedema, and anxiety in advanced illness through provision of specialist treatment interventions including personalized exercise prescription, manual treatments, provision of equipment and aids, rehabilitation, and expert guidance
- **Self-management** education and strategies to empower patients and carers to understand and cope with symptoms, maintain function and participation in meaningful activities, reduce dependence on others, and foster a sense of control and self-efficacy
- **Positive risk taking, assessment, and management:** Including comprehensive evaluation of patients' safety to manage functional activities; recommendations to actively manage risks through provision of support, activity modification, and use of equipment and aids; and enabling supportive risk taking to support patient choice and quality of life even when risks are evident
- **Complex moving and handling**: Risk assessment, personalized management plans, education, and support to patients, carers, and multidisciplinary team (Tiberini and Richardson 2015).

5.3 Participation in Activities of Daily Living

Enabling participation in activities of daily living (ADLs) which include toileting, bathing, dressing, or preparing a meal is a core element of palliative rehabilitation, central to supporting patients' priorities for maintaining normalcy and independence. Occupational therapists and physiotherapists are experts in the assessment of function with attention to a patient's capacity to manage ADLs. This holistic assessment routinely takes into account each individual's impairments, their environment, level of motivation and support relationships, alongside their personal goals and priorities.

Participation in ADLs is an important route to maintaining patients' dignity, which remains important even when a patient's capacity has diminished to a point where they require assistance to meet their basic needs. Examples of this may include patients living with advanced neurological conditions or those in the last days of life where continuing to enable participation in tasks,

where it is important to that person, such as supporting them to wash their own genitals or face when undertaking a bed wash, can make a real difference right up until death.

In advanced neurological conditions, rehabilitation has been found to be both acceptable and effective in supporting people to manage symptoms, maintain function, prevent secondary impairments, adapt constructively to change in function related to their illness, and proactively avert crisis situations (Trend et al. 2002; Khan et al. 2007; Simmons 2013). A Cochrane systematic review of 954 adults with multiple sclerosis of all severities found there was strong evidence to show rehabilitation produced short-term gains with improved levels of participation, patient experience, and quality of life (Khan et al. 2007).

Physiotherapists and occupational therapists are well placed to develop "enablement plans" for patients which provide clear recommendations for the interdisciplinary team on how to best optimize patient participation. This aspect of rehabilitative palliative care requires conscious attention on behalf of all members of the interdisciplinary to ensure patients are not unintentionally deprived of opportunities to undertake tasks themselves, especially where this may take longer than doing the task for them.

Occupational therapists are skilled in managing complex discharges which enable palliative patients to return safely to their preferred place of care, frequently home, following an inpatient stay. Due to the variable nature of advancing illness, patients' condition and their functional abilities can change quickly. This requires proactive planning to ensure the patient will be safe and supported both in phases of stability and deterioration, including at the end of life if they wish to die at home. Occupational therapists and physiotherapists work in partnership to undertake a comprehensive assessment of patients' function, environment and support network, to explore the risks and opportunities of a person returning to live in their own home. Areas of assessment may include a person's ability to climb stairs to access the bedroom and bathroom versus setting up a microenvironment on a single level or their ability to safely access and get on and off the toilet to maintain personal hygiene versus using a commode beside the bed. Home assessment is paramount, and where needed, adaptation of a person's environment can enable them to continue to actively participate in ADLs, maintain independent living, and remain at home. Simple adaptations such as installing a stair rail can allow a patient to safely, independently navigate stairs – a small intervention which can make the immense difference between being house bound and accessing the local community (Fig. 11).

Supporting patients to participate in ADLs and to return home requires an important balance to be struck which is enabling both *choice and safety*, managing both *risk and opportunity*, and acknowledging both *expectation and reality.* Positive risk taking and parallel planning, discussed later in this chapter, are effective practices to help achieve this.

Box 7: The Specialist Contribution of Palliative Care Occupational Therapists

Occupational therapists work as autonomous practitioners offering specialist assessment, interventions, and guidance specifically focused around occupation. Occupation encompasses all activities of daily living and dying. They optimize a person's quality of life by supporting maintenance of role, identity, and sense of "self" through participation in activities that are important or meaningful to them despite their disabilities or prognosis through:

- **Specialist assessment of a person's ability to function** in the unique context of their physical environment and interpersonal relationships with attention to cognitive, psychological, social, and physical aspects of a person:
  - Analysis of the individual components of occupation to enable targeted interventions to modify or adapt the activity to support participation, independence, and quality of life

(*continued*)

Fig. 11 The role of the Specialist Palliative Care Occupational Therapist

Box 7: (continued)

- Cognitive and perceptual assessment to identify factors affecting a person's ability to plan, sequence, and execute activities in order to improve or maintain existing capacities
- Assessment of care and support needs to determine a person's ability to participate in ADLs, with attention to both risk and independence in order to tailor support to enable personal choice and priorities while optimizing safety, including analysis of carer's ability to provide support
- Assessment of complex posture, seating, and manual handling issues in order to provide recommendations and interventions to manage pressure and other risks and to maximize participation in occupation

(*continued*)

Box 7: (continued)
  - Environmental assessment to evaluate a person's functioning within their home (or other) physical and social environment to identify difficulties and risks and to help maintain the person within their own home and maximize participation in occupation
- **Environmental adaptation, assistive technology, and equipment prescription**: To optimize safety in the home (or other) environment to enable people to be as independent as possible, reengage with activities of purpose and meaning, reduce burden on carers, and support people to achieve their preferred place of care and death
- **Advice and guidance on symptom control and self-management strategies** for fatigue, breathlessness, pain, anxiety, and sleeplessness using a range of interventions to facilitate occupational engagement
- **Complex discharge planning**: Including environmental modification, equipment provision, rehabilitation, supportive risk management, care support recommendations, creative problem-solving, and leadership to the multidisciplinary team to enable a safe and timely inpatient unit discharge and thereby optimize inpatient service efficiencies and to achieve the persons preferred place of care and death
- **Adjustment to loss of occupational engagement** due to progression of illness and a focus on the occupation of living with dying (Tiberini and Richardson 2015).

5.4 Non-pharmacological Symptom Management

Physiotherapists and occupational therapists play a key role in providing non-pharmacological strategies and practical advice to empower patients to understand and effectively self-manage symptoms. For many people living with advanced illness, symptoms are refractory which means that they persist despite optimizing the treatment of any underlying causes. Subsequently, it is essential that the focus of non-pharmacological symptom management is on symptom *mastery* rather than symptom reduction, although this is also a possible outcome. Mastery over a symptom is about having control over it rather than it having control over you – a concept which patients find helpful and empowering. In other words, the approach can be explained as "while we may not take away this symptom, we can help it to have less of an impact on your life."

Breathlessness is a common, distressing symptom in advanced disease, present in about 90% of people with moderate to severe COPD, 80% of people with advanced heart failure and more than half of those living with incurable cancer (Solano et al. 2006), which is amenable to non-pharmacological management. The experience of breathlessness is characterized by the distressing sensation of being short of breath but also by the reduction in physical activity and function which frequently ensues as patients seek to avoid this unpleasant experience. The resultant downward spiral, where breathlessness leads to inactivity, which leads to muscle deconditioning, which further exacerbates breathlessness and functional decline, is frequently accompanied by escalating anxiety levels and panic attacks.

In the palliative care setting, there is evidence that non-pharmacological interventions for breathlessness, including breathing techniques, exercise, facial cooling with a handheld fan, pacing and positioning, and anxiety management strategies (Bausewein et al. 2008) are "the most effective interventions currently available to palliate breathlessness in the mobile patient" in the advanced stages of malignant and nonmalignant diseases (Booth et al. 2011). These strategies equip patients with the knowledge, skills and confidence to be more in control of their breathlessness. A recent randomized controlled trial found that a comprehensive

multiprofessional approach to support patients with advanced disease and refractory breathless – integrating input from physiotherapists, occupational therapists, as well as doctors from palliative care and respiratory medicine – effectively enhanced patient mastery and ability to self-manage their breathlessness (Higginson et al. 2014). This approach focused on patients gaining control over their breathing, being functionally active and living fully alongside breathlessness, rather than just targeting the intensity of the symptom.

Through non-pharmacological symptom management, physiotherapists and occupational therapists help people live with breathlessness, enabling patients to better manage their *functioning, breathing, and thinking* so that the breathlessness has less impact on their life and they are able to achieve their best potential (Fig. 12).

For many symptoms there are non-pharmacological treatment options that may help a person have better control over the symptom or even reduce the intensity of the symptom. Examples are found in Table 3.

Fig. 12 Nonpharmacological Symptom Management – focus on mastery

Table 3 Non-pharmacological symptom management for common symptoms in advanced illness

Breathlessness	Fatigue	Pain	Deconditioning and weakness
Breathing control techniques Activity pacing Adaptation of daily activities Hand-held fan Mobility aids Pulmonary rehabilitation Secretion clearance techniques	Activity analysis Activity planning and pacing Sleep hygiene Graded exercise Mobility aids	Cognitive behavioral approaches Exploration and challenge of pain beliefs Graded exercise TENS	Personalized exercise Programs Gym-based exercise Mobility aids
Education			
Tailored exercise rehabilitation			

6 Key Strategies for Rehabilitative Palliative Care Success

In addition to the practices and specialist interventions described above, the following are strategies that are key to realizing rehabilitative palliative care in day-to-day practice.

6.1 Create a Shared *Culture* of Rehabilitative Palliative Care

Work to build a culture across the interdisciplinary team where everyone understands what rehabilitative palliative care is and what their role is to bring it to life for patients through their day-to-day clinical practice:

- Start by raising awareness of the dominant *values* for people living with serious, advanced illness – *choice, autonomy, and dignity* – and make a conscious and active commitment across the team to support these.
- Attend to the *language* we use and critically appraise whether it is fit for purpose. Adopt and integrate the active language of rehabilitation into our palliative care dialogue such as "support" (alongside care), "living with" (instead of dying from), "goals," "empowering," "enabling," "being alongside," "coping," and "managing."
- Build rehabilitative palliative care principles and practices into service strategies, operating frameworks, service standards, job descriptions, and education initiatives – including mandatory training.
- Ensure physiotherapists and occupational therapists are core members of the palliative care team to lead and support the approach.

6.2 Champion *Early Referral* for Specialist Physiotherapy and Occupational Therapy Rehabilitation

Maximize the benefit of rehabilitation interventions for people living with life-limiting illness, by making early referrals to your physiotherapist and occupational therapist for a specialist rehabilitation assessment:

- The earlier rehabilitation begins, the better the chances of preventing avoidable deterioration, delaying physical decline, and maintaining or improving function, while there is a window of opportunity.
- Proactively equip patients to deal with distressing symptoms, unwanted functional limitations, or disability before they happen – through access to individually prescribed non-pharmacological techniques and coping strategies to self-manage their condition.
- Establish personalized enablement plans to guide the interdisciplinary team in their provision of rehabilitative palliative care support.

6.3 *Engage* and *Motivate* Patients to Achieve the Things that Are Most Important to Them

The way we engage with patients and their families sets the scene for rehabilitative palliative care to take place, starting from our very first interaction:

- Create a *collaborative partnership* based on an implicit understanding that the patient and the professional each bring expertise and solutions to the relationship and that these are equally valuable.
- Make the **first priority and goal** of our professional assessment about establishing the **patient's priorities and goals**. This is key to building engagement and rapport as it values patients as *people* and ensures any support is tailored to what is most important to them.
- Place the patients' priorities at the heart of the dialogue by making simple changes in our questioning style such as asking "What matters to you?" rather than problem-focused questions such as "What's the matter with you?"
- Empower patients to come up with their own solutions and to express what support they need to achieve what is most important to them.
- Be aware of and seek to raise patients' *activation*. This describes a patient's involvement and levels of active engagement and participation in their health and care (Hibbard et al. 2005) – or put simply describes the gap between a person having the ability to undertake an activity and whether they actually do it or not. Proactively explore factors that can lower a patient's activation such as fatigue, refractory symptoms, anxiety, or loss of confidence, and bring these out into the open to overcome or work around them.

6.4 Proactively Acknowledge and Plan for *Uncertainty*

We should ensure that rehabilitation in palliative care is both meaningful and realistic by actively inviting uncertainty into the conversation and then, as far as possible, planning for how to manage it:

- Openly acknowledge that we cannot be certain what the future holds. This is upfront, honest, and frequently welcomed by patients and families who recognize the truth in this.
- Begin from the starting point of **maximizing opportunities** for people **rather than minimizing risks**. Develop a culture of *positive risk taking* which supports patients to take risks to achieve positive personal outcomes and recognizes that while the negative consequences of risk must be managed appropriately, we can't be certain of the outcomes. This involves balancing the positive benefits gained from taking risks with the negative effects of attempting to avoid risk altogether (Morgan and Williamson 2014). In the context of palliative care, avoiding risks due to concerns of negative outcomes can deprive patients of opportunities to take positive risks that may enable them to fulfill their potential or personal goals and maintain personal agency and identity.
- Support realistic hope alongside patient safety by practicing "parallel planning" – the process of actively acknowledging and planning for two or more possibilities at the same time or put simply "hoping for the best while planning for the worst" (Tiberini and Richardson 2015). Planning for several possibilities concurrently can help to (i) introduce and allow for anticipation of possible deterioration in a safe way and (ii) help prevent crisis situations which place the patient at undue risk (Fig. 13).

6.5 Provide a Support System for Patients and Their Families to *Actively Anticipate and Cope with Loss*

Losses in physical functioning frequently represent the tip of the iceberg for a cascade of less visible "network" losses, which are intrinsically

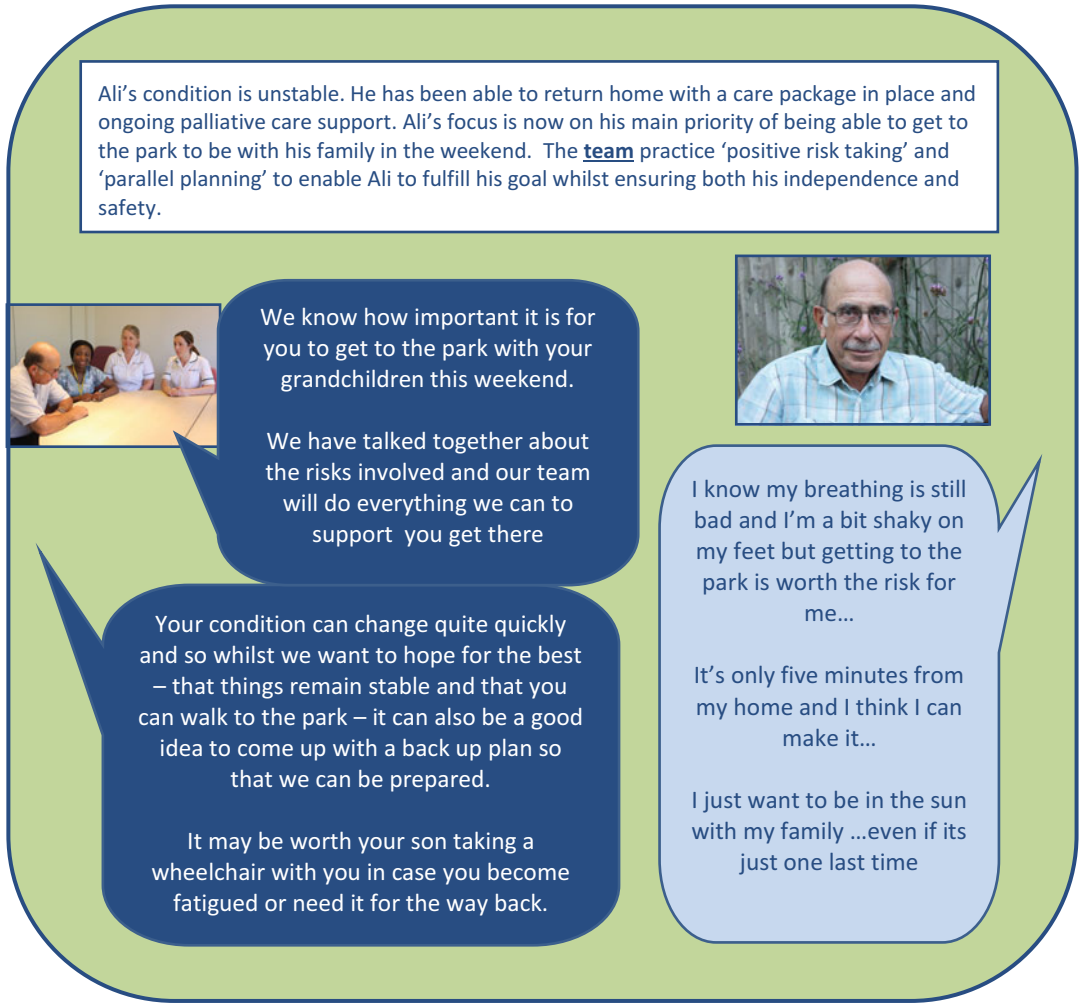


Fig. 13 Positive Risk Taking and Parallel Planning

linked with and arise from functional decline. These may include loss of independence, freedom, sexual function, career, roles, sense of self and identity, control, hope, dignity, certainty, and meaning (Jackson 2014).

- Recognize functional losses and proactively explore how these are impacting on a person's psychological, spiritual, and social well-being.
- Facilitate open, safe discussions for patients and families to share their experience of current losses and fear of future losses related to their diminishing functional capacity.
- Practice active, therapeutic listening – this can be just as rehabilitative as actually "doing" something.
- Acknowledge and validate people's grief – which can be complex as the losses are frequently permanent, unresolvable, and cumulative.
- Where possible, work in partnership with patients and families to openly anticipate future losses and come up with action and coping plans – this can be an empowering and reassuring exercise even if in the best case scenario they are never needed (Fig. 14).

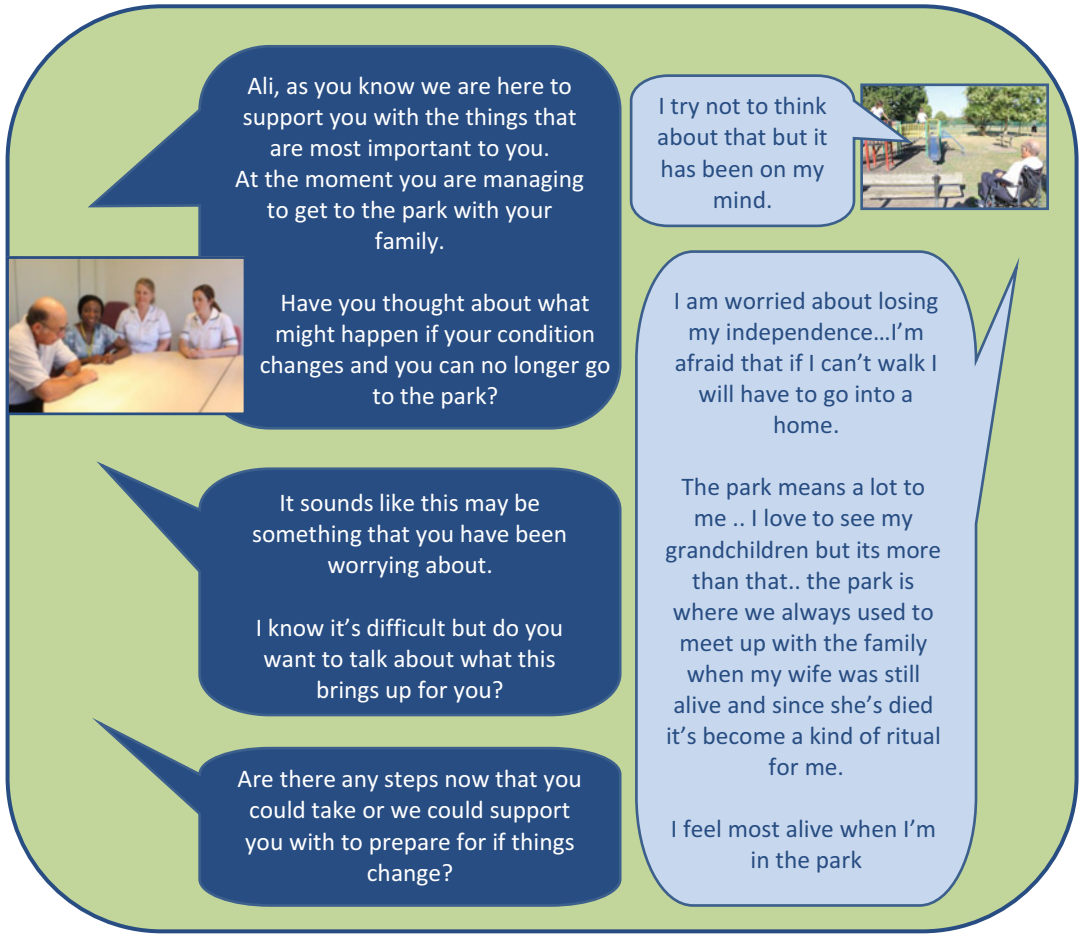


Fig. 14 Actively Planning for and Coping with Loss

7 Summary

Rehabilitation in palliative care aspires to optimize patient's choice, independence, autonomy and dignity and provides an active support system for people to live life fully until they die. It encompasses both the specialist rehabilitation contribution of occupational therapists and physiotherapists together with the crucial involvement of the wider interdisciplinary team through the practice of "rehabilitative palliative care." With patients' personal goals and priorities firmly at the heart of the approach, rehabilitation in palliative care creates a culture of enablement, through which the whole team can support patients to *live their priorities* right up until they die. Rehabilitation in palliative care is an important route to transforming people's quality of life and represents a key consideration for palliative care provision both now and in the future.

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Dietetics and Nutrition in Palliative Care

36

Cathy Payne

Contents

Abstract

Good nutritional care is a fundamental component of palliative care provision. Managing issues associated with eating and drinking, weight loss, and changes in body image towards the end of life can be challenging for many patients and families, as well as for healthcare professionals. The best nutritional care happens when patients and families are provided with early, consistent, and evidence-based dietary assessment and guidance. As well as direct provision of care to patients and families, dietitians have a significant role in educating all members of the multi-disciplinary care team on the provision of

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_36

optimal nutritional care for patients with life limiting illness and in supporting the evidence base to practice through engagement in research. The aim of this chapter is to provide an overview of the role of the dietitian as a member of the specialist palliative care team and to explore dietary interventions provided when incurable progressive illness is diagnosed and when a person approaches the end of life.

1 Introduction

Dietary issues in advanced illness can be a matter of particular concern for patients and families, turning each meal into a source of anxiety. Impaired nutritional status is associated with muscle loss, reduced muscle strength, functional limitations, and increased morbidity which all impact negatively on quality of life and may reduce length of survival (Shaw and Eldridge 2015). National reports and guidance for palliative care provision recommend that dietitians are included as members of specialist palliative care teams, or work in close liaison with them (Radbruch and Payne 2010). Specialist palliative care dietitians have an advanced knowledge and understanding of the dietary aspects of life-limiting conditions and of how nutrition impacts positively and negatively upon symptom burden. They are able to provide guidance on the management of dietary problems within palliative care settings, translating the most up-to-date knowledge on food, health, and disease into practical guidance. They also enable people to make dietary choices based on their likes, dislikes, and to lessen the impact of symptoms affecting dietary intake. Dietitians can also advise on food fortification and the appropriateness of macronutrient and micronutrient supplementation to correct dietary deficiencies, dependent on the stage of illness and goals for treatment and care (Ryan et al. 2014).

Assessing the patient's nutritional intake and requirements requires a comprehensive assessment of the patient's medical, treatment, and dietary history. This includes a review of relevant available blood biochemistry results, current weight and weight history, functional limitations, psychosocial concerns, current dietary intake, nutrition-related symptoms, and dietary goals (Shaw and Eldridge 2015).

Interventions which are employed by specialist palliative care dietitians can be broadly grouped into five types: health promotion and maintenance, support for specialized dietary needs, symptom management, nutritional support, and psychosocial support.

2 Health Promotion and Maintenance

Some patients with the diagnosis of advanced progressive illness can retain a good oral intake, with or without an appetite, until the very late stages of their illness. In the absence of sufficient anabolic drive, additional energy consumed by patients above their daily requirements may be preferentially stored as fat mass. This excess fat mass increases the metabolic demands imposed on bodily systems and may potentially lead to a worsened prognosis (Harvie et al. 2005). Dietitians can provide practical guidance on appropriate lifestyle and food choices to prevent excess fat storage while maintaining the fat free mass so vital for functional well-being and for the performance of daily activities.

3 Support for Specialized Dietary Needs

Some patients have longstanding restrictions to their dietary intake which make food choices challenging, especially if desire and ability to eat are compromised. In some situations, dietary restrictions may no longer be necessary, as the potential for burden significantly exceeds any potential for benefit, for example, the adherence to a low-fat diet for management of raised cholesterol level. In other situations, continued adherence to a specialized diet is necessary to prevent additional symptom burden, for example, the adherence to a gluten-free diet for someone with symptomatic coeliac disease. Dietitians are best placed to

provide sensible dietary advice to meet nutritional requirements without compromising patient safety or comfort. Factors affecting this decision are patient benefit, patient desire, and patient intake. This role extends to working alongside catering staff to ensure that appropriate meal options are available and that dietary choice is optimized (Pereira et al. 2016). Occasionally, a person may wish to maintain strict adherence to a special diet even if this is deemed against their best interest. Excellent communication and negotiation skills are required to ensure that the patient's rights to autonomy are maintained while ensuring that they are making informed decisions in relation to their diet.

4 Symptom Management

People with advanced incurable and life-threatening conditions often develop symptoms, associated with their illness and its management, which impact upon both their desire and ability to eat. Such symptoms include dysphagia, nausea, early satiety, sore mouth, taste changes, and constipation. Active management of such symptoms can lead to perceived improvements in quality of life. See Table 1 for examples of advice given to support nutritional intake where symptoms impacting nutritional intake are present.

4.1 Dysphagia

Dysphagia is caused by any condition that weakens or damages the muscles and nerves used for swallowing. There is a high incidence and prevalence of dysphagia among patients with neurological impairment and, with head and neck cancer. Dysphagia may also occur as a consequence of cachexia (Wakabayashi et al. 2015). While coughing during eating or drinking is a common symptom of the condition, some patients may aspirate silently due to central or local weakness or poor coordination of the pharyngeal musculature, reduced laryngopharyngeal sensation, or impaired ability to produce a reflexive cough. Speech and language therapists can assess swallow and provide recommendations on safe or safest consistencies to prevent or reduce aspiration risk (Brady et al. 2015). Dietitians can subsequently provide advice and support to patients and their families on eating a modified diet which supports food choice and enjoyment, promoting weight maintenance if appropriate.

4.2 Nausea

Nausea is an unpleasant feeling of the need to vomit. Reasons for nausea may be multifactorial and may be exacerbated by stress, fear, and anxiety. It is important to treat the symptom appropriately based on a thorough assessment of its root cause and recognizing the profoundly debilitating effect the symptom has if it persists over prolonged periods of time (Del Fabbro 2016).

4.3 Poor Appetite/Early Satiety

It is not uncommon for patients in the advanced stage of progressive illness to have little or no desire to eat or to lose their appetite after a few bites of food (Solheim et al. 2014). Some patients are able to continue to eat normally in spite of early satiety, while others require advice and support to overcome its impact. Potential causes of poor appetite and early satiety include delayed gastric emptying, abdominal ascites, constipation, and changes in food tastes and smells. Reversible causes should be investigated and the dietary plans considered in relation to irreversible symptom burden (Boltong and Campbell 2013).

4.4 Sore Mouth

A sore mouth can have many causes including infection, ulceration, micronutrient deficiency, dry mouth, tumor infiltration, and dental problems such as cavities or gum irritation due to ill-fitting dentures. It is important that pain relief is optimized before meals are offered and that oral hygiene is attended to regularly to prevent additional unnecessary discomfort at mealtimes.

Table 1 Examples of advice given to support nutritional intake based on presenting symptom

Symptom	Hints and tips
Constipation	Encourage fluid intake and review necessity of any fluid restrictions if present Encourage mobility if possible A warm drink taken first thing in the morning may stimulate bowel movement If appetite is good, encourage fiber (roughage) in the diet; if not, encourage soluble fiber sources such as soft fruit, oats, beans and pulses, or root vegetables If taking a supplement drink, consider changing this to one containing fiber
Dysphagia	Avoid mixed consistencies as the liquid portion of a food bolus may be aspirated before swallow onset Avoid distractions during eating Provide utensils to control bolus size and support independence at mealtimes, e.g., use of a teaspoon or a feeding cup with a valve to control fluid flow Ensure supervision or assistance to eat if required Discuss suitability of alternative feeding options if appropriate
Nausea	Try to stay calm and relaxed at mealtimes Ensure room is well ventilated and away from cooking smells, e.g., open a window If the smell of hot food is off-putting, offer cold meals or snacks. It may be beneficial to cool food to room temperature *before* it is provided to reduce smells Try dry foods such as toast or crackers. Having regular snacks can prevent worsening of symptoms caused by an empty stomach Encourage fluids to prevent dehydration. It may be best to drink between meals rather than with food Avoid greasy, fatty, or fried foods Foods or drinks containing natural ginger extract may also help to reduce feelings of sickness Encourage the person not to lie flat immediately after eating
Poor appetite/early satiety	Provide easy access to favorite foods Use small plates/cups and offer small portions frequently Encourage to eat small amounts even when no appetite is present Encourage eating at the table with others when possible as a distraction Encourage activity to stimulate appetite
Sore mouth	Avoid very hot food and fluids. Most people find cool foods and drinks to be soothing to a sore mouth Avoid very hot, salty, spicy or acidic foods or fluids which may sting the mouth Avoid rough textured food like toast, crisp-bread, or raw vegetables and sticky foods like doughnuts and peanut butter as they can scrape or stick to a sore mouth. Provide foods moistened with sauces and gravies Drinking may be more pleasurable through a wide straw
Taste changes	Concentrate on eating a variety of foods that taste good. Taste perceptions may change over time, so retry disfavored foods to maintain dietary variety If sense of taste has decreased, choose highly flavored foods If food tastes metallic, try using nonmetallic cutlery, marinating meat or chicken or garnishing with pickle or chutney Ensure foods are moist and easy to eat and avoid foods that remain in the mouth for long periods requiring lots of chewing Follow good oral hygiene practices Sip fluids through a straw to bypass the taste buds

Towards the end of life, oral complications increase in prevalence (Matsuo et al. 2016). Dry mouth is a common side effect of many prescription and nonprescription drugs, including antidepressants, analgesics, anxiolytics, antihypertensives, antipsychotics, diuretics, and anti-Parkinson's drugs. Dry mouth can also be a side effect of muscle relaxants and sedatives. It can also result from the side effects of certain diseases and infections including Sjögren's syndrome, HIV/AIDS, Alzheimer's disease, diabetes, anemia, cystic fibrosis, rheumatoid arthritis, hypertension, Parkinson's disease, stroke, and mumps. A review of medication can be helpful in

identifying which, if any, medications can be stopped to improve this symptom.

4.5 Taste Changes

Taste changes are a recognized contributor to loss of appetite in advanced illness, and especially in advanced cancer (Mahmoud et al. 2011). Foods can taste sweet, salty, metallic, bitter, fishy, like cardboard or cotton-wool. In a prospective cohort study of 192 Canadians with locally advanced or metastatic cancer, 74% of participants reported taste and smell aberrations. This corresponded with a consumption of 20–25% less calories per day, as well as a marked reduction in protein intake, compared to those without altered taste or smell. Symptoms included heightened, dulled, or altered perceptions in food smells, and these patients tended to lose more weight and report a poorer perceived quality of life (Brisbois et al. 2011). Other factors that influence these taste changes are many and include deficiencies in nutrients (such as zinc, niacin, or vitamin A), medications, poor oral hygiene, changes to saliva (too much and/or too little), nerve damage (in head and neck cancers), smoking or poorly fitting dentures because of weight loss, for example. It is theoretically possible to reduce the effect of these changes by supplementing the diet with nutrients and vitamins such as vitamin A, copper, nickel, zinc, niacin, or iron. These should only be added to a diet under the supervision of a health professional.

4.6 Constipation

Constipation is one of the most frequently encountered symptoms in palliative care impacting on a patient's quality of life and potentially requiring pharmacological intervention especially when the patient is receiving opioid pain relief. Both a softener and stimulant laxative are generally recommended for optimal management (Larkin et al. 2008). As part of the multidisciplinary team, the dietitian should ensure that there is early intervention and treatment of constipation and that laxative regimes and dietary intake is carefully re-evaluated when constipation has resolved (Linton 2014).

5 Nutritional Support

Unintentional weight loss is very common in advanced incurable illness, often prompting referral for dietary assessment and review. Concern over weight loss is not unreasonable since spontaneous weight loss is unnatural and poses a threat to health and well-being (Baracos and Parsons 2010). Nutrition support can be a life prolonging therapy for patients who are unable to meet nutrient needs due to mechanical or functional problems. Early intervention in such situations can prevent, minimize, or correcting reversible weight loss (Fearon et al. 2011). Calculating energy requirements in advanced illness is challenging as changes in body composition, including disease-related reduction in fat free mass, can significantly affect energy expenditure and macro- and micronutrient needs (Elmadfa and Meyer 2008). Metabolic disturbances, dietary and gastrointestinal symptoms, and psychosocial distress all combine to affect macro- and micronutrient requirements. In particular, the potential role that micronutrient deficiencies may have in inefficient energy processing and in the development and perpetuation of inflammation is a key target of ongoing nutritional research (Baracos and Parsons 2010).

Alongside the wider healthcare team, dietitians can ensure that an appropriate nutritional support care is plan is implemented, continuously evaluated, and revised to meet the individual's ongoing nutritional needs and preferences. It is never ethically defensible to withhold oral food or fluids from a patient; however, desire to eat and drink naturally declines during the dying process as the body's systems shut down (Maillet et al. 2013). As core members of the multidisciplinary palliative care team, dietitians can facilitate discussions on the potential benefits and burdens of supplemented oral, enteral and parenteral nutrition for individuals with life-limiting conditions and their families to enable

informed decision making (Schwartz et al. 2016). Nutritional support can be provided to patients orally, enterally (via a feeding tube placed within the stomach or upper bowel), or parenterally (via an intravenous catheter).

5.1 Oral Nutritional Supplements

Oral nutritional supplements (ONS) are widely used within the acute and community health settings for individuals who are unable to meet their nutritional requirements through oral diet alone. They come in a variety of different types. These include:

- Juice, milkshake, yoghurt, or soup type drinks
- Pudding or dessert type
- Flavored or unflavored powders and liquids can be used to fortify foods or drinks

These products are not intended to be a replacement for meals and snacks but rather complement or supplement usual diet (Shaw and Eldridge 2015). While these products are useful in counteracting normal starvation, ONS have not been shown to have survival benefits in those with disease-related malnutrition (Baldwin 2011; Balstad et al. 2014a, b). A recent systematic review (13 studies with 1414 participants) compared ONS interventions against standard care for malnourished patients receiving curative or palliative treatment for any cancer diagnosis (Baldwin et al. 2012). While the analysis was limited by study heterogeneity, but the authors stated that, although ONS increased dietary intake and improved some quality of life indices, such as poor appetite or global quality of life scores, there was no evidence that nutrition interventions alone could improve survival rates. Additionally, while oral nutritional supplements are frequently prescribed for those presenting with unintentional weight loss and reduced appetite, compliance with prescribed supplements is often poor and dietary counselling has been determined to be more effective in unintentional weight loss prevention (Balstad et al. 2014a).

5.2 Enteral Nutrition

Enteral feeding tube permits nutritional support for those who have a functional digestive tract but are unable to take adequate nutrition orally. Regular review by the dietitian is necessary to balance the delivery of adequate nutrition and fluids to meet the person's individual needs. Standard polymeric formulas are most commonly used, designed to mimic a normal dietary intake of carbohydrate, protein, fat, vitamins, and minerals (Shaw and Eldridge 2015). Special feeds are also available to support those who require nutrient modifications due to issues such as electrolyte imbalance, malabsorption, fluid overload, or critical illness. Where appropriate, the dietitian can advise the patient and/or their family on how to manage an enteral feeding regime at home (Howard 2009).

5.3 Parenteral Nutrition

Parenteral feeding is primarily used to permit nutritional support in those who have a nonfunctioning or inaccessible digestive tract. Since parenteral feeding bypasses the bodies' normal digestive processes, regular review is essential to ensure the delivery of appropriate levels of macro- and micronutrients. While standardized solutions can be used, total parenteral nutrition is frequently tailored to meet individual patient requirements (Pertkiewicz and Dudrick 2009). The use of parenteral nutrition within palliative care varies widely between countries and is generally discouraged in those with a life-expectancy of less than 2 months owing to the likelihood that the burdens of the intervention will outweigh any benefit (Bozzetti et al. 2009).

6 Psychosocial Support

As appetite reduces or unintentional weight loss is observed, families may feel it is their duty to encourage their loved one to eat more. Such encouragement in the face of deteriorating health can become distressing for all concerned,

especially when unintentional weight loss persists and meals are regularly refused (Amano et al. 2016). While oral nutritional supplements and artificial feeding using enteral or parenteral routes can compensate for micronutrient and macronutrient insufficiency, they are no substitute for the physical and psychosocial pleasures that most people gain from eating. If nutritional support is provided, it should not be so invasive or unacceptable that it impairs rather than improves quality of life. Dietitians are able to support families directly or to support other health professionals in the appropriate management of the physical, psychological, and social impacts of appetite loss and changes in body image. By explaining the causes of weight loss, patients and families may be able to better come to terms with body changes and are more prepared to deal with irreversible weight loss in the latter stages of active disease processes (Hopkinson et al. 2013).

Dietitians can do much to support psychological well-being and maintain positive family interactions at mealtimes. If weight loss is refractory, patients may still enjoy eating very small quantities of their favorite foods to savor their flavor and texture and to remain a part of family social gatherings. Maintaining optimal quality-of-life rather than optimizing nutritional intake is usually the primary goal of dietary interventions towards the end of life (Scott et al. 2016).

7 Dietitians as Palliative Care Researchers

Part of the role of specialist dietitians is to support the creation of better palliative care nutritional knowledge through engagement in clinical research. This is best achieved by working as part of a multiprofessional research team using robust trial methodology and recruitment strategies to ensure that nutrition-related trials are appropriately powered and conducted. Nutritional research is challenging and in the face of insufficient evidence every effort is taken to build nutritional guidance for palliative care that synthesizes all available sources of evidence (Eva and Payne 2014).

8 Conclusions and Summary

As members of the specialist palliative care team, dietitians exploit the potential to improve quality of life through the effective management of issues relating to nutrition, physical, psychological, social, and spiritual. Dietitians support the multidisciplinary team in developing nutritional management plans which reflect the best evidence and individual patient wishes and are constantly seeking to improve the evidence base for practice.

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Self-Care and Palliative Care

37

Peter Huggard and Jayne Huggard

Contents

Abstract

Working in palliative care can be intensely demanding yet enormously rewarding. To enable health professionals to actively engage in this field of work, emphasis on appropriate self-care activities is essential. Participating in a variety of professional and personal practices assists staff to be effective in their roles as well as mitigating the possible effects of stress and

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_44

burnout and avoiding the potential damaging impact of vicarious traumatization or compassion fatigue. This chapter explores the palliative care work environment and identifies potential stressors. A range of activities is suggested that have been shown to be effective in mitigating the impact of various occupational stressors.

> The care of the dying and bereaved people is a great challenge. It can be the most stressful part of our work, but it can also be the most rewarding. The rewards are likely to outweigh the stress only if our needs for support are met. (Parkes et al. 1996, p. 30)

1 Introduction

This chapter will explore the palliative care environment and the challenges faced by health professionals when working with dying and death. We will examine specific stressors in the context of palliative care, as well as the subsequent possible experiences of clinicians. Outcomes discussed, that may arise from these experiences include: vicarious trauma, compassion fatigue, secondary traumatic stress, compassion satisfaction, and burnout. We then examine the role that resilience may play in mitigating the effect of such stressors. A range of personal, professional, and organizational obligations will be discussed. Finally, several strategies for identifying and managing potential stressors will be described along with strategies for enhancing one's professional and personal life.

A number of researchers over many years have explored the palliative care environment and have reported their views as to what it is that enables people to work in this complex, difficult, and challenging role. Mary Vachon (1995) talks of health professionals who choose to work in palliative care as having a personal belief around illness, death, and the meaning one makes of one's life. She believes that these dimensions of their lives and personal belief systems contribute toward enabling health professionals to work in this demanding role. In her 1995 review of the literature of stress in palliative care over the first quarter century of the movement, Vachon found that many studies reported staff working in palliative care as having either less burnout and stress than other professionals or that they experienced no more stress than other health-care professionals working with seriously ill and/or dying persons. More recently, Pereira et al. 2011 reviewed the palliative care burnout literature from 1999 to 2009 and also found that burnout levels in palliative care, or other related health-care settings, did not seem to be higher than in other contexts. This finding was also confirmed by Gélinas and colleagues in their 2012 study of Quebec nurses working in end of life care. They found that nurses working in hospital settings such as critical care and oncology showed higher stress indicators when compared with nurses working in specialized palliative care units.

Importantly, and fundamental to being able to work in palliative care, is the view that death is part of the life cycle and is not seen as a failure of medicine or of the health professional. Death can be regarded by some health professionals as the "final enemy" and dying, a failure on the part of staff to prevent that happening. This has contributed to the notion of the "good death." Richard Egan (2008) has argued that it is not death that is the failure; rather, it is our attitude toward death that may be the failure. He believes that it is the illusion that medicine can "cure all" that incapacitates us all. This "cure all" view of medicine contrasts markedly with hospice philosophy which has at the core the concept of a good death and embraces a philosophy of openness about death and an acceptance of its reality. Such views about dying and death mean that palliative care staff are less likely to have avoidance patterns to dying and death than peers in other health settings and particularly low levels of death anxiety. It may be that palliative care professionals with low death anxiety have chosen palliative care as a preferred work specialty or that the overexposure to death, along with the hospice philosophy and specific training on this topic and staff support, has served to decrease this anxiety. It is also possible that palliative care staff have confronted their own mortality and are therefore comfortable with the meaning of life and death.

For many staff, both clinical and administrative, the choice to work in palliative care can be directly linked to experiences they may have had in relation to the death of family, friends, or dying patients they have previously cared for (Huggard 2008).

This meaning-making appears to be a key "enabler" to working in palliative care and has been discussed by several researchers. Palliative care nurses' ability to find meaning in their work is well documented (Fillion et al. 2006). Research by Desbiens and Fillion (2007) involving 120 Canadian palliative care nurses examined the use of meaning-making strategies in association with emotional outcomes. Results from this study showed that the nurses' capacity to find meaning in the work they do with the dying enabled them to not only positively adapt to the deaths of their patients but also allowed them to have a better spiritual quality of life.

Despite the possibilities of a stressful and emotionally demanding work environment working in palliative care, clinicians working in this field have described feelings of satisfaction and a heightened appreciation of the spiritual and existential elements of their life. These experiences include an appreciation of the reciprocal healing process; inner self-reflection; connection with their peers, family, and their wider professional and personal community; and an enhanced sense of spirituality (Kearney et al. 2009).

2 The Palliative Care Environment

Early research by Vachon (1987) identified that 48% of the occupational stressors in palliative care came from the "work environment," with 29% deriving from one's "occupational role" and 17% from working with "patients and families." A small percentage, 7%, was derived from illness related variables such as addressing pain management and symptom control. While there have been numerous studies done since this time, the above broad themes still remain relevant today when looking at stressors in the field of palliative care. Environmental stressors, including work overload, team conflict, administrative problems, interprofessional communication, and role conflict, are all potential stressors and may be more stressful than any stress resulting from interaction with patients and their families. (Vachon and Huggard 2010). Vachon (1995) found that professionals working in palliative care did not have higher levels of stress than others working with seriously ill or terminal patients and, in fact, had less stress than professionals working in other settings. One possibility for this may be because the struggle to find a cure is over and the palliative approach, with its realistic goals and care plans, is more manageable, and that potential stressors are anticipated and coping mechanisms are implemented, and that hospice nurses have a level of autonomy that serves to mitigate stress. The shared philosophy of care, the recognition given to staff that the work they do is of value, the evidence of support, and that generally the staff-patient ratios are manageable are all factors that may contribute to less stress in this workforce.

2.1 Nurses

The concept of nursing being a potentially stressful occupation was identified by Florence Nightingale: "The concept of stress has been of concern to nurses since 1859" (Foxall et al. 1990, p. 578). A significant stressor for palliative care nurses, and indeed nurses working in many other sectors, is role confusion, particularly often around unresolved role definition conflicts and the subsequent conflict and tensions arising between multidisciplinary staff members. Being unsupported can leave staff feeling vulnerable and emotionally fraught, particularly if the work of individuals is not acknowledged or valued. Other potential stressors can be the management of complex symptoms, administrative and communication difficulties, dealing with family dynamics, and working with doctors unfamiliar with the palliative care and hospice culture. Further organizational stressor issues include communication difficulties with managers in relation to administrative issues, heavy workload, complexities of care, and insufficient staff allocations. There

may also be a sense of pressure around time constraints in being able to provide the degree of care that staff felt was needed. This can give rise to stress and frustration as it impedes the quality of time spent with patients and limits nurse's ability to be innovative in their practice.

As in many other areas of nursing, organizational stressors can include the degree of responsibility held, workload, physically arduous work, shift work, home/work conflict, interpersonal conflict, responsibility for training, uncertainty and unpredictability, and managing change.

2.2 Doctors

Work overload and the effects of the work on home life can be two of the most significant work stressors for physicians, as well as keeping up to date with current knowledge and fear of making mistakes. However, issues related to death and dying do not appear to be significant sources of stress for palliative care physicians. What can be distressing is the absence of control and workplace social support. Issues such as dealing with management, being on call, excessive paperwork, insufficient free time, lack of personal control over clinical practice, and dealing with the emotional aspects of life can all contribute as stressors in a physician's life. The constant exposure to the dying and their families, the complex issues of symptom control, relieving pain, and the very nature of the difficult conversations necessary to be had with patients all can increase the likelihood of role strain (Kearney et al. 2009).

2.3 Working with Families

For some professionals working in palliative care, communicating with distressed family members can be one of the major stressors. The terminal illness of a family member can bring with it significant disruption to the family, along with feelings of uncertainty, fear, anxiety, and anger. Adjusting to death is one of the most difficult of the life's transitions that individuals have to make. It should not be surprising therefore that managing family dynamics can be problematic for palliative care staff. Given the nature of the holistic care given to families, nurses and other palliative care professionals usually spend more time with family members than do staff in other fields of health care. These stressors can come about as a result of the time and emotional energy spent dealing with family issues, particularly with relatives of the patient. However, this is a necessary feature of the work of a palliative care clinician and the development of a therapeutic relationship with patients and families important for maximizing care. A study by Canning et al. (2007) of Australian palliative care nurses found that developing effective communication relationships with patients and their families was an important aspect of their care. Of significance was the need to share information between the nurses and the families, keeping open the channels of communication. The nurses in this study also reported the need for mutually agreed boundaries in the therapeutic relationship particularly when there are many interdisciplinary professionals involved in the care.

There may be additional communication problems faced by staff concerning patients and families from different cultural backgrounds. Bray and Goodyear-Smith (2007) found that palliative care nurses found working with people from ethnic minorities stressful as communication can often be difficult and can give rise to issues of cultural safety due to a lack of knowledge of cultural differences. The stress associated with looking after the terminally ill, however, needs to be counterbalanced by the satisfaction gained by working with these patients and their families. Palliative care professionals acknowledge the rewards experienced in having time to develop meaningful relationships with the dying and their families and gain a sense of making a difference in what they do.

2.4 Death and Dying

Although professionals working in palliative care are repeatedly subjected to loss and grief, exposure to death and dying has not emerged as a

major source of job stress in palliative care (Huggard 2008). This supports the notion that intimate contact with dying patients, such as that experienced by palliative care staff, does not contribute to the creation of an inherently stressful job. These experiences can reinforce the work that palliative care staff do. Working with dying patients can have many positive outcomes for staff and can be a source of much personal growth and satisfaction. Being present at the deaths of many patients can be a very professionally and personally positive and spiritual experience. However, those working with dying patients and their families can have specific emotional demands not realized by those who do not (Fillion et al. 2006). Palliative care staff are intimately involved with dying and death, and the nature of this work can lead to them experiencing personal loss and grief when their patients die. There are many losses for patients before their death, and witnessing their suffering may leave health professionals feeling vulnerable and at risk of becoming overburdened.

2.5 The "Good Death"

> We talk of good deaths. We mean that we will leave the world in a mindful way. We mean that in the fullness of time and after a satisfactory journey we will engage with our deaths, make peace with the past, complete whatever is left to be done in the present and die in a dignified and companionable way. (Ward 2008, p. 335)

One of the rewarding aspects of working in palliative care is seeing patients die a peaceful, dignified, and comfortable death. Such a "good death" is seen as a success. However, not all deaths are peaceful nor are they dignified, and it is important to acknowledge what may be unrealistic expectations around the pursuit of the perfect death and that such an "unspoken ideal" is often impossible to achieve and may lead to a sense of guilt or powerlessness for staff when these "imperfect" deaths occur. Many palliative care staff do have difficulty coping with the death of a patient if they feel it has not been well managed, and this may be because symptoms were complex and not able to be adequately controlled or that pain was not able to be fully managed. Additionally, patients and their families who struggle to accept the imminence of the death, along with difficult family dynamics, can contribute to difficulties in coping for palliative care staff. Particularly in this case, if the staff feel they have not been able to give the amount of time to the patients and their families, that they feel is necessary. Multiple deaths in a short period of time may also contribute to a sense of emotional vulnerability on the part of palliative care staff. It is clear that palliative care staff need to have sufficient time to be with patients and their families and to be able to manage the intense emotional aspects of their work.

2.6 Grieving and Mourning

Health-care professionals' grief experience and its impact have not been well understood (Shimoinaba et al. 2009). Palliative care staff, and in fact all health-care professionals, need sufficient time and support to process the death of patients. Sometimes, due to staffing levels and workload commitments, staff have to move straight away from a patient death to caring for other patients and their families. Time may not be immediately available to appropriately grieve, and the grief may be disenfranchised or hidden if recognition is not given to their need and time to grieve. The emotional pain experienced by witnessing the grief of others may intensify feelings of helplessness and inadequacy. Working with the dying can mean that palliative care staff may reflect on their own past losses and grief. If staff minimize or deny this emotional distress, and if it is not addressed in the longer term, the cumulative effects of grief can become overwhelming and lead to burnout or compassion fatigue.

Early research by Smith-Stoner and Frost (1998) described cumulative stresses as stress stored in the "shadow self," and call the unresolved sadness "shadow grief." These authors believe that nurses carry a heavy load of shadow grief due to the losses they encounter on a daily basis and suggest that the personal work nurses need to do is to find ways to "lift the shadow" by

acknowledging and grieving these losses. The grieving process is the way loss is reconciled. Time must be given to staff to fully grieve the losses. If staff are not given this opportunity, the impact of such grief experiences may be cumulative and lead to burnout and compassion fatigue which can prevent professionals from being able to be emotionally present for their patients. As a means of processing one's grief, there must be time to mourn. Activities such as attending funerals or memorial services for those who need to or want to are important ways of doing this. Other ways of managing this mourning process include establishing a memo board or scrapbooks to display thank you letters and cards of appreciation from families, having various bereavement events such as memorial services that honor and remember those that have died, acknowledging the deaths at regular team meetings, engaging in rituals such as lighting a candle for those who have died, and sending bereavement cards to families.

3 Resilience

Although much of the earlier research on resilience involved studies of children and adolescents (Aburn et al. 2016), more recent research has focused on health professionals (McCann et al. 2013). Although there appears to be no universal definition (Aburn et al. 2016), a variety of definitions have emerged for resilience. The literature review by McCann took, as a definition of resilience, the ability to maintain personal and professional well-being in the face of ongoing work stress and adversity. McCann's review focused on literature discussing a number of health professional groups and reviewed the studies in relation to coping as a means to improve well-being, resilience, and hardiness and the report of any components of resilience specific to each health discipline. They found that only gender (more specifically, being female) and maintaining a work-life balance have been found to consistently relate to resilience across all of the health professional groups reporting on resilience. Other factors related to resilience included laughter/humor, self-reflection/insight, beliefs/spirituality, and professional identity.

To manage workplace stress, engagement in a variety of coping strategies is needed. These strategies include problem-focused coping, taking time out, and giving and receiving support from co-workers, seeking emotional support, realistic belief systems, self-control, and positive reappraisal. In addition to these positive coping strategies, staff need to be alert to the presence of negative strategies, such as suppression and denial, which can significantly increase the negative effects of stress. Ablett and Jones (2007), in their study of hospice nurses, reported ten themes that related to interpersonal aspects and to the participant's beliefs as to their own ability to do the work required of them. The themes were (1) an active choice to work in palliative care, (2) that past personal experiences influence care-giving, (3) personal attitudes to care-giving, (4) personal attitudes to life and death, (5) awareness of one's own spirituality, (6) personal attitudes toward work, (7) aspects of job satisfaction, (8) aspects of job stress, (9) ways of coping, and (10) personal and professional issues and boundaries. Central to these ten themes were the nurses' beliefs about their commitment to their work in palliative care and their belief that they could make a difference. A recommendation from a literature review of personal resilience in the nursing literature by Jackson et al. (2007) was that resilience can be strengthened in nurses through strategies and mentorship programs. Their recommendation was that such programs should aim to develop positive and nurturing professional relationships and encourage positivity, emotional insight, life balance, spirituality, and personal reflection. What is clear from these studies is that nurses working in hospice and palliative care employ a variety of strategies that enable them to positively and effectively manage the demands of this work and enhance resilience.

Through a qualitative online survey of 30 American physicians practicing hospice and palliative medicine, Swetz et al. (2009) found exercise and physical well-being, nurturing professional relationships, discussing feelings, and valuing relationships with others to be the most

common wellness-promoting strategies reported. Commonly reported strategies also included coping activities aimed at improving the work environment, namely, ensuring clinical variety, making time within the day for oneself, and engaging in meditation, personal reflection, and reflection with others. Shapiro et al. (2011) have presented an individualistic model for identifying strategies physicians employ to gain and regain a sense of control when caring for patients. The model had four modes of control. Positive assertive and positive yielding represent the positive modes of control, while negative assertive and negative yielding represent the negative modes of control. They suggested that interventions that aim to increase self-awareness and reflective capacity and being mindful of emotion regulation might enable physicians to cope better with loss of control. Being self-aware assists physicians to recognize their responses and to interrupt negative behaviors and reactions through mindfulness emotion regulation. This can then assist them to recognize situations where they are attempting to regain a sense of control and, instead, engage in more positive responses, such as assertion and letting go. This model does not consider the impact of organizational factors on the physician's ability to cope with low control. Chittenden and Ritchie (2011), however, include both individual and contextual factors in recommendations for improving physician work-life balance and subsequent well-being. They suggest that to achieve work-life balance physicians should maximize job fit by finding work that is flexible, consciously slow down; cultivate mindfulness; make personal and professional values and goals explicit; take care of physical, emotional, and spiritual needs; learn to ask for and accept help; and identify sources of emotional and practical support.

In a study of 253 New Zealand physicians, Huggard (2013) examined the relationship between compassion fatigue and burnout and resilience, spirituality, empathy, and emotional competence. Findings from the study indicated negative and significant correlations between resilience, spirituality, and emotional competence and burnout and compassion fatigue. The survey item having strongest and negative correlation with compassion fatigue was *I feel able to initiate access to additional support, if required, to help me to understand and manage my emotions in relation to my patients*. This provides some insight into the role that having a well-developed level of emotional competence might have in mitigating the impact of emotional distress and identifies the need for them to have someone who can support them.

A pilot study led by the current authors gave individual hospice staff – nurses, physicians, and family support staff – the opportunity to define resilience from their perspective. Results were obtained using a Delphi consensus methodology. The most commonly identified themes reported were maintaining a good work-life balance, maintaining clear professional boundaries at work, having a sense of humor, developing strong and trusting collegial relationships and support at work, having a passion for palliative care work, engaging in self-reflective practice, and having a spiritual belief system. Of these themes, engaging in self-reflective practice has appeared in other research (Jackson et al. 2007; McCann et al. 2013; Aburn et al. 2016) and seems to be key to enabling staff to work in what is an emotionally demanding work environment.

The notion of "happiness" is a key concept in relation to resilience. An understanding of this is located within the field of positive psychology and explores ways of minimizing suffering and increasing happiness. Happy people have been shown to be healthier, more successful, and more socially engaged. Recent work by Seligman (2012) has offered ways of helping individuals find ways to flourish by focusing on developing positive emotions, through engagement and enhancing relationships, by finding meaning in one's work and life, and by gaining a sense of achievement. The role played by positive emotions assists in the development of psychological resilience. These positive emotions assist to manage negative emotions and to deal with challenging situations. Research by Bolier and colleagues in 2013, and earlier by Tugarde et al. in 2007, demonstrated the role of positive emotions and self-care in assisting the development of resilience. A recent example of using this approach,

utilizing the *Three Good Things* intervention approach, was reported by Rippstein-Leuenberger et al. (2017). This study emphasized ways to encourage positive emotions, through having supportive relationships, being open in communication, engaging in common activities, and making meaningful use of time away from work.

4 Vicarious Trauma and Burnout

Individuals working in health care have been shown to experience significant personal and professional distress related to factors such as lack of autonomy, difficulty balancing personal and professional life, excessive administrative tasks, and high work load. In addition to the personal impact, such workplace stressors and subsequent burnouts have been linked to the quality of patient care. For example, a study of 115 medical residents reported that 76 percent met criteria for burnout and were significantly more likely than those without burnout to report suboptimal patient care at least monthly (Shanafelt et al. 2002).

One of the greatest privileges offered to any clinician is to provide relief to the suffering – be it physical, mental, or spiritual – of others. However, bearing witness to the suffering of others can carry an additional risk of burnout for the health professional when such exposure results in the clinician becoming overwhelmed, which may result in vicarious traumatization – often referred to as compassion fatigue or secondary traumatic stress. Perhaps it is more important in the field of caring for the dying than any other to understand the potential impact of vicarious trauma on the clinician and those in their care and for both the clinician and those managing clinical services to actively engage in strategies to mitigate its potentially distressing effects. Although there is a growing body of literature reporting the possible effects of witnessing the suffering of others, there are few published studies of processes that mitigate these effects.

Three researchers are responsible for initial explorations on the nature of distressing emotional responses experienced by health professionals. They each describe such consequences from slightly different perspectives and using different terms. Charles Figley (1995) promotes the term "compassion fatigue" to describe this phenomenon, Laurie Anne Pearlman and Karen Saakvitne refer to it as "vicarious trauma" (1995), and Beth Hudnall Stamm employs the phrase "secondary traumatic stress" (2010). Although there are conceptual differences in compassion fatigue, vicarious traumatization, and secondary traumatic stress, they all are part of the larger picture of possible negative consequences of caring for traumatized patients and their families with some researchers disagreeing as to the individual nature of these three constructs. Although there are large overlaps and ambiguity in the characterization of these constructs, this highlights the need to appraise current understandings among the literature, when discussing the distinctions and differences between the terms "compassion fatigue," "vicarious trauma," and "secondary traumatic stress."

Although these terms may all be used to describe a secondary traumatic stress response, these processes may in fact differ on a phenomenological level. There have been attempts to address the confusion that exists regarding these various terms, and while there are reported differences, the constructs are not mutually exclusive – each contributes to the overall understanding and articulation of the positive and negative aspects of caring. Current thinking is that compassion fatigue occurs when there is a combination of burnout plus experiences that lead to the development of vicarious traumatization (Huggard et al. 2013).

While some view these three constructs as different, there are also differences between them and burnout. The differences appear to be that burnout relates to feelings of hopelessness, work-related problems, high workload, lack of professional support in the workplace, and feeling as if work efforts do not make a difference in the lives of those being served and usually has a slow onset and is often the result of long-term work-related issues. On the other hand, vicarious traumatization occurs as a result of specific secondary exposure to traumatic events.

A large variety of symptoms are linked to vicarious traumatization, including those normally associated with burnout (such as emotional exhaustion, a lack of personal accomplishment, and depersonalization), increasing difficulties in bearing further witness to the suffering of others, symptoms of posttraumatic stress disorder (such as hyperarousal, intrusive imagery, and hypervigilance), physical symptoms (such as insomnia, headaches, and somatization), a variety of avoidance behaviors (particularly avoidance of certain patients), feelings of helplessness and a diminished sense of enjoyment, and an increased sense of personal vulnerability and loss of hope (Kearney et al. 2009; Vachon et al. 2015).

A further construct – compassion satisfaction – was first reported by Stamm (2002). She describes the balancing act between compassion fatigue and job satisfaction, and while health professionals may experience compassion fatigue, their role can bring much satisfaction and with this many positive benefits. Stamm describes this as "compassion satisfaction" and suggests that the belief health professionals have that what they are doing is helping others may indeed be redemptive. Earlier, Lamendola (1996) used the phrases "burning brightly" or "burning dimly" as a different way to describe compassion enrichment versus compassion fatigue. When burning brightly, compassion flows and there can be peace and acceptance, whereas burning dimly is characterized by tiredness, a lack of energy, and an inability for health professionals to be fully present with the pain and suffering around them. Being sensitive to what is happening in this state and putting self-care measures in place can prevent moving from burning dimly to burning out.

5 Caring for Ourselves: Strategies and Practice

In 2001, Barbara Dane and Esther Chachkes, in the journal *Social Work in Health Care*, wrote "Staff support is a necessity, not a luxury" (p. 46). This is a fundamental "truism" for working in health care and in particular, palliative care. Their findings indicated that a positive work environment with supportive colleagues and supervisors was found to mitigate workplace stress. One important aspect of their findings was that support from friends and family was not sufficient to sustain them, as the reality of the work they did was not understood, thereby making it difficult for family and friends to empathize in the same way that colleagues in the field were able to. This emphasizes the need to undertake debriefing within the workplace and that this opportunity needs to be offered by ones employer.

5.1 Staff Support

Support can be present and felt in a variety of ways and through different processes. The challenge for health-care organizations is to find ways to care for their staff in the same way that staff care for their patients (Huggard 2003). Positive outcomes of effective staff support have been shown to include better personal health and satisfaction with work (Hulbert and Morrison 2006). Gathering together to share experiences, in either a formal or informal way, has been shown to have positive outcomes. The use of support groups has been recommended as important in providing social support (Hawkins et al. 2007), and as far back as reported in Alexander and Ritchie's 1990 study, their role in encouraging staff to reflect on their practice resulted in reduced stress and enhanced practice. In the Dane and Chachkes' (2001) study, staff found that support groups promoted the connections between them and other colleagues and reduced the isolation they sometimes felt.

Staff support practices, within any organization, generally fall into two broad categories. Firstly, there is the need for policies that provide a professional development framework for staff such as appropriate recruitment and orientation, performance management processes, and professional development and education opportunities and secondly, policy that acknowledges and provides for the emotional and psychological support for staff, such as supervision, debriefing, feedback, healthy rostering practices, and regular

forums for communication. Organizational support and understanding are critical, and this support should be integrated into the everyday working life, rather than at a time of crisis (Danieli 2006). There is a need for further research aimed at demonstrating the value and effectiveness of a variety of supportive processes. A systematic review of staff support practices in palliative care by Ieroo Ha and the current authors (2013) identified that positive changes occurred in how staff perceived their role as a result of either staff support or educational interventions.

5.2 Organizational Support Frameworks

Inadequate and ineffective organizational support structures to care for professional caregivers have been previously highlighted, particularly with respect to managing grief (Shimoinaba et al. 2009). Meier and Beresford (2005) described the need for efficient and effective infrastructures in palliative care services so that administrative systems can reliably support the health professionals to do their job. Such infrastructure includes human resource policies and procedures, adequate staffing, effective management structures, staff support and scheduled meetings, and team briefs. Additionally, inefficient management structures and communication systems, as well as ineffective leadership and blurred role boundaries, all contribute to unnecessary stress for hospice staff. It is important that both managers and clinicians monitor the organizational climate carefully, with particular reference to staff relations and any staff conflict evident. In palliative care services, the main sources of perceived conflict were lack of psychological support, the absence of staff meetings, and problems with the decision-making process (Azoulay et al. 2009) with conflict not being dealt with having major repercussions on team functioning and are a source of stress. Another factor for staff working in palliative care is the need to constantly project a persona of being a nice, compassionate, and caring person, which can be difficult, and has led to this being described as the "tyranny of niceness" (Lee et al. 2009).

Hospice policies, especially those that are values based, can have a positive effect on staff by encouraging a healthy balance between professional responsibilities and personal needs (Louie et al. 2007). Examples of such practices include family-friendly policies such as parental leave, part time or flexible work hours, unlimited leave to care for ill family members, and sabbatical leave options to study or to travel. Additional staff well-being policies include those for both physical and emotional safety, employee assistance programs, and having professional supervision and critical incident stress debriefing available. Having access to an ethics committee has been reported as a helpful way for health-care professionals to discuss, at a multidisciplinary level, the struggles that teams have with ethical issues and clinical decision-making (Davies et al. 2008).

Feeling valued is one of the most important indicator of job satisfaction. Valuing staff, and letting them know that they are valued, is one of the most important factors in job satisfaction and reduction in workplace stress (Huggard 2008).

5.3 Emotional Safety

While most organizations focus on the legislative and clinical requirements for physical safety in the work place, there is usually much less attention to the emotional safety needs of staff. An innovative approach by a major hospice in Auckland, New Zealand, led to the development of an emotional safety policy and committee, whose aims are to protect and promote staff emotional safety in order to minimize stress and fatigue. The guiding principles of the emotional safety committee were those of the mission and values of the organization: dignity, compassion, respect, quality, advocacy, and stewardship. The hospice has introduced a range of interventions aimed at better supporting the emotional needs of all staff – clinical, administrative, and volunteers. In addition to various organizational obligations, the policy acknowledges several personal responsibilities that staff are encouraged to engage in so as to minimize the burden of their work and enhance

their emotional safety. These activities have all been identified as contributing to hospice staff health and well-being (Vachon and Huggard 2010). Such activities include effective de-roling at the end of a shift; using professional supervision effectively; using appropriate ritual to acknowledge one's own losses and attending to grief work; nurturing, caring, and valuing oneself and accepting support and help when needed; and taking regular holidays and making the best possible use of time away from the workplace (Huggard and Nichols 2011). Supporting and caring for staff in this way leads to greater care being available for patients.

5.4 Supervision

Supervision is a wide-ranging term used to describe a number of supportive process such as clinical supervision, reflective practice, mentorship, coaching, and professional supervision. Each of these practices has differences in intention and in process; however, each of them have aims of enabling the health-care professional to reflect upon, develop, and enhance their clinical practice. Davys and Beddoe (2010, p. 19) describe supervision as an opportunity that "demonstrates an ongoing professional commitment to reflection, analysis and critique by professional practitioners who take individual responsibility to use supervision to renew and refresh their practice and ensure that they continue to work within the mandate for their work with other people. A commitment to supervision demonstrates a commitment to lifelong learning." Edmonds et al. (2015) describe a process for clinical supervision that is part of an overall wellness program for their palliative care team. The supervisee meets regularly (often weekly) with the supervisor with the meetings including discussions regarding assessment, diagnosis, treatment, and administrative matters. Using a psychodynamic model of supervision, exploration of important issues such as emotional responses, clinician defense processes, transference, and countertransference is key to the professional development of the clinician. They describe the ultimate goal of clinical supervision is to "remove the veil between clinician and client such that the clinician perceives the client clearly and provides exquisite patient care, all the while protecting the clinician from the costs of caring" (p. 275).

A form of peer supervision, mostly used by physicians and to a small extent by other health professionals, called Balint groups, offers a way of reflecting on one's practice and drawing upon the wisdom of ones colleagues. The key feature of Balint group work is to explore the clinician-patient relationship, with an outcome of increasing clinician self-awareness, contributing to an enhanced sense of well-being, and heightening ones resilience (Wilson and Cunningham 2013). Interestingly, there is very little evidence of research exploring the role of individual supervision and its impact on stress and vicarious traumatization experiences. One study (Wallbank 2010) did show a reduction of levels of such traumatic responses following a 6-month period of monthly individual supervision. Participants were midwives and obstetricians who were often exposed to tragic events such as fetal or newborn deaths. Measurements of subjective stress, compassion fatigue, burnout, and compassion satisfaction before and at the completion of the supervisory process showed statistically significant reductions in subjective stress, compassion fatigue, and burnout and a statistically significant increase in compassion satisfaction scores. In this study, systematic, individual supervision appeared to have a positive impact on the reduction of stress in the participants.

5.5 Debriefing

Palliative care clinicians have experiences that, to other health professionals, may seem overwhelming, yet the majority are able to appropriately and effectively cope with such potentially traumatic events. One of the ways in which such coping is possible is through the individual and shared experiences of defusing and debriefing processes. Huggard (2013) described the process for conducting effective team debriefing meetings and emphasized the role of a trained facilitator.

Having such a trained facilitator conduct the debriefing can be beneficial in helping staff feel more comfortable about being open regarding their feelings and experiences at a time that could potentially be quite vulnerable for them. One of the advantages in holding interdisciplinary team debriefing meetings is that they can provide an opportunity for staff to hear the perspectives of other professional groups (Keene et al. 2010). The value of such debriefing was demonstrated in a study of palliative care nurses exposed to terminal hemorrhage (Harris et al. 2011). However, there are other ways in which debriefing can occur, such as during individual or group supervision, participation in peer group processes such as Balint groups, or engaging in other forms of reflective practice. Or, the debriefing process may be quite informal and be as simple as sitting with colleagues and having a cup of tea at the end of a shift.

A useful process described by Huggard (2013) is the Personal Debriefing Model (PDM). This is a simple approach to completing the days' work and can become a valuable self-care practice. The two main components of the PDM are acknowledging the day, and what was able to be achieved, and putting strategies in place that assist in separating ones professional and personal lives. This brief process can take place at the end of the working day and before one leaves work.

5.6 The Reflective Practitioner

Reflective practice is a process where in a clinician can review their clinical practice and use insight gained to learn from that experience to guide and enhance further practice. Sarah Coulson, writing in the Australian Nursing and Midwifery Journal (2014 p. 45) wrote "Personal insight into our own values and the ability to respect, explore and learn from the values and experiences of others is fundamental to delivering quality palliative care." Through engaging in a variety of reflective practices, one can gain the personal insight Coulson writes of. Reflection on one's practice and relationships with patients and colleagues can occur through effective staff support processes such as supervision and debriefing. These can occur in a groups setting (Bailey and Graham 2007; Wilson and Cunningham 2013), one-on-one with a trusted colleague (Geraci and Thigpen 2017) or trained facilitator (Davys and Beddoe 2010) or as an individual exercise using such techniques as reflective writing (Borgstrom et al. 2016).

Mehta et al. (2016) have recently reported results of a pilot study aimed at increasing resilience in a multidisciplinary palliative care team. The intervention, called the *Relaxation Response Resiliency Program for Palliative Care*, aimed to reduce stress and increase resiliency. Designed using principals of positive psychology and cognitive behavior therapy, the program's aims are to elicit the relaxation response, reduce overall stress reactivity, and increase connectedness to oneself and others. A variety of reflective processes are a component of this program. Reflective practices in palliative care would appear to be a necessary component of practice in this specialty.

5.7 Mindfulness

Discussing a proposal by Balfour Mount for a paradigm change in the way patients and their families are cared for, Cory Ingram (2014) reflects on Mount's model of care as being one that embraces the whole person and all that he or she is. Within this model, an understanding of the role and practice of mindfulness is a necessary attribute of all clinicians. Mindfulness had its origins in a Buddhist tradition and was seen as a path for happiness and enlightenment. Mindfulness is a way of training one's mind to accept what is as part of the fabric of life. It teaches one to achieve a state of calmness through being fully attentive to the present and knowing and accepting of the emotional state one is in. Antonio Fernando et al. (2014) described one approach to experience this state of calm through a simple breathing and relaxing exercise. They advise beginners to start with a 5 min exercise and gradually increase this over time.

The process of mindful communication has received attention as a valuable communication

process within palliative care. Mindful communication is the bringing together of mindfulness and reflective, genuine and adaptive communication. In their study of palliative care leaders, Omilion-Hodges and Swords (2016) interviewed palliative care leaders and identified the leader's mindful communication practices. The effective key communication strategies were to consider your audience(s); ask questions, listen, and repeat; discard scripts; and recognize your role. They found that the use of mindful communication can "increase clinician well-being, decrease depersonalization, promote sound decision-making, and improve patient safety and care" (p. 330). Thus, the practice of mindfulness can impact directly on the clinician by reducing their levels of stress and, through the use of mindful communication skills, positively impact upon patients and their families and, in that, on the clinician and patient relationship.

5.8 Taking Stock and Committing to Change

A useful tool used for several years by the current authors in self-care and professional development workshops is a check list aimed at identifying individuals self-care practices – the Self-Care Questionnaire. This 62-item inventory covers 6 domains of self-care: physical, psychological, emotional, spiritual, workplace/professional environment, and balance within one's life. The tool, adapted from one developed by Saakvitne and Pearlman (1996), has been found to be helpful for workshop participants to focus on their self-care behaviors and perhaps identify gaps in practice that they might need to pay attention to. This tool is introduced in the psychoeducational phase of workshops and can provide a prompt for participants to complete a second tool: the self-care plan. The self-care plan prompts workshop participants to identify practices they will keep doing, stop doing, and start doing and considering these at an individual, team (or department), organization, or professional association level. In addition the plan prompts answers to the following questions: Think about how you are going to make sure your goals are achieved, who you need to talk to or gather together to discuss your plan, when are your goals going to be achieved by, and do you need to consider some small steps for any of the goals. Anecdotal feedback from workshop participants indicates that many will complete the plan and check in with what they have written regularly as a prompt to their practice. Others have said they use the plan as a discussion document with their supervisor as a way of receiving support for their planned activities. Additionally, the self-care plan can be a useful adjunct used in performance appraisal processes. Copies of the two tools can be obtained from the authors.

6 Conclusion

Nowhere is there more vulnerability than at the time of death. Patients and families are often in crisis, as they struggle to cope with suffering, loss, and impending death and the emotions of panic, fear, pain, and anguish (Johnson and Jackson 2005). Within this range of human experience, health-care professionals live their professional life. In order to fully "live your professional life," we have proposed certain practices that can assist health professionals working in the demanding field of palliative care. These include:

Acknowledgement that working in palliative care can be very demanding, and this acknowledgement needs to come from within oneself as well from those responsible for management of the organization the health professional works for.

Acknowledgement of one's own losses and grief. These may be personal losses or those from ones workplace. Not processing this grief can prevent professionals from being emotionally present for their patients.

Engaging in resilience-building through developing effective coping skills, creating a professional life and personal life balance that works, engaging in support processes such as reflective practice, using mindfulness techniques, and having the insight, or acknowledging the observations of others, to know when additional support may be required.

Developing awareness of the potential impact of vicarious traumatization as well as acknowledging this and seeking support to process such experiences.

Engaging in effective professional supervision, using individual, peer, or team processes.

Requiring appropriate organizational input such as effective human resource activities, for example, regular performance feedback, appropriate orientation and mentoring, family-friendly workplace practices, appropriate rosters, access to employee assistance programs, and professional development education opportunities.

Access to individual and team debriefing as well as adopting the Personal Debriefing Model.

Taking stock and committing to change through the use of the Self-Care Questionnaire and the self-care plan.

These techniques and activities, as well as others you identify as "working for you," will significantly assist you to be a safe and effective health professional in the rewarding field of palliative care.

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Self-Management for Patients with Progressive, Life-Threatening Diseases and Their Family Caregivers

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Contents

Abstract

We are in the midst of a paradigm shift from paternalistic healthcare to more participatory healthcare, where patients' autonomy and self-determination are increasingly valued. Patients are more and more expected to be in charge of their health. Yet, patient engagement in care is not always self-evident, especially when patients can no longer be cured and care needs are high. Learning that one's disease has progressed to an advanced and incurable stage is for most patients and their relatives an overwhelming experience that often includes shifting ones goals from curative treatments to focusing on quality of life. Managing the physical, psychosocial and lifestyle consequences of severe illness often includes making complex decisions and navigating through a complex healthcare arena, with care delivered by healthcare professionals from a variety of disciplines. Patient self-management can be

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_118

supported by healthcare professionals. Still, most of the time, patients, together with their relatives, need to manage a huge part of their life and care themselves. In this chapter, we provide comprehensive insight into self-management for patients with progressive, life-threatening diseases. We describe the concept of self-management and its domains in this population, the role of the family, determinants and outcomes of self-management, the current state of affairs of self-management support programs, and possible innovations for the future.

1 Introduction

We are in the midst of a paradigm shift from paternalistic healthcare to more participatory healthcare, where patients' autonomy and self-determination are increasingly valued. This is also visible in healthcare policy and social policy. Healthcare policy is shifting toward out-of-hospital delivery of care, partly driven by a tendency to reduce costs while invoking the importance of the "participation society" in which people should create their own support and safety nets. As a result, patients are more and more expected to be in charge of their health. Patient engagement has made it to center stage in discussions of quality of care, enshrined by the Institute of Medicine's "quality chasm" report as one of the key elements of high-quality care (Baker 2001). Despite these developments, patient engagement in care is not always self-evident, especially when patients can no longer be cured and care needs are high, as is the case in palliative care.

Learning that one's disease has progressed to an advanced and incurable stage is for most patients and their relatives an overwhelming experience that often includes shifting ones goals from curative treatments to focusing on quality of life. Because patients have to live with the prospect of imminent death and are increasingly unable to continue working and fulfilling their usual social roles, they need to deal with considerable emotional, psychosocial, and lifestyle consequences (Rainbird et al. 2009). They do this in the face of increasing multidimensional symptoms, such as fatigue, pain, lack of energy, weakness and/or appetite loss, anxiety, and depression (Rainbird et al. 2009; Kirkova et al. 2012; Rosenstein 2011; Uitterhoeve et al. 2004; van den Beuken-van Everdingen et al. 2016). Managing the emotional, psychosocial, and lifestyle consequences of severe illness often includes making complex decisions and navigating through a complex healthcare arena, with care delivered by healthcare professionals from a variety of disciplines, such as nursing, oncology, general practice, social work, pharmacology, dietetics, and psychology. Patient self-management can be supported by healthcare professionals. Nurses in particular may play an important, interdisciplinary role through direct involvement in communicating with patients, relatives, and other healthcare professionals, and by providing medical, practical, and emotional support to patients and relatives (Johnston et al. 2014). Still, most of the time, patients, together with their relatives, need to manage a huge part of their life and care themselves.

Box 1 and 2 describe examples of patients who are managing the consequences of a progressive, life-threatening disease.

Box 1 Self-Management in Context: Mrs. Ying

Mrs. Ying was 45 years old when she got diagnosed with breast cancer. Despite intended curative treatment, 4 years later the cancer had metastasized to her bladder and kidney, and a renal drain was inserted. Mrs. Ying had a strong wish to live as long as possible. She had two sons aged 14 and 17 years and knew that they needed her daily support for at least another few years. In order to fully focus on therapy and healthy living she stopped working as a management assistant in her husband's store selling hearing aids. She went to the hospital one to three times a week (depending on the type of treatment she

(*continued*)

Box 1 Self-Management in Context: Mrs. Ying (continued)

received). She experienced many treatment side effects, such as alopecia, neuropathic pain, fatigue, nausea and vomiting, and serious anorexia and weight loss resulting in cachexia. She spent much time and energy on balancing her diet, while experimenting with pharmacological and non-pharmacological interventions, vitamins, and cannabis to decrease her nausea and anorexia. Furthermore, she went out for a walk every day. Her husband accompanied her during each hospital visit, cared for her when she was feeling ill, kept the house clean, and supported the boys in their activities at school and sports. Therefore, he eventually decided to close his store. When family or friends wanted to visit Mrs. Ying, she asked them to bring their walking shoes to accompany her outside. During these rounds she talked about (the joy of) living; she did not want to talk about death and the imminent parting from her husband and children. Gradually, her physical condition deteriorated and new metastases were found in the uterus, stomach, and liver. She increasingly experienced pain, fatigue, severe weight loss, sleeping problems, and anxiety. Every time a treatment failed to succeed she insisted on another therapy. She searched the internet for information and experiences from peers and learned about the value of peer support. Only at these moments she showed some awareness of her imminent death, although even then she kept hoping that her life could be extended a little more. After 1 year her oncologist initiated a discussion about her preferences regarding end-of-life care. Although she was shocked (do I really only have a few months left?), she realized she did not want to die at home. Home was a place to live and she aimed to protect her boys from the remembrance of her death at home. She continued her daily walking

Box 1 Self-Management in Context: Mrs. Ying (continued)

rounds in company of her sons, her husband, or a friend. Almost a year later, she was admitted to an inpatient hospice facility and started preparing for death. She sent all her friends a short message about her situation and only allowed very close family to visit her. Two weeks later, she passed away quietly and alone during her sleep.

Box 2 Self-Management in Context: Mr. Kenston

Mr. Kenston is 74 years old and diagnosed with chronic obstructive pulmonary disease (COPD) Gold III. His wife died 2 years ago and he is now living alone in a tiny house in a small village. He has three children; one of them is living abroad and the other two are living a 30 min drive away. Twice a week the community nurse assists him with his hygiene care and 2 days per week he has a few hours help to clean his house. Mr. Kenston increasingly suffers from dyspnea, fatigue, dysphagia, anorexia and weight loss, and concentration deficits. In addition, he feels lonely and has difficulties to find a meaningful way of spending his days. Luckily, he is still able to go to his favorite pub every Sunday, where he sometimes meets with some old friends, drinks a beer, and watches football or rugby. Mr. Kenston is participating in a rehabilitation program that is offered by the multidisciplinary care team in his hospital and consists of disease treatment and symptom management. As part of the program, he receives medication and oxygen therapy, which he manages at home himself, and for which he visits his pulmonologist on a two-monthly base. Furthermore, the program includes physical activity and breathing exercises (two group sessions per

(*continued*)

Box 2 Self-Management in Context: Mr. Kenston (continued)
week), speech therapy to improve his dysphagia (one session per week), and consultations with a dietician (two per month) and an occupational therapist (two visits per month) aimed at improving his nutritional and functional status, respectively. Sometimes one of his children accompanies him to appointments, but most of the times he goes by himself, by taxi. Mr. Kenston feels supported by the rehabilitation program. He finds it difficult, however, to plan all the appointments with the various healthcare providers. Recently, he forgot to arrange a taxi. Also, he has realized that he sometimes forgets to take his pills. He increasingly struggles to fulfill his daily activities, such as going to the supermarket and preparing his meals, not only because due to a lack of energy but also because he finds the planning and maintenance of the various activities of his healthcare program to be difficult.

Self-management has frequently been studied in the context of chronic diseases, such as arthritis and diabetes (Charmel and Frampton 2008; Coulter and Ellins 2007). Although self-management in the context of palliative care, that is, for patients with progressive, life-threatening diseases, is similar or maybe even more relevant, it has received less attention. In this chapter, we will provide comprehensive insight into self-management for patients with progressive, life-threatening diseases. In the next paragraphs, we will describe for this population:

- The concept of self-management and its domains
- The role of the family
- Determinants and outcomes of self-management
- The current state of affairs of self-management support programs
- Innovations for the future

2 The Concept of Self-Management and Its Domains for Patients with Progressive, Life-Threatening Diseases

To date, self-management has predominantly been studied in the context of chronic diseases, such as asthma or arthritis. Definitions of self-management developed in the context of chronic diseases do not usefully apply to the specific situation of progressive, life-threatening diseases. Therefore, in this chapter, we define self-management as: "The strategies used by persons with the aim of managing the physical, psychosocial and existential consequences of living with a progressive, life-threatening disease and its treatment." Key to this definition is that self-management involves more than the management of physical problems alone, as it also includes the management of problems in other domains, such as psychosocial problems. In the context of progressive, life-threatening diseases and palliative care, self-management is similarly or even more relevant compared to chronic diseases. Nevertheless, self-management in patients with progressive, life-threatening diseases has received considerably less scientific attention and, consequently, still lacks thorough theoretical underpinning and conceptual delineation.

Studies describing self-management strategies used by patients with progressive, life-threatening diseases appear to cover multiple domains: medicine and pharmacology, lifestyle, mental and spiritual well-being, social support, knowledge and information, navigation and coordination, and decision-making (see Table 1) (Chan et al. 2016; Hansen et al. 2015; Johansson et al. 2006; Levy and Cartwright 2015; Norris et al. 2009; Stephens et al. 2014).

As Table 1 shows, within each of the self-management domains, a wide range of different self-management strategies can be distinguished. In the domain of lifestyle for example, patients might self-manage the consequences of their advanced disease by exercising, making dietary

Table 1 Self-management domains and self-management strategies used by patients with progressive, life-threatening diseases

Self-management domains	Examples of self-management strategies
Medicine and pharmacology	Monitoring symptoms, bodily changes, treatment effects, and/ or disease risks Self-administering medication Adhering to prescribed treatment schedules Adjusting or discontinuing treatment schedules (e.g., taking extra drug doses during breakthrough pain, replacing conventional treatment with alternative therapies, omitting use of medications)
Lifestyle	Doing exercise, reducing sedentary behavior Reducing cigarette and/or alcohol consumption Adjusting nutrition and diet Engagement in complementary and alternative medicine (e.g., medicinal herbs, meditation, massage, Reiki, homeopathy) Performing leisure activities (e.g., engaging in physical or creative activities) Maintaining daily activities (e.g., by taking breaks/sleep during the day, dividing activities into smaller parts)
Mental and spiritual well-being	Engaging in psychotherapy Keeping a diary Using mindful self-help strategies (e.g., practicing assertive self-talk, focusing on feelings and thought of control, acceptance, positivity, channeling thoughts of own death toward future well-being of loved ones) Engaging in meaningful activities (e.g., volunteering, promoting cancer awareness)
Social support	Seeking support from relatives and friends Seeking support from healthcare professionals Seeking support from other patients (e.g., participating in (online) support groups) Providing social support to friends and relatives Limiting social interactions to certain people or moments (e.g., withholding emotions, restricting social contacts to close relatives or good moments)
Knowledge and information	Seeking information about disease and/or treatment (e.g., searching the internet) Seeking information about self-care Avoiding or ignoring information (e.g., not reading about symptoms or prognosis)
Navigation and coordination	Coordinating medical services (e.g., obtaining health-related documents) Delegating certain aspects of care (e.g., obtaining medications, decisions on pain treatment approach) to others Coordinating and staying in charge of information dissemination to, for example, relatives Making financial and practical plans (e.g., arranging funeral, inheritance)
Decision-making	Making informed decisions about treatment Engaging in advance care planning Short-term and longer term goal-setting to define and fulfill wishes

changes, practicing complementary and alternative medicine, or engaging in new or existing hobbies. Psychological self-management strategies could consist of engaging in psychotherapy, practicing mindfulness, keeping a diary, or doing meaningful activities. Coordination and navigation strategies include the coordination of medical services and making financial plans. Also in the other domains, self-management strategies are numerous. How and to what extent patients use these strategies might be highly dependent on personal preferences and circumstances. Furthermore, self-management styles and strategies may change during the course of advanced illness. In the case description provided in Box 1, Mrs. Ying started to self-manage the consequences of advanced breast cancer by engaging in healthy lifestyle activities (e.g., taking daily walks), seeking information and making informed decisions about treatment options and preferences, seeking social support from her loved ones, and delegating certain household, caregiving, and healthcare

tasks to her partner. When her health condition deteriorated, she shifted focus from seeking regular and experimental medical treatments to preparing and planning for death (for instance, by making plans about where and how she wanted to die). Mr. Kenston's life is dominated by the fulfillment of his COPD rehabilitation program that mainly requires self-management strategies within the domains of the medicine and pharmacological domain and navigation and coordination. Meanwhile, he tries to maintain his daily activities, and once per week he goes to his favorite pub for some distraction. Keeping up with all these activities becomes increasingly challenging.

Self-management in the context of progressive, life-threatening diseases thus comprises a heterogeneous, multifaceted concept. In the context of chronic, nonadvanced diseases, patients also self-manage in multiple domains by applying a variety of different strategies. However, for several reasons self-management in progressive, life-threatening diseases is different and probably even more challenging than it is in chronic conditions. These challenges concern the prospect of imminent death, the magnitude of the "work," and the involvement of the family.

2.1 The Prospect of Imminent Death

Although some patients might never stop hoping for cure, in advanced disease and palliative care, most people strive for life extension and optimizing quality of life. However, when living with the prospect of inevitable deterioration and imminent death, the concept of quality of life can be very diffuse and susceptible to competing values and priorities. Self-management strategies and attitudes might therefore not only be various, but (seemingly) ambivalent and strategies could change over time. Mrs. Ying, for example (see Box 1), initially wanted to support her sons for at least another few years. After a while, however, she became aware that her metastasized breast cancer would not allow her to. Whereas on the one hand, she might have wanted to keep fulfilling her usual caregiver role and remain the mother she had always been, on the other hand, she felt that she had to delegate certain aspects of care to her husband. Also, despite potentially needing the emotional support of her sons, Mrs. Ying decided not to share all her emotions with them to protect them from sadness.

Studies about self-management in patients with progressive, life-threatening diseases showed that social support might indeed range from providing and seeking social support to limiting and even avoiding social support (Johnston et al. 2014; Baile et al. 2011). Although most patients experience social support as essential, for some of them, seeking and accepting it is hampered by fears of becoming a burden to their loved ones and losing their established roles and identity. A recently published literature review on life values of elderly people suffering from incurable cancer (Ebenau et al. 2017) also found that besides seeking social support, many patients consider maintaining independence and withholding emotions to contribute to a good death, as this is perceived to minimize strain on their loved ones. Facing the end of life also demands strategies to prepare for life closure and death, which might include seeking support and care for children or a partner, making decisions about the arrangement of a legacy or funeral, and/or preferred care at the end of life. More generally, ambivalence in self-management strategies of patients with advanced diseases often seems to reflect a conflict between two seemingly opposing attitudes: appreciating life in the present versus planning for the future; readjusting purpose and expectations versus maintaining normality and a sense of established identity; preparing for death versus hoping to live longer; and taking control versus letting things happen.

2.2 The Magnitude of the "Work"

Problems and needs of patients with advanced diseases are highly multidimensional and complex, making their daily management far more

time and energy intensive than that of chronic nonadvanced diseases. The work has often been compared to a full-time job, like for Mr. Kenston who was treated for many symptoms and problems at the same time. Among advanced cancer patients a median number of 11 symptoms have been demonstrated (Higginson and Costantini 2008). Physical symptoms, such as pain, breathlessness, fatigue, anorexia, constipation, and insomnia, occurred in some combination in virtually all of these patients (Higginson and Costantini 2008). Managing physical symptoms involves taking numerous medications in different dosages at different times of the day according to the physician's instructions, and monitoring their therapeutic and adverse effects (Lau et al. 2009). Patients and family caregivers report that they are often not able to manage such complex medication regimes (Joyce et al. 2014). Further, although not always recognized and treated properly, depression and anxiety are common symptoms for a large proportion of patients (Delgado-Guay et al. 2009). Depression is associated with decreased health-related quality of life scores and poor treatment adherence (Arrieta et al. 2013). Patients and their family caregivers also have urgent psychosocial issues/problems, such as loneliness and hopelessness (Steinhauser et al. 2000). In addition, patients have deteriorating capacity to independently perform activities of daily living. All these problems and needs make healthcare navigation and coordination increasingly complex, because care is often delivered by various providers from a variety of disciplines in various settings, hampering integrated and coordinated care (Daveson et al. 2014). Furthermore, many complex preference-sensitive health and healthcare decisions need to be made, for instance, about medical care and changing or sacrificing certain lifestyle habits (e.g., reducing sedentary behavior, quitting smoking) that may potentially, but would not necessarily improve outcomes. Adequate and timely communication between patients, family caregivers, and healthcare providers is a prerequisite for adequate self-management, but this is often also time consuming and difficult (Higginson and Costantini 2008; Slort et al. 2011).

2.3 Involvement of Family Caregivers

Another reason why self-management is especially complex in advanced diseases concerns the people involved. As a result of progressive physical and/or cognitive decline, patients' self-management skills may be increasingly limited and family caregivers play an important role in the daily illness management. They spend on average 8 h per day on care tasks, often feel overwhelmed, and suffer from high levels of caregiver burden and numerous health-related problems, such as sleep-disturbances and depressive symptoms (Aranda and Hayman-White 2001). As such, they are often called the "hidden patients." In the next paragraph, we discuss the role of the family in more depth.

3 The Role of Family in Self-Management in Palliative Care

While most patients prefer to receive end-of-life care at home (Gomes et al. 2012), this is not possible without depending heavily on contributions by family (Aranda and Hayman-White 2001). Various terms are used to describe persons who are involved in the unpaid or nonprofessional care for a patient, such as informal caregivers, family caregivers, care from relatives and friends, and carers (Payne 2010). In this chapter, we will use the term "family caregiver" and the definition of Stajduhar et al. (2010) of family caregivers at the end of life, i.e., "Individuals who provide any physical, emotional, and instrumental support and assistance to individuals with life-limiting illness that they view as family members. These family caregivers are not acting in a professional or occupational capacity. They may or may not be co-residing with the care recipient and the care recipient may be either in a home or institutional setting" (Stajduhar et al. 2010). This definition implies a broad definition of family that goes beyond formalized relationships. In the past decades, there has been an increase in informal caregiving as a primary source of patient care. It has been estimated that family caregivers in Canada and Australia provide 80–90% of all

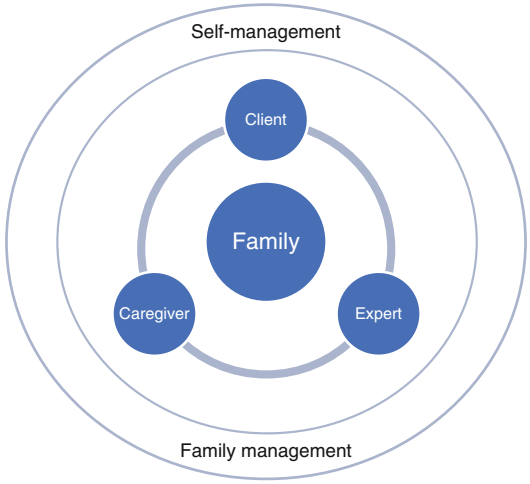

Fig. 1 Conceptual model of the family roles in self-management and family management at the end of life

care provided at home. Currently, 8–16% of adults in the European Union serve as family caregivers, a proportion that is expected to further increase (Börsch-Supan 2008).

Although some work has been done to conceptualize the roles of family caregivers in self-management of chronic conditions (Ryan and Sawin 2009; Schulman-Green et al. 2012), only little is known about these roles in palliative care. In this context especially, the role of the family seems to be multifaceted (see Fig. 1). First of all, a family caregiver supports the patient in uptaking self-management strategies (e.g., monitoring symptoms, providing assistance with activities of daily living). Second, a family is an expert, for instance, in the contact and collaboration with healthcare services. A family caregiver knows the patient usually best, including his or her personal history, values, goals, preferences, and self-management challenges and strategies. Finally, a family caregiver of a patient at the end of life can be considered to be a "client" as well, affected by the patient's disease and the imminence of approaching loss of their beloved. In addition, family members may have their own chronic conditions themselves (Turner et al. 2016).

The roles of caregiver, expert, and client may not always be distinguishable, and the family is moving between and within the various roles, depending on the patient's condition, their own condition, and other contextual factors at stake. When the roles of caregiver and expert predominate, the family takes over various self-management activities of the patient, such as monitoring symptoms, coordinating care, seeking information or support, and dissemination of information about the patient's condition to others. The role of the family then becomes "self-management by proxy," which is in the figure expressed as family management. In their role as client, family members have to take care of themselves, that is, to self-manage the situation in combining caring activities with preparing for loss of their beloved and with, for example, their own living, employment, and house holding. At the same time, they need to prevent overburdening.

Of the three family roles described in Fig. 1, the role of caregiver is most extensively studied and in practice probably best acknowledged.

From the patient's perspective, being cared for and dying at home is likely to improve quality of life and quality of dying (Gomes et al. 2013). However, for family caregivers this might be burdensome: family caregivers of patients with advanced cancer spend on average 25 h per week on family caregiving for a patient, with approximately 25% spending over 40 h a week (Van Houtven et al. 2010). Involvement in the life of and care for a beloved patient in the last phase of life can engender positive feelings for the family caregiver, such as self-esteem and a sense of meaning. These responsibilities may nevertheless be very demanding, physically, emotionally, and financially. As the death of a loved one does usually (fortunately) not occur frequently, many family caregivers lack (any or extensive) experience in caring. Many family caregivers have hardly any knowledge about disease management and do not know what they can expect in the last stages of life. Family caregiving causes physical, psychosocial, and existential strain, and family members are at increased risk for caregiver burden (Guerriere et al. 2016; Park et al. 2012), defined as a psychological and emotional experience related to the perception of the demands that are

specifically associated with accompanying and providing care for a dying person (Dumont et al. 2008). Reviews addressing the quality and problems related to end-of-life care found that intensive family caregiving is linked to numerous health-related problems (Stajduhar et al. 2010; Gysels et al. 2012), which worsen as the patient's physical function and symptom burden increase (Palos et al. 2011; Schulz and Beach 1999). Most reported are psychological difficulties, such as depression and anxiety, and physical and emotional stress; financial and occupational difficulties, e.g., occupational disruption and financial strain; and difficulties with patient care, such as being able to leave the patient unattended or dealing with the physical demands of providing care (Stajduhar et al. 2010; Gysels et al. 2012). The percentage of family caregivers experiencing moderate to severe burden has been showed to increase from 32% 3 months prior to death up to 66% in the last week of life (De Korte-Verhoef et al. 2014). Modifiable and nonmodifiable factors predicting the risk of caregiving burden have been identified, such as patient and caregiver gender, duration of family caregiving and of unpaid work, patient's functional status, increasing healthcare costs, and emergency department visits (Guerriere et al. 2016).

Self-management at the end of life often takes place in the dyad of patient and family caregivers. They are interdependent and are balancing their lives with all disease-related activities (Hardy et al. 2014), while trying to maintain a normal life (Turner et al. 2016). At moments during which the patient feels reasonably well and is able to self-manage her disease and related activities rather adequately, the family caregivers' role in disease management and decision-making may be fairly limited. Yet, family caregiver's support will be more demanding when the patient's condition deteriorates and for instance accompanying her to healthcare visits and treatment is needed. Vice versa, when family caregivers have to opt out for a while, for example, due to responsibilities at home or at work or because they feel exhausted, the patient needs to expand self-management activities or arrange assistance of other relatives or healthcare services. The same accounts for the expert role. When the patient is able to decide for himself, he does not necessarily need the support of family as expert in therapeutic relationships. Deterioration of the patient's condition increases the need for shared or surrogate decision-making. This need for balancing and flexibility of family caregivers is possibly very demanding. As most self-management strategies are built upon cognitive and mental skills, such as adherence to medication therapy, seeking information, coordinating care, and decision-making, family management may be especially demanding in patients with dementia. Then patients and family have to deal with patients' deteriorating cognitive and mental capacities and various self-management problems occur early in the disease trajectory. These mostly long-lasting and far-reaching processes of gradually changing roles in the patient and family dyad are an important risk factor for psychological distress in the family (Moore et al. 2017).

Being caregiver, expert, and client at the same time, family caregivers need acknowledgment of their position and contribution to the care and understanding of their experiences (Aparicio et al. 2017). They may need assistance in handling difficult situations, such as suffering from pain and anxiety, to improve quality of life and well-being of both the patient and themselves. A close therapeutic relationship, including supportive attitudes such as kindness, empathy, attention to the family, and closeness are important (Aparicio et al. 2017). By being concomitant caregiver and expert, family caregivers try to achieve a life as normal as possible. When self-management of both disease-related activities and daily activities are in balance, this so-called family management is effective (Hardy et al. 2014). However, family members are at risk of burden as they feel the responsibility but not the power to advocate for the best care for their beloved (Teno et al. 2001), especially when the patient is admitted to the hospital or nursing home. Family caregivers may fear that the needs of the patient are being neglected (Teno et al. 2001; Witkamp et al. 2016) when they have to leave.

4 Determinants and Outcomes of Self-Management in the Palliative Phase

As described in the previous paragraphs, patients are increasingly expected to be in charge of their health (Henselmans et al. 2015). It is questionable, however, whether all patients and their family members are able to fulfill this role. In addition, few studies have addressed the outcomes of self-management. To describe the determinants and consequences of self-management of patients and their family members in the palliative phase, we have developed a preliminary conceptual framework, visualized in Fig. 2. It builds on Stewart's palliative care model (Stewart et al. 1999) and on the revised self- and family-management framework of Grey et al. (Grey et al. 2015). The model hypothesizes that patient, family, and system factors (Rademakers et al. 2015) are related to self-management skills and practices of patient and family members. Studies in chronic diseases show that more than half of patients struggle with self-management (Rademakers et al. 2015), especially older people (Korfage et al. 2015), people with low SES (Rademakers et al. 2014), and people with low health literacy (Berkman et al. 2011). A few studies conducted in the palliative phase also give insight in possible related patient factors. Norris et al. (2009) showed that younger patients with advanced cancer tend to participate more frequently in cancer support activities, while patients with higher levels of physical functioning were more likely to practice physical exercise (Norris et al. 2009). Chan et al. (2016) showed that higher education scores, lower levels of depressive symptoms, and higher total and global self-efficacy scores were positively associated with perceived effectiveness of self-management behaviors (Chan et al. 2016). Furthermore, patients with more anxiety and/or depressive symptoms and lower self-efficacy reported more self-management concerns (Baile et al. 2011). In psychology, some constructs explain why certain people are better at dealing with harsh circumstances than others, which can be considered the crux of self-management. Coping refers to the way individuals deal with stress (Taylor and Stanton 2007); self-efficacy is the belief in the own ability to accomplish a difficult task (Bandura 1977), and resilience is the ability of positively adapting to adverse events and to thrive despite adversity (Cosco et al. 2016). It may well be that these constructs as mediators play an important role in explaining why some people have difficulties with self-management and others have not. A few studies already provide some evidence for the role self-efficacy (Lorig and Holman 2003; Lorig et al. 2001).

Fig. 2 Conceptual framework showing possible determinants and outcomes of self-management of patients with progressive, life-threatening diseases and their family caregivers

Drawing from mostly observational studies about problems and needs in the palliative phase (Higginson and Costantini 2008; Bekelman et al. 2016; Given et al. 1992), the model further postulates that poor self-management may be associated with a reduced quality of life, depressive symptoms, high treatment burden, high caregiver burden, and overuse of care (Hibbard and Cunningham 2008). Our ongoing research aims to study the proposed conceptual framework in depth.

5 The Current State of Affairs of Self-Management Support Programs in Palliative Care

A considerable group of patients is interested in self-management support (Henselmans et al. 2015). However, comprehensive self-management support interventions for patients in the palliative phase are lacking. Comprehensive self-management support programs have been developed for patients with chronic, nonlethal diseases (Bodenheimer et al. 2002). They were shown to improve self-management skills (Hibbard and Cunningham 2008) and resulted in reduced symptom burden (Barlow et al. 2002), less hospitalizations (Barlow et al. 2002), and improvements in quality of care (Coulter and Ellins 2007), patient safety (Coulter and Ellins 2007), and reduced healthcare costs (Charmel and Frampton 2008).

Within oncology, several attempts have been made to develop and evaluate intervention programs aimed at supporting self-management of patients and/or their family caregivers. However, most of these interventions have been directed at patients with early stage, curative cancer or cancer survivors (Bennett et al. 2016; Grimmett et al. 2013; Hochstenbach et al. 2017; Jahn et al. 2014; Kanera et al. 2016; Kim and Park 2015; Kuijpers et al. 2013; McCusker et al. 2018; Mishra et al. 2012; van den Berg et al. 2012, 2013). Thus far, only few interventions have addressed self-management in advanced, incurable cancer. An elaborate example of such an intervention concerns the ENABLE II (Educate, Nurture, Advise, Before Life Ends) project (Bakitas et al. 2009a, b), which aims to encourage patient activation and self-management in multiple domains by means of a case management, psychoeducational approach. During four-weekly educational sessions (either by telephone or during clinic visits) and monthly follow-up sessions conducted by advanced practice nurses with palliative care specialty, patients with advanced cancer are coached using an educational manual including modules of problem solving, communication and social support, symptom management, advance care planning and unfinished business, and an appendix listing supportive care resources. A randomized controlled trial that assessed the incremental effects of the intervention compared to usual oncology care only has shown promising, positive effects on quality of life and mood, yet limited effects on symptom intensity scores and use of resources.

In the past decades, several interventions to support self-management in COPD have been developed. The support of patients with advanced COPD requires a more integrated approach compared to support of less severely ill patients. Wagg (2012) has described a spectrum of support for COPD patients, showing that especially for the most severe patients a comprehensive pulmonary rehabilitation is of importance (Wagg 2012). This includes focus on self-management and the maintenance of ones' health status. According to Effing et al.

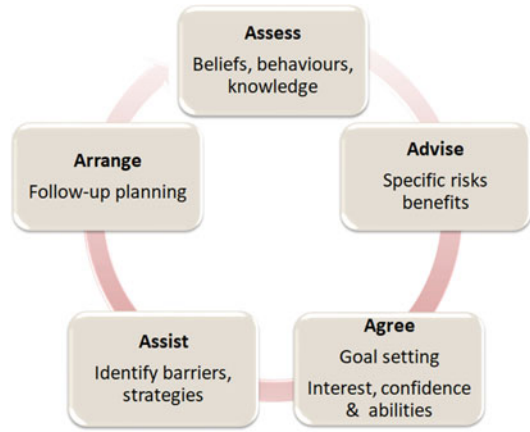

Fig. 3 5-A model of healthcare professionals' competences of self-management support (Glasgow et al. 2003)

(2012), the change of behavior, including cognitive behavioral techniques to achieve this, is a fundamental element of self-management programs in this patient population (Effing et al. 2012). In 2016, an international expert group reached consensus on the requirements of adequate COPD self-management interventions. Its core aims and elements are described in Box 3. The process of iterative interactions between patients and healthcare professionals as described in element 3 is also nicely conceptualized by the 5-A model (see Fig. 3) (Glasgow et al. 2003). In the 5-A model, five competencies of healthcare professionals are central to adequate self-management support: Assess patients' beliefs, behaviors, and knowledge, Advice on benefits and risks, Agree (e.g., on goal setting), Assist patients in their strategies of choice and possible barriers they may experience, and Arrange follow-up planning.

Box 3 Core Aims and Elements of COPD Self-Management Support Programs (Effing et al. 2012)

1. A COPD self-management intervention is structured but personalized and often multicomponent, with goals of motivating, engaging, and supporting the patients to positively adapt their health behavior(s) and develop skills to better manage their disease.
2. The ultimate goals of self-management are: (a) optimizing and preserving physical health; (b) reducing symptoms and functional impairments in daily life and increasing emotional well-being, social well-being, and quality of life; and (c) establishing effective alliances with healthcare professionals, family, friends, and community.
3. The process requires iterative interactions between patients and healthcare professionals who are competent in delivering self-management interventions. These patient-centered interactions focus on: (1) identifying needs, health beliefs, and enhancing intrinsic motivations; (2) eliciting personalized goals; (3) formulating appropriate strategies (e.g., exacerbation management) to achieve these goals; and if required (4) evaluating and readjusting strategies. Behavior change techniques are used to elicit patient motivation, confidence, and competence. Literacy-sensitive approaches are used to enhance comprehensibility.

In a meta-analysis of 22 studies among COPD patients with different disease stadia (including advanced COPD), Lenferink et al. (2017) summarized the effectiveness of COPD self-management interventions on outcomes of health-related quality of life (HRQoL), overall and respiratory-related hospital admissions, and mortality (Lenferink et al. 2017). They concluded that these COPD self-management interventions are associated with improvements in HRQoL and lower probability of respiratory-related hospital admissions. Not all studies included in the meta-analysis already met the requirements as described in Box 3 and not all studies provided detailed information regarding the intervention components. As many patients with COPD have comorbidities, the investigators recommended to take comorbidities into account when COPD self-management action plans are used in the wider population. Self-management interventions with a smoking cessation program showed significant improvements in HRQoL when compared to interventions without such a program. Neither the number of behavioral change technique clusters that were used in the intervention nor the duration of the intervention and the adaption and maintenance of medication did affect HRQoL.

6 Conclusions and Innovations for the Future

In an era where participatory healthcare is increasingly valued and stimulated, patients more and more need are expected to be co-responsible for their health and care. In this chapter, we showed that self-management of patients with progressive, incurable diseases is complex and multifaceted, covering multiple domains, such as medical and psychological self-care, lifestyle, the organization of social support, the acquirement of relevant knowledge and information about the disease, navigating the medical arena, and participating in decision-making about future treatments and care. The prospect of imminent deterioration and death further adds to its complexity. Patients' family caregivers have an important role in self-management in this phase of life, especially when the patient's health status further deteriorates. This is complex, as family members may have a role in supporting the patient, provide information to professional caregivers, and need to take care of themselves as well. In our chapter, we also demonstrated that people may differ in the extent to which they are able or prefer to engage in self-management strategies, and also in the type of strategies that they prefer. Disentangling why some people seem to be able to deal rather effectively, with what may be the hardest event in life – an approaching death – and others are not, is crucial. Such insight would highly advance theory-building of patient engagement and would yield important opportunities to close the gap between current policy and actual practice. This could promote effective and efficient self-management support interventions, that might benefit from a tailored approach, in the vulnerable population of patients with advanced cancer and their family caregivers.

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Advance Care Planning in Palliative Care

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_25

Abstract

Advance care planning is a patient-centered process to enable a person to express his or her preferences for future healthcare. Advance care planning is an integral component of palliative care for people at various stages in the illness trajectory. This chapter provides an overview of advance care planning; the potential benefits, barriers, and facilitators; the key components of advance care planning at various stages of health; strategies for the advance care planning conversation; and areas for future research.

1 Introduction

Advance care planning is a process of supporting a person to express his or her preferences and priorities for future healthcare in consultation with healthcare providers, family members, and other people who are important to him or her. It typically includes a discussion about end-of-life care. It's a patient-centered initiative that facilitates shared decision-making. It is highly relevant to palliative care and core business for palliative care providers.

Advance care planning as a concept has been around for decades, initially developing in the USA as a legal mechanism to guide use of end-of-life care interventions. Legally binding documents such as advance directives were established to allow a person to specify his or her preferences for medical treatments prior to loosing capacity. However, various factors have limited the uptake of advance care planning.

This chapter explores definitions of various terms relevant to advance care planning, the benefits and evidence supporting advance care planning, the gaps in evidence and barriers to uptake of advance care planning, the advance care planning over the trajectory of health/illness, and the tips for advance care planning discussions in palliative care settings.

2 Definitions

2.1 What Is Advance Care Planning?

Two recently published international Delphi studies have been conducted to establish consensus around the definition of advance care planning. A European consensus process defined advance care planning as *"the ability to enable individuals to define goals and preferences for future medical treatment and care, to discuss goals and preferences with family and health-care providers, and to record these preferences if appropriate"* (Rietjens et al. 2017). Another international consensus process was led from the USA and defined advance care planning similarly as *"a process that supports adults at any age or stage of health in understanding and sharing their personal values, life goals, and preferences regarding future medical care. The goal of advance care planning is to help ensure that people receive medical care that is consistent with their values, goals and preferences during serious and chronic illness"* (Sudore et al. 2017).

2.2 What Is an Advance Care Plan?

An advance care plan is the ideal outcome of an advance care planning discussion. Regardless of whether or not the person wishes to formally

document his or her preferences in a legal way, the outcomes of advance care planning discussions should be documented to inform care provision. Advance care plans *"state a person's preferences about health and personal care, and preferred health outcomes. They may be made on the person's behalf and should be prepared from the person's perspectives to guide decisions about care"* (Australian Commission on Safety and Quality in Health Care 2015).

2.3 What Is an Advance Directive?

An advance directive is a type of advance care plan. It is a formal document signed by a competent adult. It can record the person's preferences for future care and include specific instructions, such as refusal of certain interventions. Other names used in various jurisdictions include advance health directive, advance care directive, living will, and medical directive. The legal standing of advance directives varies from country to country and state to state. In some Western countries, advance directives are supported by specific legislation (statutory advance directives) and are legally binding. In other jurisdictions advance directives may be recognized under common law. Advance directives only come into effect when the person loses capacity to make his or her own decisions.

3 Appointment of a Substitute Decision-Maker or Legal Healthcare Proxy

In many countries, people can formally appoint a trusted person to make medical decisions on their behalf should they lose capacity to do so. Substitute decision-makers have legal authority to make medical decisions on behalf of a person whose decision-making is impaired, with legislation varying between different jurisdictions. Various names are used for this role, such as enduring guardian, health attorney, medical agent, and guardian. This is usually different to a person appointed to make financial decisions (for whom terms include power of attorney).

4 Evidence/Benefits for Advance Care Planning

Patients cite the benefits of advance care planning as including preparation for end-of-life care and death, greater personal empowerment and hope, better medical care, avoidance of prolongation of dying, strengthening of personal relationships, and relieving burdens placed on family (Davison and Simpson 2006; Singer et al. 1995, 1999). Studies conducted in a range of healthcare settings suggest that advance care planning may improve patient and family satisfaction with care (Detering et al. 2010; Molloy et al. 2000), increase the likelihood of medical staff and family members' understanding and complying with patients' wishes for end-of-life care (Rietze and Stajduhar 2015; Houben et al. 2014; Martin et al. 2016), reduce hospitalization and aggressive medical care near death (Rietze and Stajduhar 2015; Martin et al. 2016; Khandelwal et al. 2015; Robinson et al. 2012), and increase palliative care and hospice use (Rietze and Stajduhar 2015; Robinson et al. 2012) and the likelihood of a person dying in his or her preferred place of care (Martin et al. 2016). Furthermore, advance care planning may also reduce levels of stress, anxiety, and depression in surviving relatives (Detering et al. 2010; Molloy et al. 2000; Silveira et al. 2010; Wright et al. 2008). At a clinician level, advance care planning can reduce moral distress related to decisions to withdraw treatment (Elpern et al. 2005). At a health system level, advance care planning has potential to increase cost-effectiveness by ensuring resources are not misspent on care that is unwanted or likely to be futile (Klingler et al. 2016; Dixon et al. 2015). Although evidence for benefit at a societal level is limited, improved bereavement outcomes in relatives seem likely to translate into quicker return to productivity both economically and socially.

5 Facilitators and Barriers to Advance Care Planning

While the range and extent of benefits demonstrated across the literature as a whole is impressive, there has been significant heterogeneity

between studies. This finding has refocused attention away from the overarching question of whether advance care planning *can* have benefits toward a more nuanced analysis of which advance care planning elements may be more or less effective and in what contexts. Advance care planning is a "complex intervention," as defined by the UK Medical Research Council, in that it has multiple interacting components, and is dependent on contextual factors for successful implementation (Medical Research Council 2006). Untangling the contributions of each component and contextual factor is challenging. However, research has identified a number of ingredients for success, as well as key problems.

5.1 Organizational Support

At the organizational level, systematic reviews suggest that advance care planning needs to be assigned due priority in terms of training, resources, and time and supported by an appropriate administrative system for communicating and reviewing advance care plans and monitoring adherence during end-of-life care (Gilissen et al. 2017; Travers and Taylor 2016; De Vleminck et al. 2013; Lovell and Yates 2014). Transitions between care settings (e.g., aged care and hospital) are especially disruptive to communication about advance care planning and other aspects of care (Coleman 2003). Ensuring advance care plans are kept up to date improves clinicians' confidence that they represent the person's current wishes; as concern that the person may have changed his/her mind since the plan was written is a common barrier to adherence. Other system-level approaches to advance care planning include embedding it into routine care (e.g., on admission) to ensure it is consistently offered; however, care is needed to ensure advance care planning is individualized to each person's needs rather than takes a "one-size-fits-all" approach. A further "double-edged" system-level approach is to defer advance care planning within an organization to one or more highly trained advance care planning specialist rather than allocate time and training to all clinicians. Although cost-effectiveness analyses are lacking, this approach may be less sustainable in cost terms and overlooks the importance of advance care planning occurring opportunistically within a trusting therapeutic relationship (Lund et al. 2015).

5.2 Clinician-Patient/Family Interaction

At the clinician level, good relationships with the patient and family involved are important, as are motivation, confidence, knowledge, and communication skills (Gilissen et al. 2017; Travers and Taylor 2016; De Vleminck et al. 2013; Lovell and Yates 2014). Clinicians may be uncomfortable with having "difficult conversations" about end-of-life care, even when they are competent communicators more generally. Difficulty with prognosticating often leaves clinicians uncertain about the best time to initiate advance care planning, with many concerned that they will undermine hope if they commence too soon. Even in the later stages of illness, clinicians may worry that patients aren't psychologically "ready" to discuss end-of-life care, so they wait for patients to initiate the discussion rather than doing so themselves. In fact, research suggests that patients typically welcome the opportunity to take an active role in deciding future care, but may not be sufficiently aware of advance care planning to request it. Patients and families may also have limited knowledge about their disease and available treatments and be unaware that they have management choices, including the option to have no treatment at all. Limited health literacy and low education in general have been found to be barriers to advance care planning (Lovell and Yates 2014), requiring communication to be appropriately tailored for content, timing, quantity, and form, as well as checking for comprehension (Dy and Purnell 2012).

5.3 Patient and Clinician Characteristics Associated with Increased Likelihood of Advance Care Planning

The likelihood of advance care planning being undertaken is associated with higher patient age and having a cancer diagnosis (Lovell and Yates

2014), perhaps reflecting clinician assumptions about conditions under which a conservative care pathway may be more or less desirable. While advancing age may increase the likelihood of cognitive decline and need for health-related decision-making, age alone should not influence decisions to forego life-sustaining treatments. Similarly, while religious views, family roles, and community support may confer genuine reasons why advance care planning is less attractive to people from certain cultural backgrounds (e.g., African Americans (Sanders et al. 2016)), care is needed to ensure that mistrust in the health system is not a reason for exclusion, and concerns that advance care plans may be used to reduce costs are addressed where these exist. Culture may influence the attitudes not only of patients but also of clinicians, making them more or less likely to offer advance care planning (Frost et al. 2011). An experiential approach to advance care planning training may help clinicians reflect on their own attitudes and values to limit bias in their practice, as well as develop empathy for patients and skills for sensitive communication (Weiner and Cole 2004). Clinicians' perceived norms may also be determined by their clinical experience, in turn dependent on their discipline and specialty. Multidisciplinary team meetings and case conferences have been used to ensure a diversity of professional perspectives, especially where considerations are complex, as in the context of multi-morbidity (Phillips et al. 2013).

5.4 Substitute Decision-Maker Considerations

With notable exceptions, patients typically prefer their substitute decision-maker to be a close family member (Kelly et al. 2012). However, the role can be burdensome, especially when the decision-maker is uncertain of his or her loved one's preferences or feels unable to enact known preferences because of emotional ties, or when there are divided opinions among the family more generally (Vig et al. 2007; Lord et al. 2015). If decisional conflict is not addressed at the time, it can damage family relationships and complicate bereavement and recovery following the patient's death. Addressing this problem requires skillful facilitation and support that, wherever possible, should engage with diverse perspectives across the family rather than focus only on the legal obligation to involve the substitute decision-maker.

6 Who May Benefit from Advance Care Planning?

Any adult may choose to start advance care planning when healthy before an unexpected health crisis. It may also be relevant for children with a life-limiting illness, although this is beyond the scope of this chapter. Advance care planning may be especially relevant for:

- People diagnosed with a life-limiting or chronic illness
- A person whose doctor would not be surprised if he or she were to die within 12 months
- Any person admitted to a residential aged care facility
- People 75 years of age of older
- Any person requesting to discuss advance care planning
- A person at risk of losing capacity to make decisions (e.g., due to progressive cognitive impairment)

7 Advance Care Planning Across the Trajectory

While advance care planning may be relevant for any adult, the approach and areas to be covered in an advance care planning discussion are different for people at different stages of the illness trajectory. Palliative care providers have various roles in the provision of advance care planning. This includes direct involvement in ongoing advance care planning and goals of care discussions with patients and families referred to palliative care services. Importantly it also includes provision of education and support for clinicians working in other settings to facilitate advance care planning discussions with their own patients, and an advocacy role in education of the public. The

following section shows the authors' recommendations for advance care planning across the trajectory of health.

7.1 Advance Care Planning for a Well Adult, Less Than 75 Years of Age

The main intervention for this population is public education and enabling family discussions about advance care planning. Health professionals do not necessarily need to be involved in the discussion. The key messages for this group are:

1. To prompt the person to consider who he or she would want to make medical decisions for him or her if he or she couldn't speak for himself or herself in case of a sudden illness or injury. If this person is different from the person who would normally be consulted according to the hierarchy in their jurisdiction, then encourage the person to consider formally appointing a legal medical SDM. In some jurisdictions only legally appointed medical substitute decision-makers can refuse treatment on behalf of the person, which is another reason the person may wish to consider such an appointment.
2. Suggest they have discussions with key family members about the values, goals, and preferences they would want considered if they ever had a serious injury or were in a prolonged period of incapacity. For example, what makes worth living, what level of function and ability to do things would be acceptable to them, their funeral wishes, other things that would be important for their family to know if they died suddenly, and any wishes regarding organ donation.

It is also important for well adults to know they are likely to be called upon to have input into decisions for their family members when they are dying or incapacitated. Resources for enabling early family discussions about advance care planning are shown in Box 1.

Box 1 Advance Care Planning: Example Resources

Resources for clinicians

- ACP Australia www.advancecareplanning.org.au
  - This includes elearning/workshop materials, fact sheets, legal information, webinars
- Canadian ACP website http://www.advancecareplanning.ca
  - Provides range of information and resources and educational materials for health professionals, consumers, and researchers
- NZ ACP website http://www.advancecareplanning.org.nz
  - Provides range of information and resources and educational materials for health professionals and consumers
- Singapore ACP website https://livingmatters.sg
  - Provides range of information and resources and educational materials for health professionals and consumers
- The ADVANCE Project website www.caresearch.com.au/advance
  - Provides training and resources for clinicians working in primary and chronic/complex care setting to initiate discussions about advance care planning and screen for older and/or chronically ill patients' supportive and palliative care needs

ACP workbooks or websites for consumers

Resources relevant for early discussions about ACP

- Dying to talk discussion starter http://dyingtotalk.org.au

(*continued*)

Box 1 (continued)

- Conversation Project http://theconversationproject.org
- Singapore Advance Care Planning Workbook https://livingmatters.sg
- ACP Australia www.advancecareplanning.org.au
  - Includes resources for patients and links to other websites. This includes resources in languages other than English

Resources for more in-depth discussion about ACP

- New South Wales of Australia Central Coast ACP workbook: http://www.cclhd.health.nsw.gov.au/patientsandvisitors/CarerSupport/cpa/Documents/ACP_Workbook.pdf
- PREPARED https://www.prepareforyourcare.org/
- Canadian workbook http://www.advancecareplanning.ca/resource/acp-workbook/
- NZ website includes an e-learning module for consumers http://www.advancecareplanning.org.nz/how-to/

7.2 Advance Care Planning for Someone with Chronic Illness or a Well Elderly Person

This group has a greater risk of dying, and/or risk of losing capacity to make healthcare decisions, than a healthy adult younger than 75, but they are not yet likely to be approaching the final months of life. For these patients, health professionals should proactively educate and "plant the seed" about advance care planning. Some key components of advance care planning for this group include:

- Asking the patient about his or her preferred substitute decision-maker; prompting the patient to consider legally appointing a substitute decision-maker, especially if his or her preferred substitute decision-maker is someone different according to the hierarchy in their state; and ensuring there is a record of the patient's preferred substitute decision-maker in the medical record
- Encouraging the person to consider an advance care planning discussion with his or her preferred substitute decision-maker, a health professional(s), and any significant others to help him or her reflect on his or her values and preferences if he or she were ever to be unwell to speak for himself or herself.

If the patient is ready to discuss advance care planning, a workbook or web resource (see Box 1) may help patient reflect on his or her wishes and guide the discussion. Regardless of whether or not the patient wants to complete an advance directive, it's helpful to record a summary of where the discussion is up to in the medical record. It is also important that this documentation is accessible in emergency situations and at the time of transitions between care settings, for example, in the electronic medical record or in a patient-held medical record.

7.3 Advance Care Planning for Someone Whose Health Is Deteriorating and Approaching the Last Months (or Weeks/Days) of Life

This is the population where palliative care providers are most likely to be involved in the discussion. If the patient is likely to have only months to live, the clinician should review what advance care planning discussions have already taken place and any advance care planning documents that have been completed. The person should also be provided a further opportunity to reflect on his or her priorities and try to establish a clear plan for the goals of care if/when the person's health deteriorates. It is important to remember that, even if the patient likely has months to

live, he or she may still wish to pursue disease-specific therapies. Questions suggested by Atul Gawande (2014) to help patients consider whether particular treatments are worthwhile for them include the following: *"What is your understanding of the situation and its potential outcomes? What are your fears and what are your hopes? What are the trade-offs you are willing to make and not willing to make? And what is the course of action that best serves this understanding?"*

If the patient is already in the final weeks or days of life, discuss "good dying" rather than offering interventions like CPR if he or she is unlikely to have therapeutic benefit. Explore the person's preferred place of care during terminal phase and preferred place of admission if required.

For people whose health is already deteriorating (likely life expectancy is months or less), it is important to translate advance care plans into actionable medical orders that can transition across care settings in case of an emergency, e.g., Physician Orders for Life-Sustaining Treatment (POLST) or Medical Orders for Life-Sustaining Treatment (MOLST) forms, resuscitation plans and/or ambulance plans.

Once a person no longer has capacity to take part in decisions about his or her care, health professionals need to review any previously completed advance care plans and talk with the person's substitute decision-maker(s) to ensure treatment plans are consistent with the person's preferences and appropriate to his or her circumstances.

8 Tips for Advance Care Planning Conversations

The general aims of the advance care planning conversation are to:

- Establish who the person would like to speak for him or her, if he or she ever became unable to speak for himself or herself
- Ensure the person understands his or her medical situation to the level that he or she wishes
- Explore the person's
  - Values, beliefs, goals, fears, and concerns relevant to his or her current and future care
  - Concept of a "reasonable outcome" or health state (if appropriate and the person health is not already approaching the final days of life)
- Determine if there are any treatments that a person does, or does not want now or in the future
- Explore any other wishes the person may have about his or her care in the future and at the end of his or her life
- Facilitate documentation of the person's wishes in an advance care directive if he or she wishes and/or document any verbal wishes in his or her electronic and paper medical record

General recommendations for advance care planning discussions are shown in Table 1. Further strategies and example questions and phrases for advance care planning discussions are shown in Table 2. Other resources that may be useful are shown in Box 1.

The key to initiating advance care planning is to sensitively offer to discuss the topic. Describe simply and clearly what advance care planning is. Give a rationale for why having these conversations may be helpful for the person, their family, and the healthcare team. While it is important to be proactive about initiating advance care planning discussions, it is also important to give the patient the option not to discuss it or to defer the discussion to another time if he or she prefers. Not all patients want to discuss and plan for future care. If the patient does not currently wish to discuss the topic, raise it again when the person's condition or situation changes. Some patients prefer their families to be involved in such discussions on their behalf.

Subsequent steps in the advance care planning discussion include (Johnson et al. 2016):

- Assessing the patient's and/or family's readiness to discuss future care

Table 1 Summary of recommendations for discussing advance care planning and end-of-life issues with patients with advanced life-limiting illnesses and their families, modified from the PREPARED framework

P	**Prepare for the discussion**, where possible
	Confirm the clinical situation and appropriate treatment options
	Try to ensure privacy and uninterrupted time for discussion
	Mentally prepare yourself
	Gauge the person's readiness to discuss his or her future care
	Negotiate who should be present during the discussion
R	**Relate to the person**
	Introduce yourself and explain your role and develop rapport
	Show empathy, care, and compassion during the entire consultation
	Consider cultural and contextual factors which may influence preferences
	Use appropriate body language and actively listen
E	**Elicit patient preferences**
	Clarify the patient's or caregiver's understanding of their situation, and how much detail they want to know, before giving new medical information
	Identify the patient's preferred substitute decision-maker (if not already identified)
	Elicit the patient's goals, values, and beliefs relevant to the discussion
	Elicit the patient's priorities for care and preferences regarding current and future treatment
	Explore the family's concerns and priorities where applicable
	Summarize the patient's (and family's) most important priorities and check if you have it right
P	**Provide information** tailored to the individual needs of both patient and their family
	Ask permission to discuss what to expect
	Pace and tailor delivery of information about the clinical situation and prognosis to the patients'/families' current understanding and wish for information
	Use clear, jargon-free, understandable language
	Explain uncertainty, limitations, and unreliability of prognostic information
	Consider offering recommendations for the patient's medical care that are clinically appropriate and align with the patient's priorities
A	**Acknowledge emotions and concerns**
	Explore and acknowledge the patient's and caregiver's fears and concerns and their emotional reaction to the discussion
	Respond to the patient's or caregiver's distress regarding the discussion, where applicable, and consider their needs for additional support
	Acknowledge your own emotions – discussing end-of-life issues is challenging
R	**Realistic hope** should be fostered (e.g., peaceful death, support):
	Be honest without being blunt or giving more detailed information than desired
	Do not give misleading or false information to try to positively influence a patient's hope
	Reassure that all support and care will be given to control pain and other symptoms
	Explore and facilitate realistic goals and wishes and ways of coping on a day-to-day basis, where appropriate
E	**Encourage questions** and further discussions
	Encourage questions and information clarification; be prepared to repeat explanations
	Check understanding and if information provided meets needs
	Leave the door open for topics to be discussed again in the future
D	**Document**
	Assist the patient to document his or her wishes in an advance care directive if desired and/or the formal/legal appointment of a substitute decision-maker
	Write a summary of what has been discussed in the medical record
	Speak or write to other key healthcare providers involved in the patient's care. As a minimum, this should include the patient's general practitioner

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Table 2 Strategies and example questions and phrases for advance care planning discussions

Strategy	Example phrase or question
Describe simply and clearly what advance care planning is. Give a rationale for why these conversations can be helpful for families and the healthcare team	*"Have you thought about the type of medical care you would like to have if you ever become too sick to speak for yourself? This is the purpose of advance care planning to ensure that you are cared for the way you would want to be, even when communication may be impossible"*
	"Have you ever talked about your wishes, values, and beliefs about medical treatment and care in case you were ever injured or became too ill to speak for yourself?"
	"It's often easier to talk through tough decisions when there isn't a crisis"
	"Is this something that you would like to discuss further?"
Involve the potential proxy decision-maker in the discussions and planning so that he or she understands the patient's wishes	"*Sometimes people with your type of illness lose the ability to make decisions or communicate their wishes as the illness progresses. Who would you like to make decisions for you if you were unable to do this yourself?"*
	If the person can identify a substitute:
	"Have you spoken to this person about what would be important to you about your care if you were very ill?"
	"Would you like to talk this through with them?"
	"Would you like me to assist you with this?"
Use open-ended questions to develop an understanding of the patient's values and to help him/her to work out goals and priorities related to their remaining life and treatment of the illness, and document the patient's preferences	*"What is most important to you now (or regarding your care in the future)?"*
	"What aspects of your life do you most value and enjoy?"
	"When you look at the future, what do you hope for?" "What concerns you?"
	"Do you have any thoughts about how you would like to be cared for in the future if you became more unwell?"
	"How would you want decisions regarding your care to be made?"
	"Is there a specific person that you would like us to speak to?"
	"Is there anything you worry about happening?"
	"What would you not want to happen to you in terms of your care?"
	"Are there any situations where you would regard life-prolonging treatments to be overly burdensome?"
	"Is there anything else you would like me to know about your values and priorities for care if you were very unwell?"
Consider using clinical scenarios to structure the discussion, particularly if the patient is still at an early stage of his or her illness	Consider referring to an advance care planning workbook; see consumer resources in Box 1
Emphasize that advance care planning is an ongoing process that will need to be reviewed and updated periodically, as the patient's wishes may change over time, particularly with major health changes	*"These are discussions we may need to revisit if there are changes in the course of the illness"*

(*continued*)

Table 2 (continued)

Strategy	Example phrase or question
Ensure that other health professionals who are involved with the patient's care are aware of the patient's wishes. If an advance care directive is completed, make sure its existence is known by all the treating health professionals and is available when the patient's place of care is being changed (e.g., from nursing home to hospital, during hospital transfers)	

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- Exploring the patients' understanding of their medical situation and any unmet information needs
- Providing information as appropriate to the person's information needs and medical situation
- Exploring the patient's values, goals, priorities, hopes, fears, and concerns for the future
- Exploring if there are any situations, treatments, or health states the patient would find unacceptable
- Summarizing your understanding of the person's most important wishes for future care
- Considering any other specific treatment options relevant to the person's circumstances that may need to be discussed
- Considering offering to make a recommendation for future medical care, if the person were to become too sick to speak for himself or herself, based on his or her values and wishes
- Helping the patient to document his or her wishes

Discussions about advance care planning can be thought of as a process that unfolds over many conversations and which evolves as the person's illness progresses. Preferably such discussions should commence prior to illness onset or early in the course of a life-limiting illness and revisited over time. A hypothetical question can be a useful way of gently initiating advance care planning discussions for patients who are still very focused on treatments for their underlying illness, for example, *"While we are hoping that things go well with this treatment, if by some chance you didn't get better, what would be most important to you?"* Phrases such as *"we can hope for the best at the same time as preparing for the rest"* may be useful. When patients or family members ask for treatments that you do not think will be beneficial, the use of an *"I wish"* statement can allow the clinicians to align themselves with the patient, being supportive as well as being honest (give reference), for example, *"I wish that that treatment would help. I am concerned in your case that it would make you more unwell rather than better."*

9 Future Research Directions

Much more research is needed to help us better understand how to optimally deliver advance care planning. The following are suggested as topics in particular need of research.

A wide range of tools have been developed to help with clarifying risks and benefits of treatment and eliciting patient preferences based on his or her values, but evidence is limited regarding their efficacy (Cardona-Morrell et al. 2017).

Certain populations have particular advance care planning needs that warrant special attention. For example, more research is needed into ways of involving people with dementia in advance care planning to whatever extent is possible.

While preferences for end-of-life care are relatively stable over time in people with advanced life-limiting illness versus earlier in the disease trajectory (Auriemma et al. 2014), more research is needed to explore why preferences change in a minority of patients and to confirm the utility of written advance care plans for future decision-making. Likewise, further research is needed to determine the best ways to support and prepare

substitute decision-makers for their role in future decision-making on behalf of a patient.

Rapid development in information and communications technology (ICT) affords exciting opportunities for advance care planning, including interactive tools to support decision-making and clarify values and preferences, as well as means of digitally recording, updating, and sharing advance care plans (Ostherr et al. 2016; Oczkowski et al. 2016; Luckett et al. 2015). There have even been a number of national initiatives linking advance care plans with electronic health records to improve accessibility at the point of care and enable regular updates (e.g., Australian Government Department of Health 2016). From the clinician user perspective, ICT solutions present an opportunity to see how plans may have changed over time and, when integrated with other electronic health systems, prompt on when to review plans with the patient (Huber et al. 2017). Evidence to date has largely been limited to processes (i.e., whether advance care planning was undertaken) rather than whether interventions improved end-of-life care.

Further evidence is also needed concerning the processes of advance care planning and mechanisms by which these translate into improved outcomes. For example, there is only low-level evidence that documentation of advance care plans or directives prompts clinicians to further discuss end-of-life care with patients rather than assume that no further discussion is needed (Lewis et al. 2016). Recent rhetorical emphasis on the importance of the advance care planning process over documentation has yet to be matched by research showing how the quality of the process – however measured – influences end-of-life care received.

Given established evidence for benefits from advance care planning versus usual care, head-to-head comparisons are now needed to evaluate the most cost-effective approaches in terms of clinician training (Chung et al. 2016), role allocation within multidisciplinary teams (Rietze and Stajduhar 2015), and intensity/frequency of initial advance care planning discussion and review. Evaluations of cost-effectiveness need to take into account the full extent of costs and benefits from the perspectives of the patient, healthcare system, and society, including any impacts on burden for informal carers and requirements for community-based care (Klingler et al. 2016; Dixon et al. 2015; Weathers et al. 2016).

10 Conclusion and Summary

Advance care planning is a core skill for palliative care professionals for direct care provision, to provide support and education for other clinicians involved with caring for patients with life-limiting illnesses, and as part of our role as advocates for improving end-of-life care more broadly in the community. This chapter has provided tips for advance care planning discussions across the disease trajectory. Evidence suggest that advance care planning can improve outcomes for patients and families and improve satisfaction with care. Nonetheless there remain many unanswered questions about the best ways to implement advance care planning in practice. Further work is needed to ensure that patient preferences that are discussed during advance care planning discussions are made readily available and able to assist decision-making at the point of care and to equip caregivers to be adequately prepared for their substitute decision-making role.

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Prognostication in Palliative Care

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_26

Abstract

Prognostication occupies a central role in medical decision-making. An understanding of prognosis and relevant disease trajectory models is key for healthcare professionals caring for patients with progressive life-limiting conditions. It is a challenging aspect of professional practice for many, both because of its inexact nature and fears regarding the impact of prognostic disclosure. The research literature presented provides insight into the fallible nature of clinical predictions of survival and factors that may mitigate against this, including an understanding of prognostic indicators. Prognostic indicators including biomarkers and prognostic tools, which may be applied in advanced cancer and life-limiting nonmalignant conditions, are reviewed. Desire for prognostic information varies between individuals and within individuals over time; the outcomes of research studies that elicited the views and preferences of patients and bereaved relatives regarding prognostic disclosure are presented. The challenges inherent in diagnosing dying and key considerations are discussed, within the context of recent discontinuation of the Liverpool Care Pathway in the United Kingdom.

We look for medicine to be an orderly field of knowledge and procedure. But it is not. It is an imperfect science, an enterprise of constantly changing knowledge, uncertain information, fallible individuals, and at the same time lives on the line. There is science in what we do, yes, but also habit, intuition, and sometimes plain old guessing. The gap between what we know and what we aim for persists. And this gap complicates everything we do. Atul Gawande, Complications: A Surgeon's Notes on an Imperfect Science, p. 7.

1 Introduction

To prognosticate is to foretell future events according to present signs or indications. It occupies a central role in assessment of patients' needs and decision-making, by clinicians caring for patients at the end of life. Yet, it is an inexact science, with many caveats. As a result, prognostic uncertainty can be a source of anxiety for both clinicians and patients and their families. The challenge for healthcare professionals imparting prognostic information to patients or family members is to provide information which is as accurate as possible using all relevant information and to communicate this sensitively while openly acknowledging the limitations of the information. In this chapter, the research literature relating to prognostic accuracy and possible determinants will be reviewed. Prognostic indicators in malignant and progressive nonmalignant conditions and available prognostic models or tools are presented, and key considerations to guide individualized prognostic disclosure are outlined. Finally, the evidence relevant to diagnosing dying is presented, with reference to key documents published since the discontinuation of the use of the Liverpool Care Pathway in the United Kingdom.

2 The Role of Prognostication in Palliative Care

A prognostication is a statement about what you think will happen in the future. Requests to prognosticate are a frequent occurrence for clinicians caring for patients with terminal illnesses.

However, readiness to seek a prognostication, or hear one, varies between individuals and within individuals over time. When seeking information about the future, patients and families often seek both qualitative information about what to expect from their condition or treatment and quantitative information regarding life expectancy. Knowing what to expect from one's disease and having one's family prepared for death are key priorities for patients with life-limiting conditions (Hagerty et al. 2005). Patients and families seek information regarding expected symptoms and effectiveness of symptom control, how the condition or treatment may impact on physical and cognitive functioning, and the prospect of recovery from acute complications.

Knowing what to expect from their condition and having an understanding of life expectancy can empower patients to choose how they spend their time. It also underpins their ability to engage in informed shared decision-making with clinicians regarding treatment options, including ceilings of medical care and resuscitation status. Families request prognostic information to help them prepare and to inform considerations such as the likely duration of a caring role or timing of taking time from work or visiting from abroad.

Prognostication also plays a key part in decision-making by clinicians. For many clinicians, prognosis determines the timing of referral to specialist palliative care services. In the United States, eligibility for Medicare hospice benefit is dependent on a physician certifying that expected prognosis is 6 months or less. For physicians, decision-making regarding potential treatment options for progressive disease is underpinned by consideration of both life expectancy and anticipated course of the disease. As an example, consider the case of a 50-year-old woman with metastatic breast cancer and lung metastases, who has recently had superior vena cava obstruction managed by stent insertion, who has a functional status of ECOG 3, and who has just been diagnosed with brain metastases. She doesn't wish for life-prolonging measures. Her preference is for optimal symptom control, and she is keen to avoid progressive dysphasia. In this situation the physician wishes to avoid subjecting the patient to cranial irradiation if she is unlikely to survive long enough to obtain benefit. The physician must assess the competing risks of death due to progressive extracranial disease and life expectancy exceeding time to dysphasia becoming refractory to steroid treatment. Such assessments can be informed by relevant literature where it exists, such as randomized controlled trials, which examine outcomes following treatment in similar cohorts.

3 Prognostication: An Inexact Science

The impact of erroneous prognostication at the end of life is well understood by patients, families, and the general public. Reports of inaccurate or unreliable predictions cause significant distress. Examples, which received significant media attention, include the case of Abdelbaset al-Megrahi who was convicted for the Lockerbie bombing and the results of recent systematic reviews of the accuracy of the "surprise question." Mr Megrahi was released from prison in Scotland in 2009 on compassionate grounds, after it was predicted that he would die from prostate cancer within 3 months; he died 2 years and 9 months later. The "surprise question (SQ)," which has been widely adopted as a method to identify patients with progressive nonmalignant life-limiting conditions, who may be nearing end of life and may benefit from a palliative approach to care, prompts clinicians to ask themselves if they would be surprised if the patient died within 12 months. The results of the reviews suggest that this method has poor to moderate accuracy and yields a high proportion of false positives (White et al. 2017; Downar et al. 2017). Media coverage of these findings prompted concern among the public that patients may have been inappropriately denied active treatment. Conversely, overestimations of life expectancy place patients at risk of being denied a good palliative care.

These high-profile cases demonstrate the fallible nature of prognostication in progressive or life-limiting conditions. In one pioneering study, which examined the accuracy of clinicians'

survival predictions, each physician referring a patient to outpatient hospice services within Chicago was asked to provide a clinical estimate of survival (CPS) for that patient. This data was compared with actual survival (AS). Three hundred and forty-three physicians provided survival estimates for 468 patients of whom 65% had a cancer diagnosis. Median AS was 24 days. The survival predictions were poorly accurate and systematically optimistic. An accurate CPS was defined as between 0.5 and 2 times the AS; only 34% of predictions were accurate. The mean ratio of CPS to AS was 5.3, and the correlation between CPS and AS was only 0.28. This study also shed some light on patient and physician factors associated with accuracy. Predictions for patients with longer AS had greater accuracy. Patients with cancer were more likely to have overoptimistic predictions. However, predictions of oncology specialists were more accurate than those of non-oncologists. Longer duration of doctor-patient relationship was associated with decreased accuracy (Christakis and Lamont 2000).

Vigano et al. studied the accuracy of oncologists in predicting survival for 233 cancer patients with terminal disease. The estimated median survival time for the group overall was 15.3 weeks. Again, prognosis was overestimated; the median overestimation was 4.8 weeks. The correlation between CPS and AS was moderate at 0.47 (Vigano et al. 1999). Although specificity of a CPS of less than 2 months was high (95%), the sensitivity was low (31%), indicating that participants failed to recognize a high proportion of patients with short life expectancy (see Box 1 for guide to methods of expressing the accuracy of predictive or diagnostic tests).

Box 1 Commonly Used Methods for Expressing the Accuracy of a Predictive or Diagnostic Test

Sensitivity, specificity, positive, and negative predictive values

Sensitivity, specificity, positive, and negative predictive values are illustrated using data extracted from Vigano et al. as referred to in the text (Vigano et al. 1999).

Actual survival (AS) ≤2 months	Clinical prediction of survival (CPS) ≤2 months		
	Yes	No	Total
Yes	23	51	74
No	8	151	159
Total	31	202	233

Sensitivity is the proportion of true positives correctly identified as such.

$= 23/74 = 31\%$

Specificity is the proportion of true negatives correctly identified as such.

$= 151/159 = 95\%$

Positive predictive value (PPV) is the proportion of patients with a positive test who are correctly diagnosed.

$= 23/31 = 74\%$

Negative predictive value (NPV) is the proportion of patients with a negative test who are correctly diagnosed.

$= 151/202 = 75\%$

Area under the Receiver Operating Characteristic curve (AUROC) and c-statistic

The area under the Receiver Operating Characteristic (ROC) curve represents the ability of a continuous measure (such as a prognostic score based on a number of variables) to discriminate between individuals who will experience one of two outcomes. The ROC is a plot of sensitivity against 1-specificity for different choices of cutoff. The higher the plotted line is above the 45° line (AUROC = 0.5), the better the prognostic ability of the tool. An AUROC of 1 would represent 100% sensitivity and specificity.

For binary outcomes, the AUROC is equivalent to the c-statistic or concordance statistic. The underlying assumption of the c-statistic is that for a discerning test or

(*continued*)

Box 1 (continued)
measure, for pairs of subjects within a dataset, an individual with a particular outcome will have had a higher probability for that outcome predicted than an individual who doesn't experience the outcome. The c-statistic represents the proportion of such pairs out of the total number of pairs with discordant outcomes.

Harrell's c-index is a variation of the c-statistic, which allows for inclusion of survival data that is censored. The interpretation of a censored survival is that the survival time represents the time at which an individual exited the study without experiencing the outcome of interest. Harrell's c-statistic is not equivalent to the AUROC.

Kappa statistic (κ)

This is used to express agreement between measures, which are categorical variables: in this case, predicted survival and actual survival. A weighted kappa statistic allows for classification into adjacent categories to be considered as partial agreement. $\kappa = 1$ represents complete agreement, and $\kappa = 0$ shows no more agreement than would be expected by chance alone (Kirkwood and Sterne 2003).

$\kappa > 0.67$ represent excellent agreement

$\kappa = 0.4$–0.75 represent fair to good agreement

$\kappa < 0.4$ represent moderate to poor agreement

Glare et al. conducted a systematic review of the literature on accuracy of physicians' CPS in patients with advanced cancer. They included survival predictions relating to 1563 patients, originating from 8 studies. In seven of the eight studies, survival was systematically overestimated; meta-analysis showed that AS was 30% shorter than predicted. They also demonstrated a linear relationship between CPS and AS until CPS reaches 6 months, after which it lacks predictive value, thus supporting the concept of a "horizon effect," a term borrowed from meteorology, whereby predictions are more accurate closer to the event. As the survival data was not normally distributed, correlation was assessed using nonparametric tests. Calculation of the Spearman rank correlation showed a strong association ($r = 0.60$) between log (AS) and log (CPS). The authors concluded that physicians' survival estimates are strongly correlated with actual survival but are miscalibrated, with systematic tendency to overestimation (Glare et al. 2003).

4 Impact of Characteristics of the Patient, Doctor, and Doctor-Patient Relationship on Accuracy of CPS

4.1 Patient Factors

The nature of the datasets included in the review and meta-analysis by Glare et al. precluded analyses of the impact of characteristics of the doctor and the doctor-patient relationship on accuracy. Regarding the effect of patient characteristics on accuracy of CPS, analysis of data from two studies that collected data pertaining to possible prognostic indicators, in addition to CPS, demonstrated greater accuracy of CPS in patients with lower performance status (Glare et al. 2003).

In a study of accuracy of CPS in 214 patients referred for palliative radiotherapy in Germany, researchers sought a CPS from referring physicians (A) and a radiation oncologist with more than 10 years experience (B) plus the cohort of radiation oncologists attending daily review meetings (C). CPS was recorded as a categorical variable of either less than 1 month, 1 to 6 months, or more than 6 months. They found, as per Vigano et al. that accuracy of CPS was extremely poor in the cohort of patients who died within the shortest time frame – in this case 1 month. Survival was overestimated in 96%, 71%, and 87% of the 33 patients by raters A, B, and C, respectively. The authors postulated that this might be due to physicians' reluctance to accept imminent death (Gripp et al. 2007). An alternative

hypothesis is that some deaths may have resulted from relatively unpredictable events: sepsis, venous thromboembolism, bleeding, or cardiac events. These have been shown to be the most common causes of death in patients who die with cancer and receive a postmortem (Pautex et al. 2013).

For patients with advanced disease, the nature of the diagnosis may impact on prognostic accuracy, specifically whether the patient has a cancer diagnosis or other progressive nonmalignant condition. Distinct illness trajectories have been described for progressive chronic illnesses (see Fig. 1). In malignant conditions, there is usually a slow overall decline in performance status, followed by a relatively rapid period of decline in function. Most weight loss, reduction in performance status, and impaired ability for self-care occur in patients' last few months (Murray et al. 2005). Recognition of these changes and lack of response to antineoplastic treatment facilitate relatively easy identification of the terminal phase of the illness.

It is noted that a change in trajectory has been observed in some cancers, such as breast or prostate cancer with bone metastases, which have increased survival but increased morbidity and lower functional level. Their illness course may

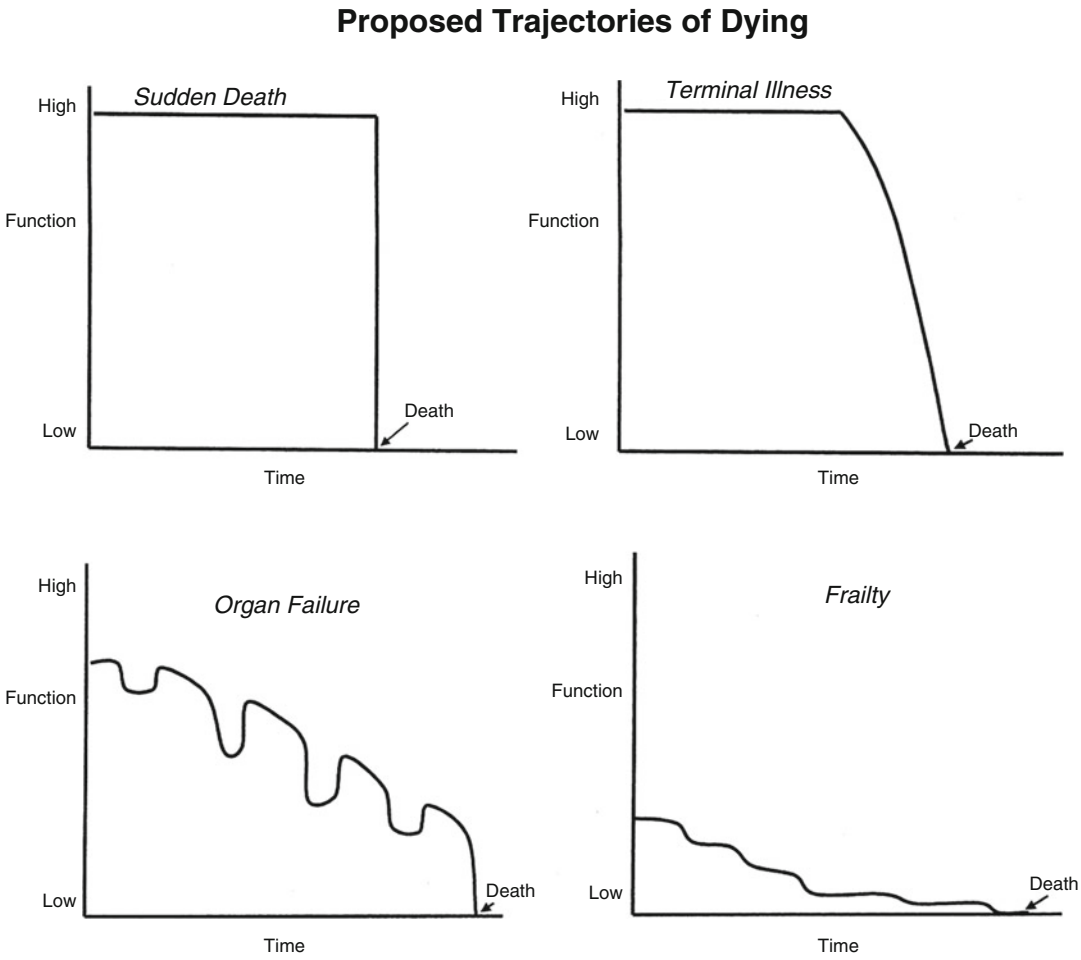

Fig. 1 Trajectories of dying. (Reproduced with permission from Lunney JR, Lynn J, Hogan C (2002) Profiles of older medicare decedents. J Am Geriatr Soc 50:1108–1112. Copyright © 1999–2017 John Wiley & Sons, Inc. All Rights Reserved)

be more similar to that of a chronic nonmalignant disease (Murtagh et al. 2004).

Patients with organ failure are usually ill for many months or years with occasional acute, often severe exacerbations. Deteriorations may be associated with hospitalizations and intensive active treatment, which may result in death or recovery, making recognition of dying or the terminal phase of illness especially difficult. With each episode the patient survives, a gradual deterioration in health and functional status is noted. The timing of death, however, remains uncertain. This is also referred to as "entry-reentry" disease trajectory.

Prolonged dwindling is a progressive disability from an already low baseline of cognitive or physical functioning as seen in brain failure (such as Alzheimer's or other dementia) or generalized frailty of multiple body systems. Such patients may lose weight and functional capacity and then succumb to minor physical events that may in themselves seem trivial but, occurring in combination with declining reserves, can prove fatal (Murray et al. 2005).

Hence, prognostication in progressive nonmalignant conditions is generally viewed as more challenging, and palliative care clinicians have professed to be more confident when estimating prognosis for patients with a cancer diagnosis. There is little data available to facilitate comparisons of prognostic accuracy. In one relevant study, researchers in the United States sought to assess the accuracy of prognostic estimates of hospital physicians, including trainees and specialists in internal medicine, cardiology, and oncology by asking them to estimate survival for three standardized patients: one with lung cancer and two with heart failure, one of whom had reduced ejection fraction and the other preserved ejection fraction. Accuracy of clinical estimates of survival was assessed against estimates generated by validated prognostic models: the surveillance, epidemiology, and end results (SEER)-Medicare database and Seattle Heart Failure Model, respectively. The proportion of accurate survival estimates was much higher for the lung cancer patient than the patients with heart failure (Warraich et al. 2016).

4.2 Clinician Factors

One might expect that prognostic accuracy improves with experience. However, there is limited reliable evidence to support this. Gripp et al. did not detect greater accuracy of CPS by the single prognosticating "experienced radiation oncologist with more than ten years experience" than the cohort of 15 more junior doctors who had a median of 1.7 years of professional experience in radiation oncology (Gripp et al. 2007). Conversely, Maltoni et al. assessed the accuracy of CPS against AS for four oncologists working full time for a Home Care Service for patients with advanced cancer. They observed that the correlation coefficient between CPS and AS was lower for the oncologist who had worked with the Home Care Service for the shortest time than for the oncologist with most experience with the Home Care Team (Maltoni et al. 1994). However, due to very small number of prognosticators in some or all of the comparator groups in both studies, it is quite possible that the observations relate to characteristics of the prognosticator other than years of experience. Authors of a recent systematic review sought to improve understanding of the impact of clinician-related factors on prognostic accuracy in advanced cancer (White et al. 2016). They encountered studies with apparently conflicting results. Due to heterogeneity between studies relating to characteristics of clinicians and patient populations plus, in some cases, limited description of clinician and patient cohorts, it was not possible to draw conclusions regarding the relationship between duration of experience and accuracy of CPS. However, examination of studies that describe characteristics of prognosticating clinicians and involve greater numbers of prognosticators might shed some light on this.

Bivariate analysis of data in the study by Christakis et al. showed no association between accuracy and years in medical practice, board certification, number of hospice referrals in past year, or number of medically similar patients in the past year. However, multivariate analysis showed that doctors in the top quartile of clinical experience were more likely to make accurate predictions (Christakis and Lamont 2000).

A multicenter study of the accuracy of survival predictions of palliative care clinicians relating to 1018 patients with advanced cancer did not demonstrate a relationship between prognostic accuracy and years of professional experience (Gwilliam et al. 2013). In the study by Gwilliam et al., results from bivariate analysis suggested that accuracy of palliative care clinicians' predictions is not affected by years of professional experience or board certification. The variation in observed relationship between accuracy and duration of professional experience between these two studies may result from differences relating to the analysis, characteristics of the prognosticating clinicians, or the duration of the doctor-patient relationship. Whereas in Christakis' study, the prognosticating physicians were heterogeneous in terms of specialty, all prognosticating clinicians were working in specialist palliative care in the study by Gwilliam et al. (2013). It is conceivable, that because consideration of prognosis plays such an integral part of assessment of patients' palliative care needs, that new palliative care staff quickly gain significant experience in prognosticating, acquiring knowledge relating to prognostic indicators from more senior staff relatively early. Early acquisition of these skills could account for the observed absence of relationship between duration of professional experience and accuracy.

This brings us to the question of whether prognostic accuracy varies with specialty. The report by an EAPC working group on prognostication in advanced cancer states that lack of experience in oncology and palliative care reduces accuracy (Maltoni et al. 2005). This was based on consensus opinion or inconclusive studies. Within the relevant literature, studies in which CPS is estimated by oncology or palliative care specialists do report greater accuracy than the study by Christakis, where CPS was estimated by a cohort of doctors from different specialties (Bruera et al. 1992; Glare and Virik 2001; Gwilliam et al. 2013; Christakis and Lamont 2000). This could be partly attributable to the difference in case mix, whereby all or the majority of patients in oncology or palliative care studies had advanced cancer, which has a slightly more predictable disease trajectory, than in the study by Christakis, in which 35% of patients had nonmalignant life-limiting conditions. However, one would expect experience and training in oncology and palliative care to be associated with greater accuracy, in predicting prognosis in patients with cancer. There is some evidence that specialty-specific experience and training can improve prognostic accuracy in other patient cohorts. In the study by Warraich et al. discussed above, cardiologists were more accurate at predicting prognosis in the hypothetical patient with heart failure and reduced ejection fraction than oncologists and generalists. No difference in accuracy for the patient with preserved ejection fraction was demonstrated. Cardiologists were less accurate than generalists and oncologists in estimating survival for the patient with lung cancer (Warraich et al. 2016).

Some researchers have sought to understand how prognostic accuracy varies among different members of the multidisciplinary team. In one early study, each member of a hospice inpatient team (a doctor, senior nurse, staff nurse, chaplain, and healthcare assistant (HCA)) estimated life expectancy of consecutive admissions, at the time of admission and at weekly intervals until death or discharge (Oxenham and Cornbleet 1998). For each team member, accuracy of the final prediction was more accurate than the initial prediction. While the doctor's predictions were the most accurate at time of admission and the HCA's the least accurate, the predictions of the HCA were the most accurate at the time of final prediction. The results of a similar study by Twomey et al. are not inconsistent with this; HCAs were the least accurate members of the multidisciplinary team (MDT) when it came to estimating survival of patients within 48 h of admission to an inpatient hospice (Twomey et al. 2008). The results of these small studies must be interpreted with caution because, again, the observations could reflect characteristics of the individuals involved, other than their profession. However, it may be that staff who work closely with patients and assist them with activities of daily living are well placed to detect changes in functional ability, severity of symptoms, and

patients' outlook, which are of prognostic significance in the last weeks of life.

There are conflicting results from other studies regarding the superiority of prognostic accuracy among doctors and nurses working within MDTs. Again, it is likely that these variances are attributable to heterogeneity among studies regarding other relevant factors such as timing of prediction, duration of clinician-patient relationship, or conclusions based on observed accuracy of a small number of prognosticators (White et al. 2016). One might expect that a CPS informed by MDT discussion would improve accuracy. The studies by Gripp et al. and Gwilliam et al. compared the accuracy of predictions by single prognosticators with consensus estimation by radiation oncology and palliative care MDTs, respectively. While both demonstrated that a higher proportion of patients had an accurate CPS when formulated by MDT consensus, the observed differences didn't reach statistical significance.

4.3 Doctor-Patient Relationship

In the study by Christakis et al., in multivariate analysis, longer duration of doctor-patient relationship was associated with decreased accuracy. In this study, the mean duration of the doctor-patient relationship was 159 weeks. Based on this, the authors proposed that accuracy of CPS might be improved by obtaining a second opinion from a colleague who doesn't know the patient well and is therefore less likely to have their judgment influenced by personal investment. Conversely, Gwilliam et al. did not detect a relationship between length of time that the clinician had known the patient and accuracy of predictions. However, in this study, in more than 90% of cases, the clinician had known the patient for less than 1 month.

There is some limited data to suggest that prognostic accuracy may improve with repeated measurements. In one study, doctors and nurses estimated survival of patients admitted to St Christopher's Hospice in London, on the day of admission. A subset of patients had a repeat CPS 7 days later. The correlation between AS and CPS was improved for both professional groups at 1 week compared with time of admission (Parkes 1972). Similarly, accuracy of final survival prediction before death was better for all members of the MDT, compared with the initial prediction at time of inpatient hospice admission, in the study by Oxenham and Cornbleet. Although there is evidence to suggest that treating a patient for an extended period of time may be associated with reduced prognostic accuracy, it stands to reason that a CPS formulated after an interval, such as 1 week in the case of a hospice inpatient, would be superior than one formulated at the time of admission. At the second time point, the clinician would have better knowledge of the patient, insight into their performance status, and be able to make an assessment regarding rate of deterioration.

5 How Do Palliative Care Clinicians Prognosticate?

This brings us to the question of what doctors consider when formulating a CPS for patients with progressive life-limiting diseases. It is probable that this varies somewhat, both between doctors and within the practice of individual doctors, depending on what the most salient prognostic factors are felt to be for a given patient. Specialist doctors and nurses in palliative care who participated in a qualitative study on prognostication referred to considering objective factors such as blood indices, extent of disease, and performance status, plus observations regarding rate of disease progression, symptom burden, and rate of overall deterioration. Rate of deterioration was considered to be particularly important, and participants highlighted the value of repeated patient assessments over time and incorporation of observations and opinions of nurses and HCAs, when formulating a CPS. Participants also described drawing upon relevant experience, pattern recognition, and intuition (Pontin and Jordan 2013).

In summary, while clinical predictions of survival are flawed, in that they are systematically miscalibrated and influenced by factors relating to the patient, doctor, and the doctor-patient relationship, they are strongly correlated with AS, at least

in the case of malignant diagnoses. The EAPC working group on prognostication in advanced cancer recommend that survival should be estimated using a combination of CPS and other prognostic factors, such as clinical signs and symptoms, biological markers, or prognostic tools which have been demonstrated to be of prognostic significance (Maltoni et al. 2005). They also recommend seeking a second opinion if the patient and doctor have a close relationship and repeated evaluations of CPS at fixed intervals.

Meta-analysis of data from two studies which assessed the accuracy of CPS and other possible prognostic indicators in advanced cancer demonstrated that CPS alone accounted for 51% of the variation in AS, while the other prognostic factors accounted for only 35% of the variance in AS, thus illustrating the supremacy of CPS over traditional prognostic indicators alone (Glare et al. 2003). This isn't altogether surprising, as physicians describe incorporating prognostic indicators, pattern recognition, and the other less tangible elements into their CPS (Pontin and Jordan 2013). In addition to the factors discussed above, CPS can encompass considerations such as the potential to respond to antineoplastic treatment or will to live.

6 Prognostic Indicators

Prognostic indicators are factors demonstrated to be associated with survival. They encompass features of the disease, characteristics of the patient, clinical signs and symptoms, biological indices, and complications of disease, such as hypercalcemia of malignancy or onset of dysphagia.

7 Prognostic Indicators in Advanced Cancer

Prognostic indicators in cancer can be considered to relate to the features of the patient, the tumor, or patient-tumor interaction. While at the relatively early stages of incurable cancer, selected characteristics of the patient, tumor, and patient-tumor interaction all seem to have prognostic significance, in the advanced stages of cancer, only clinical symptoms and signs, in other words, features of the patient-tumor interaction retain prognostic significance.

Hauser et al. conducted a systematic review of studies examining prognostic indicators in patients with incurable solid tumors and only included studies in which the median survival was 3–24 months. For each variable they reported the number of studies testing it, the total number of patients in the studies, the types of cancer examined, and the frequency of statistically significant results from univariate and multivariate survival analyses (Hauser et al. 2006). They did not comment on methodological quality of studies or level of evidence available for each variable. The variables found to have a statistically significant association with survival in multivariate analysis, in at least half of studies that conducted multivariate analysis for that variable, are listed in Table 1. In particular, performance status was shown to be associated with survival in multivariate analysis, in 33 of 34 studies, totaling more than 10,000 patients. The symptoms associated with the cancer anorexia cachexia syndrome shown to be associated with survival were weight loss, anorexia, and nausea.

The EAPC working group on prognostication in advanced cancer conducted a systematic review of prognostic variables identified in studies of patients with median survival less than or equal to 90 days (Maltoni et al. 2005). The authors graded the strength of their recommendations based on the level of evidence as determined by study design and methodological quality. Characteristics of the patient or the tumor were not associated with survival. A number of variables were shown to be associated with survival, all of which relate to signs and symptoms of advanced disease. These variables are listed in Table 1. For each, the association with survival has been demonstrated, either consistently in exploratory studies with low risk of bias or in one heterogeneous meta-analysis or confirmatory study with low risk of bias. The symptoms associated with the cancer anorexia cachexia syndrome shown to be associated with survival were anorexia, weight loss, dysphagia, and xerostomia.

Table 1 Prognostic factors in advanced cancer (see text for explanatory notes regarding level of evidence)

	Prognostic factors identified in patient cohorts with median survival 3–24 months (Hauser et al. 2006)	Prognostic factors identified in patient cohorts with median survival less than 90 days (Maltoni et al. 2005)
Patient factors	Number of comorbidities	
Tumor factors	Presence of metastatic disease	
	Lung primary versus other primary	
	Liver, visceral, or cerebral metastases	
	Pleural effusion	
Patient-treatment factors	Receipt of antineoplastic therapy	
	Response to antineoplastic therapy	
	Performance status	
Patient-tumor interaction	Symptoms associated with cancer anorexia cachexia syndrome	
	Dyspnea	
	Patient-rated emotional quality of life	Delirium
	Patient-rated physical quality of life	

As Table 1 shows, symptoms of the cancer anorexia cachexia syndrome, dyspnea and poor performance status, are of prognostic significance in both the earlier and later stages of incurable cancer.

7.1 Biomarkers

Biomarkers can be defined as objective, quantifiable characteristics of biological processes, quantifiable in bodily fluids and tissues. Researchers and clinicians have attempted to produce a variety of prognostic models incorporating biomarkers to determine patient suitability for treatments and predict longer-term survival. However, there is less evidence available for biomarkers and models that are useful in prognostication in the last weeks and days of life. If identified, we must consider the additional benefit of any biomarker, in the context of current best clinical assessment available for predicting prognosis. In the clinical setting, any biomarkers identified must primarily provide additional information that cannot be gleaned from other assessments, such as physical examination, clinical observations, or functional assessment. Secondly, the test must be accessible to clinicians, acceptable to the patient, and not be prohibitively time consuming, complex, or expensive. Finally, the results of the test should help inform decision-making. Biomarkers in nonmalignant diseases are discussed separately below.

7.2 Biomarkers of Prognostic Significance in Advanced Cancer

A recent systematically structured review by Reid et al. summarized the current evidence for prognostic biomarkers in patients with advanced cancer (defined as study populations with median survival $\leq$90 days) (Reid et al. 2017). In malignant disease, established prognostic biomarkers relate to the inflammatory response and hepatic and renal dysfunction.

7.2.1 Hematological and Systemic Inflammation

Malignancy prompts an inflammatory response, and evidence of progressive change in inflammatory markers toward the end of life has prognostic significance. Elevated levels of interleukin-6 (IL-6) have been demonstrated toward the end of life, particularly peaking in the last week of life. It is hypothesized that circulating macrophages and T lymphocytes produce IL-6 in response to tumor burden or plasma IL-6 is produced by the tumor mass itself (Iwase et al. 2004). Interleukin-1 (IL-1) and IL-6 both stimulate hepatic synthesis of C-reactive protein (CRP) and ultimately the

systemic inflammatory response. Accordingly, it has been consistently observed that elevated serum CRP is associated with poor prognosis, in predominately retrospective studies across different cancer groups. The magnitude of CRP elevation may correlate with survival; studies using >10 mg/l as the threshold for defining "elevated" CRP show higher mortality than those using >5 mg/l. In addition, there is clear evidence of variation across cancer types, and therefore it may be that the use of CRP in prognostication would be most helpful in predicting cancer-specific survival (Dolan et al. 2017).

Several studies have identified a positive correlation between white blood cell count (WBCC) and poor prognosis. Lymphopenia, in particular, has been identified as the key abnormality, with a high neutrophil: lymphocyte ratio also associated with poorer prognosis (Maltoni et al. 2005; Dolan et al. 2017). This is in keeping with the known, but not clearly understood, immunodeficiency toward the end of life in patients with advanced cancer.

7.2.2 Hepatic Dysfunction

It is recognized that an elevated serum lactate dehydrogenase (LDH) level is associated with a poor prognosis. It has also been used in some contexts to monitor tumor aggressiveness and response to treatment and has been incorporated into prognostic models for patients with malignancy. In addition, early evidence suggests that LDH levels may increase significantly in the last 2 weeks of life. This may identify it, among others, as a useful biomarker in prognosticating toward the end of life, although the quality of the evidence of its prognostic value in the dying phase is limited by small sample size in a single study (Reid et al. 2017). More research is indicated in this particular phase of illness before it could reliably be used in prognosticating in the last weeks of life.

An association between high vitamin B12 levels and poor prognosis in patients with advanced cancer has been established. One study carried out by Geissbühler et al. demonstrated this relationship, showing a significant correlation between poor prognosis and elevated serum B12 (Reid et al. 2017). Interestingly, this study again showed CRP to be one of the most significant biomarkers, but B12 remained an independent marker of prognosis. The mechanism is unclear.

Low serum albumin levels have been shown to be associated with poor outcomes across cancer groups. In meta-analysis, the association between serum albumin <35 g/l and overall survival in patients with advanced cancer was significant, with HR 2.21 (Dolan et al. 2017). Serum albumin has therefore been incorporated as a biomarker into prognostic models such as the Prognosis in Palliative care Study (PiPS) model (Gwilliam et al. 2011). Albumin levels have been shown to decline into, and including, the last weeks of life in some studies, while in other studies of patients in the last weeks of life, it did not have adequate prognostic impact to be retained in the final prognostic model. It has been postulated that this may be because other correlated variables, such as reduced oral intake, explain more of the variation during this phase (Maltoni et al. 2005; Hauser et al. 2006). Alanine transaminase (ALT) was found to be associated with prognosis in the last 2 weeks of life by Gwilliam et al. (Gwilliam et al. 2011). Elevated alkaline phosphatase (ALP) and aspartate aminotransferase (AST) have also been shown to be useful in predicting prognosis.

7.2.3 Renal Dysfunction

The utility of assessment of renal dysfunction in predicting prognosis in advanced cancer is unclear. An elevated urea level was identified as an independent predictor of 2-week and 2-month survival in patients with advanced cancer who participated in the PiPS development study (Gwilliam et al. 2011). However, the evidence for other markers of renal dysfunction being useful in prognostication at the end of life in this group is inconclusive.

8 Prognostic Tools in Advanced Cancer

A number of tools have been devised to assist prognostication in patients with advanced cancer. These are described in Table 2. The included components of the Palliative Prognostic Index

Table 2 Prognostic tools for use in advanced cancer and selected validation studies

Tool	Variables included	Patient cohort	Accuracy	Comments
Palliative Prognostic Index (PPI) (Morita et al. 1999)				
Total score predicts survival of less than 3 weeks or less than 6 weeks or 6 weeks or more Independent validation study	Palliative Performance Scale, oral intake, presence of edema, dyspnea at rest and delirium	Hospice inpatients $N = 95$	For prediction of less than 3 weeks PPV = 80%, NPV 87% Sensitivity 83% Specificity 85% For prediction of less than 6 weeks PPV = 83%, NPV 71% Sensitivity 79% Specificity 77%	
Independent validation study (Stone et al.)		Hospitalized patients or community-based patients referred to SPC Services $n = 194$	For prediction of less than 3 weeks PPV = 86%, NPV 76% Sensitivity 56% Specificity 94% For prediction of less than 6 weeks PPV = 91%, NPV 64% Sensitivity 63% Specificity 92%	43% were receiving palliative radiotherapy or chemotherapy
Palliative Prognostic Score (PaP Score) (Maltoni et al. 1999)				
Total score predicts probability of 30-day survival, according to three categories: (A) >70%, (B) 30–70%, and (C) <30%	CPS, Karnofsky Performance Status, anorexia, dyspnea, total white cell count, lymphocyte percentage	Multicenter study. Details of centers not described $N = 451$ Median survival =33 days	The 30-day survival = 86.6% for group A, 51.6% for group B, and 16.9% for group C	Patients with hematological malignancy or renal tumors excluded
Independent validation study (Glare and Virik 2001)		Hospitalized patients referred to SPC Service $N = 100$ Median survival =30 days	The 30-day survival = 66% for group A, 54% for group B, and <5% for group C	Patients with all cancer diagnoses included
Prognosis in Palliative care Study (PiPS) (Gwilliam et al. 2011)				
Total score predicts survival of less than 14 days ("days"), 14–55 days ("weeks"), or more than 55 days ("months")	PiPS-A and PiPS-B are separate models. PiPS-B incorporates blood test indices. Score is calculated using web-based algorithm.	Multicenter study Hospice inpatients and hospitalized patients or community-based patients referred to SPC services $N = 1018$	PiPS-A Harrell's c-statistic =0.69 PiPS-B Harrell's c-statistic = 0.67	Blood tests not conducted in patients who lacked capacity to consent
Independent validation study (Baba et al. 2015b)		Multicenter study Hospice inpatients and hospitalized patients or community-based patients referred to SPC Services $N = 2212$ (PiPS-A) (PiPS-B) $N = 1257$	PiPS-A; absolute agreement between PiPS and AS in 56–60% of cases Weighted kappa =0.39–0.48 PiPS-B; absolute agreement in 60–62% of cases Weighted kappa =0.48–0.51 (Results reported separately for each care setting)	Modification of original PiPS, whereby AMT ≤3 was determined by physician proxy rather than patient interview

See Box 1 for guide to interpretation of statistical tests used
PPV positive predictive value, *NPV* negative predictive value, *SPC* specialist palliative care, *CPS* clinical prediction of survival, *AMT* abbreviated mental test

(PPI) and Palliative Prognostic Score (PaP) generally reflect the variables that have been found to have prognostic significance in cohorts with median survival less than 90 days.

The PiPS incorporates two different models, one for patients who have had the relevant blood tests within 4 days (PiPS-A) and another for those who haven't (PiPS-B) (Gwilliam et al. 2011). In addition to factors relating to patient-tumor interaction or signs and symptoms of advanced disease, the models include some tumor-related factors and blood indices such as albumin. While this may initially appear inconsistent with the findings of the EAPC working group's systematic review, instead, it probably reflects the way in which the models were developed, with the aim of discriminating between patients who will live for "days" defined as up to 13 days, "weeks" defined as 14–55 days, or "months" defined as more than 55 days. While tumor-related variables and some of the blood result indices were not included in best-fit models for explaining survival of "days" or more, they did appear to explain some of the variation in survival between "weeks" and more. The median survival for patients predicted to survive "months" was 92 days and 101 days in the PiPS-A and PiPS-B models, respectively. The variables included and access to the web-based algorithm is available at http://www.pips.sgul.ac.uk.

It is difficult to directly compare the accuracy and utility of the different tools from results abstracted from separate validation studies due to differences in methods, patient cohorts, and methods of presenting results. One study, published in 2015, sets out to compare the feasibility and accuracy of the tools in a single cohort of patients (Baba et al. 2015a). The PPI, PaP Score, D-PaP Score, and modified PiPS were completed for 2361 patients referred to 58 palliative care services (hospital-based, hospice inpatient, and community-based) in Japan. The modification to the PiPS model was related to the method of determining the Abbreviated Mental Test variable as outlined in Table 2. Accuracy and feasibility was assessed for patients not receiving active chemotherapy for each setting and for patients receiving chemotherapy in any setting. The D-PaP Score is a modification of the PaP Score that includes delirium as a variable. The PPI and modified PiPS-A had highest completion rates (>90%) for all four subgroups. Progressively lower proportions of community and hospice-based patients had adequate data for completion of all items on the PaP Scores (PaP and D-PaP) and PiPS-B, respectively. This finding reflects the proportion of patients in these settings who had the relevant blood results available for completion of the PaP Scores (total white cell count and lymphocyte percentage) and PiPS-B (C-reactive protein, total white cell count, platelet count, lymphocyte count, neutrophil count, alkaline phosphatase, alanine transaminase, albumin, and urea). The PaP Scores were completed in 62% and 37% of patients in hospices and at home, respectively. Accuracy, defined as the sum of true positive and true negative cases, divided by the total number of cases was greater than 69% for all tools, in all subgroups. Differences in accuracy between tools across subgroups were within 13% in all cases. The c-statistic was calculated for the PPI and PaP Scores. Although all had a c-statistic $\geq$0.75 in all settings, this was lower for the PPI for all four subgroups, with the exception of predicting survival less than 3 weeks in patients receiving chemotherapy. The authors concluded that all tools have reasonable accuracy although this is marginally lower for the PPI. However the PPI was convenient to use as it contains only five items and can be calculated at the bedside without the need for blood results.

Is there evidence that using a prognostic tool can improve accuracy of CPS in patients with advanced cancer? Morita et al. compared the accuracy of experienced palliative care physicians at predicting survival in hospice inpatients using the PPI, with accuracy of the same physicians estimating CPS without the use of prognostic tools in an historical cohort. The use of the PPI was associated with reduced incidence of serious prognostic errors, defined as a difference between CPS and AS of $\geq$28 days or CPS at least twice or as long or half as long as CPS. A palliative care MDT in an Australian cancer center compared the accuracy of CPS estimated by the MDT, with accuracy of the PaP Score (which incorporated

the same MDT formulated CPS) for a series of outpatients and inpatients (Mendis et al. 2015). Correlation coefficients between AS and MDT CPS and AS and PaP Score were very similar at 0.53–0.57 for outpatients and 0.64–0.66 for inpatients. The Harrell's c-index for the PaP Score in outpatients and inpatients, respectively, was 0.611 and 0.709, while the corresponding Harrell's c-index for the MDT CPS was 0.658 and 0.720, respectively, thus showing no clear advantage of the PaP score over the MDT CPS alone.

Although we do not, as yet, have consistent evidence that the use of prognostic tools improves accuracy of CPS in advanced cancer, the available evidence demonstrates that the tools provide accuracy comparable to the CPS of physicians who are experienced in oncology and palliative care. The observed agreement between predicted and observed survival of at least 69% in the study by Baba et al. for the PPI, D-PaP and PaP Scores, and PiPS models compares favorably with the CPS of palliative care clinicians admitting patients to palliative care services as reported by Gwilliam et al. (56–57.5%) and is similar to reported accuracy of two experienced palliative care physicians at predicting survival less than 4 weeks (68%) (Bruera et al. 1992). It is also probable that, by virtue of their relatively objective nature, the use of a prognostic tool may improve accuracy of all physicians in circumstances associated with reduced accuracy of CPS, such as a close relationship between doctor and patient.

9 Prognostic Indicators and Tools in Life-Limiting Nonmalignant Conditions

Many tools have been developed to help predict outcomes for patients with progressive nonmalignant conditions. Although in the main, they incorporate key prognostic indicators, they have generally been designed to prognosticate over longer terms. The components of some have been determined by expert consensus, while others are derived from clinical cohorts attending specialist clinics or data obtained in the course of clinical trials. Hence, the utility of many of these tools within palliative care practice is uncertain, due to poor generalizability and lack of validation in patients considered to have palliative care needs.

9.1 Heart Failure

The prognosis for patients with heart failure is poor; 30–40% of patients diagnosed with heart failure die within 1 year. It is a disease that predominantly affects older people. The disease trajectory is characterized by a slow decline, punctuated by sudden dips in functioning related to acute exacerbations, from which the patient has a risk of dying or recovering. Prognostication is challenging, and widely used tools have been shown to be inaccurate at predicting survival of less than 12 months. The best-known and most widely used prognostic tool is the Seattle Heart Failure Model (SHFM) which incorporates demographic and clinical information, etiology, and blood result indices and takes account of the classes of medication and devices being used to manage the condition. However it has been shown to overestimate survival in cohorts of community-dwelling patients with heart failure, patients awaiting cardiac transplantation, and elderly patients with heart failure admitted acutely to hospital (Haga et al. 2012). The SHFM predicted that only 6 of 138 community-dwelling patients with New York Heart Association class III and IV heart failure would have a life expectancy of 1 year or less in a study by Haga et al. Forty-three of the 138 died within 1 year. The sensitivity of a predicted survival of 1 year or less was low at 12%, while specificity was high at 99%. The SHFM model was derived and validated from data collected during randomized controlled trials. Hence the participants were not representative of the general population of people living with heart failure, in that they were younger and did not have significant renal impairment, leading to reduced sensitivity of the tool. Neither renal impairment nor brain natriuretic peptide (BNP) is included in the SHF, although both have been demonstrated to be of prognostic importance

(Haga et al. 2012). Haga et al. also tested the ability of the Gold Standards Framework (GSF) Prognostic Indicator Guide to predict survival of a year or less in the same cohort. The use of the GSF is advocated within Europe to assist identification of patients who may be nearing end of life and would benefit from palliative care, based on an assessment that they meet two of the following four criteria: New York Heart Association (NYHA) stage III or IV heart failure, an answer of "No" to the "surprise question" "Would you be surprised if this patient died in the next 6-12 months?," repeated hospital admissions with symptoms of heart failure, and difficult physical or psychological symptoms despite optimized tolerated therapy. This predicted survival of 1 year with sensitivity of 83% but specificity of 22% and overall accuracy of 41%.

Biomarkers in heart failure have been isolated, which not only have prognostic value but, in some cases, show improvement in response to treatment escalation or have become a focus for targeted interventions. Inflammatory processes have been implicated both in the pathogenesis of cardiac failure and with adverse outcomes. Sympathetic nervous system activation and its negative consequences have been identified in heart failure, prompting research into associated neurohormonal markers, including BNP and endothelin (Braunwald 2008). Pro-BNP has been identified as useful in the context of predicting longer-term survival (Huang et al. 2016). It has also been identified as the most significant predictor of mortality and hospitalization for patients with heart failure (Braunwald 2008). Big endothelin, a neurohormone which stimulates smooth muscle contraction, proliferation, and vessel fibrosis, is also a useful biomarker in predicting prognosis. To date, better understanding of its role has not translated into effective novel treatments, as the endothelin-receptor antagonists trialled have not been successful.

In the context of pathological remodeling of the ventricles in patients with heart failure, markers of collagen biosynthesis have been shown to be particularly elevated in those with worse outcomes. ST2, a receptor for interleukin-33, has been implicated in cardiac remodeling. Raised levels of serum ST2 are indicative of ventricular biomechanical overload and of prognostic significance (Bhardwaj and Januzzi 2010).

Due to the challenges in prognosticating in heart failure, it is generally recommended that access to generalist and specialist palliative care is determined by need, in relation to symptom burden and psychosocial distress, rather than prognosis.

9.2 Chronic Obstructive Pulmonary Disease

A number of factors that indicate severity of disease have been identified for chronic obstructive pulmonary disease (COPD). The forced expiratory volume in 1 s (FEV1) is the best known of these but is imperfect on its own at predicting survival. It is combined with other prognostic indicators in the BODE index, a tool devised to predict outcomes in patients with COPD. The BODE index incorporates body mass index (BMI), the degree of airflow obstruction (FEV1), severity of dyspnea measured by the modified Medical Research Council dyspnea scale (MMRC), and exercise capacity measured by distance covered during the 6-min walk test. In the original validation study, its ability to accurately identify four differing survival profiles among patients with stable COPD attending outpatient clinics was demonstrated; the c-statistic was 0.74. However, it predicts survival over a relatively long time range. Median survival of participants in the quartile with the shortest survival was 39 months.

The B-AE-D is an alternative tool developed to address some of the limitations of the BODE relating to ease of application. It was designed to be applicable during acute exacerbations of COPD (AECOPD) and during periods of stable disease and was derived from a multicenter observational study of prognostic indicators (PROMISE). It doesn't require patients to perform either the 6-min walk or pulmonary function tests. Instead it incorporates BMI, frequency of AECOPD requiring hospital attendance in the past year, and dyspnea measured by the MMRC,

in order to predict 24-month mortality. The ability to discriminate 1-year and 2-year mortality, measured by the c-statistic, was comparable to that of the BODE index, when both were applied to the data from the PROMISE participants. External validation studies, conducted by secondary analysis of data from two separate COPD cohorts, showed that 1-year mortality was well predicted (c-statistic 0.68 and 0.74, respectively) (Smith et al. 2017).

In summary, the available tools have been derived from cohorts with relatively long survival and have not been designed to predict prognosis over a short time period, such as 1-year survival, and hence may be of limited utility in improving prognostic accuracy in patients referred for palliative care. Tools designed to predict short-term prognosis and derived from cohorts with median survival of 12 months or less may identify that alternative prognostic indicators or combinations of indicators best explain survival at this stage. Other factors associated with poor prognosis in patients with COPD include increasing age, comorbidities, partial pressure of oxygen in arterial blood, and cor pulmonale.

9.3 Renal Failure

Patients with end-stage renal failure (ESRF) may die as a result of either deteriorating renal function or other complications of associated comorbidities, such as diabetes or cardiovascular disease. Median survival for patients with stage 5 kidney disease is 21 months with conservative management and 67 months with renal replacement therapy (RRT). However, older age is associated with shorter survival as older patients and those with multiple comorbidities are less likely to be treated with RRT and the survival advantage associated with RRT decreases with increasing age. Ongoing tobacco use also is a negative prognostic indicator (Reindl-Schwaighofer et al. 2017).

With regard to biomarkers of prognostic significance in chronic renal impairment, there is some commonality with other life-limiting conditions; a chronic inflammatory process has been identified and is associated with survival in patients with end-stage renal disease. A systematic review by Desai et al. examined several biomarkers in relation to mortality. In this review, high CRP and IL-6, low lymphocyte counts, and hypoalbuminemia were found to predict poor prognosis (Desai et al. 2009). Fourteen studies were identified which examined the relationship between mortality and CRP. Of these, ten used relative risk as the measurement of effect; the weighted mean relative risk (RR) across the studies was 3.23 when examining the association between CRP and mortality. Cardiac troponin t (cTnT) was found to have a predictive value in patients with renal failure, out with the acute cardiac setting. The mean RR of mortality conferred by raised cTnT was 3.69 across 15 studies, encompassing 1700 patients.

Other biomarkers found to be associated with survival in those with renal failure included tumor necrosis factor, hematocrit, and markers of dialysis adequacy such as the urea reduction ratio (URR) and Kt/Vurea (k = dialyzer clearance, t = dialyzer time, Vurea = volume of distribution of urea). Interestingly, some of the markers traditionally thought to be useful in prognostication, such as parathyroid hormone, were not found to be statistically significant, and newer markers, not previously included in discussions around prognosis, such as CRP, have now come to the fore in this area.

9.4 Liver Failure

The use and application of prognostic models, incorporating biomarkers, is well established in hepatology, whereby models are commonly used both to provide prognostic information and trigger modification of treatment plans. The Child-Pugh score has been in use for over 30 years and uses prothrombin time (PT), bilirubin, and albumin, alongside subjective assessments of the presence of encephalopathy and ascites, to prognosticate in those with end-stage liver disease. The inclusion of subjective measures within this scoring system poses challenges for its generalizability. There is also debate regarding the weighting of the

biomarkers within the Child-Pugh score; for example, both albumin and coagulation strongly correlate, and therefore the inclusion of both gives the synthetic function of the liver significantly greater weighting (Durand and Valla 2005).

The older Child-Pugh score has been somewhat superseded by incorporating creatinine, replacing PT with INR, and removing albumin and clinical assessment from the calculation, to form the Model for End-Stage Liver Disease (MELD) (Kim and Lee 2013). This was originally developed to predict survival in patients undergoing transjugular intrahepatic portosystemic shunt (TIPS) procedure. Subsequently the United Kingdom Model for End-Stage Liver Disease (UKELD) built on this by incorporating sodium. Both MELD and UKELD are useful in their generalizability due to the lack of subjective assessment. Recent evidence has suggested that the addition of sodium is helpful in prognostication and decisions regarding treatment, as it is an independent predictor of mortality in patients with cirrhosis (Kim et al. 2008). However, in post-transplant patients, MELD was better at predicting mortality than UKELD (Ling et al. 2017). The aim of these models has been to stratify patients into groups based on predicted mortality. It is worth noting that these models have been developed for predicting shorter to mid-term survival of 3 months to 1 year.

9.5 Dementia

Median survival from time of diagnosis of dementia is 3 to 6 years. While some patients with dementia have coexisting life-limiting illnesses, which may determine survival to a greater extent, the classically described disease trajectory in dementia is one of a slow progressive decline in physical and cognitive functioning. Prognostication is challenging. Negative prognostic indicators include increasing age, male gender, cardiovascular disease, low BMI, poor performance status, insufficient oral intake, weight loss, dyspnea, spending most time in bed, and at least one pressure ulcer. However prognostic tools incorporating key indicators have only moderate discriminatory capacity. The Advanced Dementia Prognostic Tool (ADEPT) was derived using minimum dataset information on more than 200,000 residents in licensed US nursing homes with advanced dementia and contains 12 items, including those listed above. It was shown to have an AUROC of 0.67 when used to predict 6-month mortality as a continuous variable in a prospective validation study. The optimal cutoff point for prediction of 6-month survival had an AUROC value of 0.63, sensitivity of 55.0%, and specificity of 71.3% (Mitchell et al. 2010). Recognition of sentinel events is suggested as a possible alternative method of identifying patients with a short prognosis. In a prospective study of care provided to patients with advanced dementia in US nursing homes, of the 323 participants, 55% died during the 18-month study period. Development of pneumonia, a febrile episode, or an eating problem heralded a poor prognosis; after adjustment for age, gender, and disease duration, the 6-month mortality rate for residents who had pneumonia was 46.7%; a febrile episode, 44.5%; and an eating problem, 38.6% (Mitchell et al. 2009).

10 Communication of Prognosis

Communication of prognosis is an emotive issue for both patients and doctors. Doctors describe avoidance of prognostic disclosure for fear of being wrong, of causing patient distress, or of damaging the doctor-patient relationships. Studies of patients with incurable cancer and their doctors consistently report that doctors overestimate their patients' understanding of their disease, that prognosis is infrequently discussed, and that consultations with oncologists tend to focus on scan results and logistical aspects of treatment options (Hagerty et al. 2005).

Patients' desire for prognostic information varies between individuals and over time. Some feel that they cope better without knowing their predicted life expectancy, while others describe not seeking prognostic information, as they perceive that it may be inaccurate or that it is an unfair request to make of their doctor.

In one US-based multicenter study, whereby several hundred patients with progressive cancer who had received at least one line of chemotherapy were interviewed, 71% said that they wished to know their life expectancy. Eighteen percent reported that their doctor had discussed prognosis with them. In analysis adjusted for age, gender, ethnicity, recruitment site, cancer type, and performance status, disclosure of prognosis was not associated with higher levels of sadness/depressed mood or feeling worried/anxious as measured by the McGill Quality of Life Questionnaire. There was no difference in the proportion of patients reporting a strong doctor-patient relationship between those who received prognostic information and those who did not. This was an observational study, which did not take account of patients' satisfaction with the way in which prognosis was disclosed or who initiated the conversation. Although it is plausible that patients who received prognostic information were a self-selected group, who perceived that knowing their estimated life expectancy would help them cope, this study does suggest that meeting patients' informational needs needn't cause ongoing distress or impact on the doctor-patient relationship. Of note, almost 30% of participants said that they did not wish to know their estimated prognosis (Enzinger et al. 2015). The variation in preferences, between individuals and within individuals over time, suggests that clinicians should assess patients' informational needs, with respect to prognosis, on an ongoing basis.

With regard to characteristics of communication of prognosis, some preferences, such as who is present during the discussion and physical aspects, such as proximity to the doctor or physical touch, vary between individuals. However, several themes consistently emerge from studies of patients' preferences regarding the nature of prognostic disclosure. Patients wish for honest and clear information, ideally from a doctor who is well known to them. In addition to information about estimated life expectancy, they want to know what to expect from their illness as it progresses, in terms of functional ability, symptoms, and ability to fulfill roles. They value having some control over what is discussed and the opportunity to ask questions. There is a need for honesty to be balanced with sensitivity and for the conversation to engender a sense of control and support hope (Hagerty et al. 2005). A good knowledge and understanding of the patient should facilitate this somewhat daunting task. By better understanding what is important to the patient, the clinician can identify where the opportunities lie to support hope and tailor information in a way that gives a sense of control.

As with delivery of bad news, the pacing and initial extent of prognostic disclosure should be informed by knowledge of what the patient already understands about the nature, extent, and implications of their disease. Patients should be informed that predictions of life expectancy are best estimates only and approximate. Patients may find it difficult to understand or misinterpret statistical data, which is not individualized, such as median survival time or probability of survival until a certain time point. Instead, it is common practice to express prognosis as the likelihood that the patient will die within days, weeks, or months and on some occasions to give an indication of whether we estimate this to be in the region of short days, weeks or months, or several. Although expressing prognosis in this way avoids conveying unfounded precision to patients and their families, it is not known how patients and families assimilate this information and whether they infer a specific numerical estimate from the information provided.

An understanding of prognosis plays an important role in informed decision-making by the patient regarding preferred treatment, ceilings of care, and place of care. Patients with cancer who have an understanding of their prognosis are more likely to opt for supportive rather than life-prolonging treatment, have a DNAR in place, and have completed a living will, than those who overestimate their survival (Enzinger et al. 2015).

For patients with other life-limiting illnesses, such as organ failure or frailty, prognostication can be particularly challenging. In one study conducted in Canada, telephone interviews were conducted with 67 bereaved relatives of patients who had died in hospital. In particular, they placed value on being informed early during the

admission that the patient was sick enough that they could die. Although doctors frequently cite uncertainty as a reason for not disclosing the possibility of death during severe exacerbations of diseases characterized by the entrant-reentrant trajectory, participants in this study who described being told of the lack of certainty regarding the possibility of death or recovery reported high levels of satisfaction with communication. Participants also valued clear information and avoidance of euphemisms, giving false hope, and conflicting information (Krawczyk and Gallagher 2016).

11 Diagnosing Dying

> Death is a process, not an event, despite medical and legal imperatives to give it a date and hour. James W. Green, Beyond the Good Death, p. 188.

11.1 Background

Diagnosing dying is not straightforward and can be difficult, even for an experienced physician. The process of diagnosing dying can be "viewed as part art, part science and is often regarded as skill of individuals rather than an objective assessment of signs and symptoms" (Kennedy et al. 2014). There are no definitive criteria for diagnosing dying. The ensuing uncertainty is often challenging for healthcare service providers. Current prognostic tools and models are limited and are not yet, or may never be, sensitive enough to reliably identify those who will die within hours or days. One literature review reported an "overarching theme of uncertainty." Diagnosing dying should be viewed as a process and not an event. Recognizing that death is imminent is integral to ensuring appropriate management that is focused on comfort and dignity and avoidance of unnecessary interventions and facilitates timely discussions and shared decision-making with patients and their loved ones.

Events in the United Kingdom (UK) during the past decade have brought scrutiny upon the scientific evidence-base for diagnosing dying. The Liverpool Care Pathway for the Dying Patient (LCP) was a care pathway covering palliative care options for patients in the final days or hours of life. The purpose was to help doctors and nurses provide quality end-of-life care. It was developed in the late 1990s for the care of terminally ill cancer patients and then extended to include all patients deemed to be dying. Its development was prompted by an increasing consensus within the UK medical community that standards of end-of-life care were variable. It was widely used throughout the United Kingdom and internationally, and initial reception was very positive. Key components included discontinuation of non-essential treatments and medications and prescription of medication for symptom control at the end of life and prompt to discuss dying with patients and families. However, its use was subject to heavy criticism in the media from 2009, with reports that it was being widely abused as a "tick box exercise" and some patients were being incorrectly diagnosed as dying. This naturally caused considerable distress to patients and their loved ones. It was claimed that patients had been inappropriately sedated and denied food and water, while some felt it had hastened death in relatives not dying imminently. Many patients and their relatives were not informed or consulted that the patient was being placed on the pathway. Controversially in some English NHS trusts, there were financial payments for meeting targets when using the LCP.

In July 2013, the results of More Care, Less Pathway, an independent UK government review into the LCP led by Baroness Julia Neuberger, were published (Neuberger et al. 2013). It acknowledged that the LCP can provide a model of good practice when used properly. However, it concluded that it was not being applied properly in all cases and that use of generic protocols was the wrong approach. They recommended that use of the Liverpool Care Pathway be replaced within 6 to 12 months by an end-of-life care plan for each patient. Following the review, it was also recommended that financial incentives for hospitals relating to care for dying patients, including the LCP, should cease immediately.

In response to the recommendations of the Neuberger Report, the Leadership Alliance for the Care of Dying People (LACDP) in 2014 published their report One Chance to Get it Right (Leadership Alliance for the Care of Dying People 2014). This advocates an approach to caring for people in the last few days and hours of life which keeps people and their families at the center of decisions about treatment and care. More Care, Less Pathway called on the National Institute for Health and Care Excellence (NICE) to issue clear guidance around death, and in 2015, NICE guidelines entitled Care of dying adults in the last days of life were published (National Clinical Guideline Centre 2015).

11.2 Factors to Consider when Diagnosing Dying

More Care, Less Pathway affirmed that diagnosing dying is an incomplete science and that there are no precise ways of telling accurately when a patient is in the last days of life. It recommended that there should be clear guidance on clinical decision-making processes at the end of life and, in particular, managing the uncertainties around diagnosing dying or recovery phases.

The NICE guidelines reported the following signs and symptoms that may suggest the person is entering the final days: multiple organ failure, progressive weakness, reduced mobility, reduced ability to carry out normal activities of daily living, and increased periods of sleep. Other features include reduced oral intake and a reduction in cognitive function, awareness, and communication (National Clinical Guideline Centre 2015). Spiritual and psychological changes including withdrawal, social isolation, declining interest in daily life, agitation, and anxiety, particularly in the evening may also occur. Social and psychological decline usually runs in parallel with physical deterioration.

Signs that may indicate death within hours include variations in respiratory cycle, weakening of pulse, shutting down of skin circulation, and noisy respiratory secretions. While some symptoms of death are specific, e.g., Cheyne-Stoke breathing and noisy respiratory secretions, these symptoms are not universal. A benefit of using clinical symptoms and signs to recognize death is that the technique is noninvasive and does not cause harm to the patient.

Functional performance scales can also be used to aid the diagnosis of dying. Specifically, deterioration in ECOG indicates a likelihood of entering the last days of life, although utility is limited in people with chronic disability (National Clinical Guideline Centre 2015). Other useful scores include Barthel Activities of Daily Living Index, Karnofsky Performance Status Scale, and Australia-modified Karnofsky Performance Scale.

It is very important that any potential reversible causes that may mimic dying are considered and excluded. These potential causes of deterioration include infection, dehydration, bleeding, acute renal impairment, drug toxicity, and hypercalcemia. These conditions are likely to be elicited by good history taking and clinical examination but may also require simple laboratory tests.

The evidence for diagnosing imminent death with laboratory tests is weak, and the use of measurements such as renal function or performing imaging may not be appropriate due to invasiveness and limitations of use. Clinical tests in the last 2–3 days of life should only be undertaken if there is a clinical imperative to do so.

When diagnosing dying, it is important to consider the patient's medical history and clinical context, including the underlying diagnosis and associated disease trajectory. Understanding trajectories may allow for more practical planning around death, but they do have their limitations. Individual patients will die at different stages along each trajectory, and the rate of progression may vary. Challenges can also arise from illnesses following different trajectories, and there may be numerous underlying conditions causing death. It is important to take into account the patient's underlying robustness or frailty, associated symptoms, and the speed of deterioration.

The setting may also play a role in diagnosis; studies have shown that care in an acute hospital is more likely to result in active treatment as opposed to the nursing home, where comfort or rehabilitative care may be the focus (Kennedy et al. 2014).

11.3 Challenges in Diagnosing Dying and Ongoing Care

Clinicians must be alert to signs of recovery in patients felt to be dying. This may be indicated by improvement in signs and symptoms or functional status. Assessment of whether a patient is nearing death, stabilizing, or improving should be informed by information gathered by the multiprofessional team, patient themselves, and those important to them (National Clinical Guideline Centre 2015). It is important that the clinical team discuss and reach agreement on the likely phase of care, in order to avoid provision of inconsistent care and advice.

Factors relating to the clinician, the doctor-patient relationship, and healthcare setting can potentially impact on how soon dying is recognized. As discussed above, a strong doctor-patient relationship can be associated with overly optimistic survival predictions, and there is every reason to assume that this may continue into the dying phase. There is sometimes a reluctance to diagnose dying if any hope of improvement exists. This may reflect the strength of the doctor-patient bond or characteristics of the healthcare setting. Making an assessment of the probability of survival in a disease-orientated context is inextricably linked with the perceptions of "success" and "failure." Murtagh et al. propose that there needs to be a willingness to switch focus away from the disease about which the clinician may know a great deal, toward a focus on the person before us, about whom we may know much less. Listening to patient preferences and enabling their end-of-life choices will lead to greater patient empowerment (Murtagh et al. 2004). Obtaining insights and information from the observations of other members of the MDT, or a second opinion from a colleague, may attenuate these biases.

When it is recognized that a patient may be dying, it is essential that this is communicated, not only to the clinical team but to the patient, if appropriate, and their loved ones. This should be communicated clearly and with sensitivity and avoidance of euphemisms (Krawczyk and Gallagher 2016). Recognizing death allows the dying person to spend valuable time with those who are important to them. This time may also give opportunity to ascertain the patient's wishes and goals, if not already known, and the views of those important to them and to focus on their physiological, psychological, social, and spiritual needs.

NICE recommends that doctors and nurses need to communicate with patients and relatives about the difficulties in diagnosing the dying phase. This includes admitting to and being explicit about uncertainty and dealing in likelihoods, not certainties. Although it can be uneasy to acknowledge uncertainty, this openness can clarify and build trust between patients and professionals. Uncertainty around recognizing dying can lead to poor communication and avoidance of frank discussions. This may cause delayed or inappropriate clinical decision-making and unnecessary distress (National Clinical Guideline Centre 2015).

Uncertainty may never be removed from the dying process, as dying can be as much a social as a medical process. The timing of a patient's death may be influenced by symbolically meaningful occasions such as birthdays, anniversaries, and festivals (National Clinical Guideline Centre 2015). It is poorly understood if a patient's will to live or desire to die affects survival, but their attitude to dying is likely to impact on their healthcare choices, such as acceptance or rejection of interventions to treat potentially reversible complications.

11.4 Biomarkers of the Dying Process

There has been increasing interest in the biology of dying and identification of biomarkers as indices of disease processes as a result of the LCP review processes. Biomarkers have the potential to assist clinicians in distinguishing dying from reversible acute deterioration. Few studies have specifically investigated changes in biomarkers in the last days to weeks of life. A number have been found to be elevated in the blood of cancer patients in the last 2 weeks of life including WBCC, platelet count, serum CRP, urea, urate,

alanine transaminase (ALT), lactate dehydrogenase (LDH), sodium, and plasma IL-6 (Reid et al. 2017). Explanations for raised serum urate concentrations have been hypothesized, including renal dysfunction and cellular injury caused by hypoxia and/or inflammation (Shin et al. 2006). In one small study of serial serum concentrations of inflammatory markers in terminally ill cancer patients, IL-6 was detected in all 28 terminal cancer patients sampled. It was seen to gradually rise during the early stages of cachexia followed by a sharp rise in the week prior to death (Iwase et al. 2004). The number of volatile organic compounds (VOCs) in urine has been shown to increase in the last weeks of life, using gas chromatography mass spectrometry (GC-MS), with the steepest rise is seen in the last week of life (Reid et al. 2017).

Increased understanding of the physiology of dying, along with interpretation of biomarkers and use of prognostic tools, will hopefully improve clinicians' identification of the dying process. This will, in turn, facilitate optimal care for patients and their families. However, the diagnosis of dying is likely to remain challenging despite ongoing work into diagnostic aids, and continued education and training is required. Meanwhile, clinicians must get better at accepting and acknowledging uncertainty and communicating this uncertainty to patients and their loved ones.

12 Conclusion

As clinicians caring for patients with life-limiting conditions, we must strive both to improve our understanding of prognostication and get better at accepting and acknowledging prognostic uncertainty.

Evidence from existing research literature highlights ways in which we might seek to improve accuracy in individual cases, such as basing prognostic estimates on serial assessments over time and seeking opinions from other members of the MDT and from distanced clinicians in situations where we know the patient very well.

Having an understanding of the typical disease trajectory and recognition of relevant biomarkers, clinical signs, and symptoms facilitates recognition of the period of terminal decline in advanced cancer. Prognostic tools are available which predict relatively short-term survival with accuracy comparable to that of doctors experienced in oncology and palliative care. However, we must be cognizant that advances in disease-modifying treatments may render traditional prognostic models inaccurate. One such example is the use of abiraterone for hormone-resistant prostate cancer, which Abdelbaset al-Megrahi is reported to have received following his release from prison.

Conversely, there are few tools available which have been designed to predict short-term survival in progressive nonmalignant conditions, and it is generally difficult to recognize the last weeks and months of life. Prognostic uncertainty should not be viewed as a reason to avoid discussions regarding prognosis with patients but instead serve as a trigger for discussions regarding this uncertainty.

Current and future research may help identify biomarkers for dying and prognostic indicators and tools designed to predict short-term prognosis in nonmalignant diseases. Other research questions, yet to be addressed, include whether doctors are more accurate when providing qualitative prognostic information compared with quantitative predictions and whether training on prognostication improves accuracy.

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Spirituality in Palliative Care

41

Carlo Leget

Contents

Abstract

Patients who are confronted with a life-threatening disease may experience the limits of their existence. In many patients, this confrontation results in struggles and questions on an existential level, which can be discerned, but hardly separated, from questions that are primarily related to the psychosocial or physical dimension of human existence. In this contribution an overview will be given on the state of the art of spiritual care in palliative care. After having given a definition of spirituality, we will focus on how to identify the aspect of spirituality, what a spiritual process and a spiritual crisis look like, what is needed for a conversation on spirituality, how spirituality can be measured and how effective spiritual interventions are, how one can deal with the hope of patients and families, how one can deal with intercultural issues, what conditions are needed

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_28

for providing good spiritual care, and how to report and refer this dimension in palliative care.

1 Introduction

According to palliative care definitions of organizations like the WHO or the EAPC, providing spiritual care is an intrinsic part of providing good palliative care. How to define spiritual care and spirituality, however, is a subject of continuous debate (Steinhauser et al. 2017; Balboni et al. 2017). Reasons that it is hard to reach consensus on this issue are either related to a difference in cultural and academic backgrounds according to which the concepts that play a central role in the definition have a different meaning or they stem from the fact that the method used to come to a definition is different. Despite the difficulty to define what spirituality is, there seems to be a general agreement that spirituality is broader than religion. Religion is one specific way in which people live and express their spirituality.

In this text spirituality will be defined according to the world consensus definition of Puchalski et al. that was published in 2014. According to this definition spirituality is defined as follows.

> Spirituality is the aspect of humanity that refers to the way individuals seek and express meaning and purpose and the way they experience their connectedness to the moment, to self, to others, to nature, and to the significant or sacred.

The reason that this broad definition is chosen is that it has a wide span of agreement. It builds on an earlier consensus definition of palliative care experts from the United States, from which also the definition was formed that is used by the taskforce spirituality of the European Association for Palliative Care (Puchalski et al. 2009; Nolan et al. 2011).

Having defined how spirituality can be understood, in this chapter we will expand on how spiritual care can be delivered in palliative care as an aspect of interdisciplinary care.

2 Identifying the Aspect of Spirituality

As an aspect of humanity related to seeking and expressing meaning, purpose, and connectedness, spirituality can be identified in many ways and on many levels. It is intrinsically related to the physical and psychosocial dimensions of human existence and mutually influencing each other. It does not, however, mean that each patient at every moment is in need of spiritual care. Often the spiritual dimension in the lives of patients and families is implicit and hidden. On the other hand, attention to the spiritual dimension might be valuable to patients and families also when there are no specific questions or problems in this field. Moments of transition are meaningful moments, and paying attention to this meaningfulness is a way of providing care for the spiritual dimension.

Spiritual needs may be explicit, but often they are intertwined with needs in other dimensions. Kellehear distinguishes three situations of transcendence that are connected with spiritual needs: situational (purpose, hope, meaning and affirmation, mutuality, connectedness, social presence), moral and biographical (peace and reconciliation, reunion with others, prayer, moral and social analysis, forgiveness, closure), and religious (religious reconciliation, divine forgiveness and support, religious rights/sacraments, visits by clergy, discussions about God, eternal life, and hope) (Kellehear 2000).

As patients are different, the ways in which they live their spirituality may vary according to their character and culture. For some spirituality is lived in an intellectual way, studying and reading books, discussing and trying to understand what is happening to them, and relating it to a larger framework of meaning. For others the spiritual quest is more a journey to the inner world, using meditation or ways of soul searching that focus more on experiencing and feeling what is happening to them. A third group is more focused on action, bringing things in order, helping other people, or contributing to a better world (Weiher 2014).

Research has demonstrated the importance that patients and families attach to spiritual care (Cobb

et al. 2012). This might either be religious care in the form of being sustained in carrying out religious duties and needs, spiritual care in the sense of being helped in making sense of what is happening, or an attitude of attentiveness to implicit spiritual needs, by listening carefully to the spiritual dimension of the situational and moral biographical needs.

One could even argue that genuine humane and open nonjudgmental attention, as it is witnessed in dignity therapy, is also a form of providing spiritual care, as the patient is supported in finding meaning, purpose, and connectedness (Chochinov et al. 2011).

3 The Spiritual Process

People experience meaning at many levels in daily life. Situational meaning makes sense of everyday experiences and is often produced automatically and implicitly. As long as situational meaning is in congruence with the global meaning of a person – the larger framework of meaning which is related to existential values – the existential level often stays undiscussed. When the actual experiences are difficult to fit into the global meaning framework, forms of distress will begin to develop (Park 2010). A spiritual struggle is the struggle to deal with this stress and to search for ways to achieve a new balance between global meaning and situational meaning making processes. This can be achieved in a number of ways, including acceptance of the new situation, the integration of a stressful experience in a changed identity, and changes in personal goals. The process of struggling for meaning comes to rest when the discrepancy has sufficiently come to rest for the patient.

The process of spiritual struggle is a normal reaction to life-changing events like being confronted with a life-threatening disease. The way this process develops, however, may change from patient to patient. Some patients will experience a difficult process or even a spiritual crisis; other patients will hardly struggle with spiritual issues. There seem to be differences between the spiritual processes of patients suffering from different diseases.

As we look at the outcome of the spiritual process, however, there seems to be agreement that this may entail one or more of the following options: a sense of having "made sense," acceptance, reattribution and causal understanding, perceptions of growth or positive life changes, changed identity or integration of the stressful experience into identity, reappraised meaning of the stressor, changed global beliefs, changed global goals, and restored or changed sense of meaning in life (Park 2010). From a psychological perspective, all these outcomes may be good. From the perspective of a specific spiritual or religious tradition, however, one outcome may be considered as a better sign of spiritual development or growth than another outcome.

4 Spiritual Crisis

When the process of spiritual struggling results in an amount of stress that the patient is no longer able to manage, one can speak of a spiritual or existential crisis (Agrimson and Taft 2009; Yang et al. 2010). This crisis can be defined as an acute and profound questioning of the self, the world, and/or the transcendent, by external stressors, in which an individual reaches a turning point or crossroad, leading to a significant alteration of the way life and the world are viewed.

When people are confronted with a spiritual crisis, it is important to determine to whom they can be referred. In case of referral, it is important to look at the match between the identity and wishes of the patients on the one hand and the availability of specialist caregivers on the other. The first disciplines to think of in these cases are the chaplain, spiritual caregiver, or psychologist. Apart from these, one can think of a minister of the spiritual or religious network of the patient and family, like a reverend, priest, imam, or pundit.

Sometimes a spiritual crisis is accompanied by a psychiatric component. These are the cases when one has the feeling that perhaps a patient suffers from a major depression, rather than normal distress which is characterized by

demoralization, grief, loss of dignity, and loneliness. Or the experience of moral guilt is so strong and unbearable that one suspects an obsessive compulsive disorder. In cases like these, referral to a psychiatrist might be important in order to avoid undertreatment. In order to distinguish between normal spiritual distress and a psychiatric disorder, a number of questions can be asked. Griffith and Norris (2012) formulate seven helpful questions in such a case:

1. Did onset of the distress coincide sharply with a stressful life event?
2. Is the intensity of distress proportionate to the severity of the event?
3. Does distress remit when the stressful event remits?
4. Are there associated symptoms of a psychiatric disorder?
5. Are there identifiable biological or psychosocial risk factors for occurrence of a psychiatric disorder?
6. Is there a past history of a psychiatric disorder? If so, has it shown a pattern of relapse and recurrence?
7. Has there been a robust response to a psychiatric medication in the past?

After having answered these questions, plan for treatment and/or accompaniment can be made, in which the disciplines mentioned above might cooperate to the benefit of the patient.

5 Conversation About Spirituality

Because for many patients the spiritual dimension is interwoven with situational, moral, and biographical needs, a spiritual conversation may take place on different levels. Realizing that for many patients, spiritual issues are not clear-cut issues that can easily be separated from their situational and biographical context, and knowing that many patients are in search of language to address the existential level that in normal life often remains unarticulated, listening carefully and in a nonjudgmental way is perhaps the most important competence for spiritual care. Asking open-ended questions and being unconditionally interested in the patient fosters a climate of confidence and trust that is needed for communicating about personal and intimate issues such as spiritual ones. One needs to realize, however, that patients respond to caregivers anticipating on what they think is appropriate or desired. Generally speaking, a compassionate physician will get different answers than a compassionate nurse or chaplain will.

Developing the right attitude starts with being conscious of one's own inner space (Leget 2017). Working in a healthcare system can be demanding in terms of goals that have to be achieved and time constraints. Moreover, we all bring a specific intellectual, emotional, and spiritual framework into the conversation that is limited and determined by our cultural biography. All this, combined with the particular circumstances and moods we are in, has impact on our ability to listen with attentiveness and openness. The better we know our inner world, the more we are able to know our limitations and biases.

Next to developing an open and nonjudgmental attitude, one can educate one's ability to listen. Many things patients and family members say do not just have one meaning, but express many things on more than one level. The German chaplain Erhard Weiher developed a framework of listening to patients distinguishing between the factual, emotional, biographical, and spiritual content of what is said (Weiher 2014). When a woman of 43 years old, lying in the hospital for chemotherapy, says "It seems like I will not be able to be at home with my four children this weekend," any caregiver might hear a factual statement about her physical location. Every good caregiver will also hear an emotional content related to feelings of love, sadness, longing, and regret. There is, however, also a biographical content in this saying, revealing that she is a loving mother of four children. Interpreting this sentence in her biographical context might help to grasp its spiritual depth, referring to what is most meaningful in her life.

Having developed our listening capabilities, there are a number of easy tools to start a conversation with patients in an open and inviting way. A

somewhat structured way of getting into conversation can be making use of the three questions that were developed by the Mount Vernon Cancer Network (2007):

1. How do you make sense of what is happening to you?
2. What sources of strength do you look to when life is difficult?
3. Would you find it helpful to talk to someone who could help you explore the issues of spirituality/faith?

The three questions of the Mount Vernon Cancer Network open up the spiritual dimension of what patients and families experience, starting from what is important to them and what has been helpful to them. They do so in a very open way without directly asking for what this means for the care they receive.

A second example of a conversation tool which has been developed for patients, families, and caregivers is the ars moriendi model (Leget 2017). This model is based on five central themes that are important at the end of life and can be summarized in five questions that patients may be struggling with:

1. Who am I and what do I really want? (autonomy)
2. How do I deal with suffering? (control)
3. How do I say goodbye? (farewell)
4. How do I look back on my life? (guilt)
5. What can I hope for? (afterlife)

The ars moriendi model has been developed as a conversation tool for patients, families, and caregivers. In accordance with the WHO definition of palliative care, it was designed from the idea that dying is a social process. Nevertheless, the patient is the first and central person who should be offered assistance in answering the existential questions that may come up at the end of life. In the model this is facilitated by presenting the five central questions against the background of five tensions that are characteristic for the ways in which people answer the question: the tension between being able to connected to oneself versus the other (autonomy), doing versus undergoing (control), holding on versus letting go (farewell), remembering versus forgetting (guilt), and knowing versus believing (afterlife). The ars moriendi tool is used in different ways. In some Dutch and Belgian healthcare settings, it is offered to patients as a mirror to reflect on their position; in other settings it is used for structuring the work of general practitioners (Vermandere et al. 2015).

Other assessment tools are directly designed to gather information which is important to take into consideration for caregivers. A very direct and effective single question that proofs to be acceptable for patients is the so-called Patient Dignity Question (PDQ): "what do I need to know about you as a person to take the best care of you that I can?" (Johnston et al. 2015). This question expresses a person-centered concern and leaves it to the patient what he or she thinks is appropriate to tell the caregiver.

Next to the Patient Dignity Question, there are a number of spiritual history tools that are known by acronyms like FICA, FAITH, SPIRITual, and HOPE. Spiritual history-taking tools can have an important role in identifying the spiritual needs of patients at the end of life. According to a recent study, the "HOPE" tool seems to be most comprehensively addressing the spirituality themes identified as important within the healthcare literature (Lucchetti et al. 2013; Blaber et al. 2015). The HOPE tool asks for (H) sources of hope, meaning, comfort, strength, peace, love, and connection, (O) organized religion, (P) personal spirituality/practices, and (E) effects on medical care and end-of-life issues.

6 Measuring Spirituality

Next to conversation tools, instruments for measuring spirituality can be used. According to a literature review comprising 90 papers and 58 measures, it is important to specify what one really wants to know (Best et al. 2015). Dependent on the construct, Best et al. recommend different measures: suffering (PRISM, MSSE), hopelessness and demoralization (HAI, Kissane's Demoralization Scale), hope (HHI), meaning

(FACIT-Sp, LAP-R), spiritual well-being (FACIT-Sp), quality of life (FACIT-Sp, MQoL), distress (SAHD), and spiritual pain, distress, or struggle (no recommendation).

Measuring spirituality might be interesting for the purpose of doing research. The distress, however, of patients who are receiving palliative care will often take a toll on their reserves. This makes lengthy assessment tools burdensome in clinical contexts and pleas for using short measures. For that reason Best et al. propose further research in this area to focus on single-item measures like: "Are you at peace?" (Bayes et al. 1997) and "How long did yesterday seem to you?" (Steinhauser et al. 2006). Next to the issue of burdensomeness, it is important to realize that the nature of suffering is very personal in the way it is multidimensional, culture, and context specific. For this reason it is more important to be sensitive to subjective components and alertness to verbal and nonverbal cues to the patient. In the end, caring requires the ability to connect and be attentive to the patient, especially in this very sensitive area of deeply personal feelings and experiences.

7 Effectiveness of Interventions

Attention to the spiritual dimension of what patients and families experience is an intrinsic part of palliative care according to the WHO definition. It is an expression of the respect for persons and confirms their dignity. Research into the effectivity of spiritual interventions, however, is scarce and has produced only small evidence. Measured with the strict criteria of a Cochrane Review, one must conclude that there are so few RCTs, and the quality of them is so problematic that there is hardly any evidence for the effectiveness (Candy et al. 2012). Nevertheless researchers continue to study the correlation between interventions and positives outcomes. Narrative interventions seem to have a moderate short-term positive effect on the well-being of patients (Kruizinga et al. 2016). The combination of meditation massage seems to have a more positive effect on the quality of life than meditation alone in a population with end-stage AIDS (Williams et al. 2005). Also, a life review program among Chinese patients seemed to have a positive effect on the well-being of patients compared to standard palliative care (Xiao et al. 2013). The training of physicians and nurses by chaplains has also shown positive results reported by patients (van de Geer et al. 2017).

Other research has not been able to demonstrate positive effects on the quality of life of patients. There is small evidence that meditation compared to standard care or massage does not seem to improve quality of care (Williams et al. 2005). Neither have positive effects on quality of life been proven for dignity therapy and a structured spiritual anamnesis compared to standard care or counseling (Martinez et al. 2017).

Although the positive effect of spiritual interventions on the quality of life or quality of care for palliative patients is hard to prove, they can still be meaningful way of caring for patients. Because spiritual care interventions are so tied up with careful and sensitive communication, attention for the spiritual dimension is an important measure of good quality care, as can be demonstrated by the example of dealing with hope.

8 Dealing with Hope

Hope plays an important role in the lives of patients and families. It is a vital and helpful source that can have different contents simultaneously and shift during the palliative phase. Dealing with hope can be difficult when caregivers have the impression that the hope of patients and families is unrealistic or absent. Often this results in an ethical dilemma: on the one hand, caregivers feel that they have to inform their patients about a realistic prognosis; on the other hand, they do not want to demoralize patients and taking away hope as a positive life force. Moreover, in some cultures taking away hope from patients is equal to abandoning them and giving them not the support they deserve.

Research has shown that among caregivers three different perspectives on hope are used, often connected with the perspective of specific professions (Olsman et al. 2014a). Physicians and

nurses often adopted a realistic perspective on hope, seeing hope as an expectation that should be truthful, so that futile treatments are avoided and patients may focus on unfinished business. Hope, thus, could be destroyed by a negative prognosis or conversations about death and dying.

A second perspective, adopted by physicians, nurses, and psychologists, was hope as a way of coping with the impact of the disease. Hope was seen as something motivating and helpful in order to live life as normal as possible. Hope-fostering strategies according to this functional perspective were offering treatment, providing comfort or pain relief, and talking about death and dying.

A third perspective of hope, adopted by nurses and chaplains, described hope in terms of meaning. Important for people adopting this perspective was that hope was in line with the patient's life narrative. For this reason it is called a narrative perspective, focusing on what is important and meaningful to a patient. Here hope is seen as a meaningful imagined future that helps restoring the biographical integrity of the patients and families.

These three perspectives on hope do not necessarily exclude each other. When caregivers are aware of the way they are inclined to see hope, and the alternative perspectives that are available, they can use the three perspectives in order to sustain the patients and their families. Often patients and families also have a dominant perspective on hope that is the most important to them at that very moment. Being aware of this perspective and communicating with them on the same terms enables to attune to the needs and possibilities that are detected in a particular situation (Olsman et al. 2015a).

Hope is a phenomenon that can be directed to many things simultaneously, even conflicting from a logical perspective. A patient may be convinced that there no life after death and still hoping to see his diseased wife. He may hope that his death will be soon and painless, but simultaneously hoping to be around when his first grandchild is born in a couple of months. For this reason the many hopes can be compared with the many voices of a singing choir (Olsman et al. 2015b). Voices may be more or less dominant, loud, or continuously present: the better one listens, the more one may hear of the polyphonic self (Leget 2017).

Lastly it is interesting to realize that patients use different metaphors with regard to hope: grip, source, tune, and vision (Olsman et al. 2014b). Metaphors may be helpful to make the elusive phenomenon of hope a bit more concrete, but the limits of each metaphor can also block new ways of looking at things. Being aware of the limits and possibilities of the use of metaphorical language enlarges the repertoire of possibilities one can use as a caregiver.

9 Intercultural Issues

Although spirituality as an aspect of humanity is universal, the way it is experienced, understood, and expressed is very much determined by the cultural context of patients and families. As we have seen, e.g., in some cultures the importance of not taking away hope is so strong that realistic prognoses are not shared with the patients. In spiritual care for people with a different cultural background than one's own, it is important to inform one about the specific spiritual or religious practices that might be important to patients and families, as do the assessment tools we have discussed above. Intercultural communication always focuses on seeing the unique and individual patient in his or her cultural context and being open, nonjudgmental, and authentic. There is a growing awareness of the importance of research into the importance of culture sensitive care in a globalizing world (Schrank et al. 2017). Because the majority of research into spiritual care has been done in North America and North Western Europe, there's a great need for researching and developing tools and instruments for other parts of the world (Selman et al. 2013).

10 Conditions for Providing Good Spiritual Care

There are a number of conditions that are to be met in order to be able to provide good spiritual care. In the first place the attitude and frame of

reference of the caregiver should be open to providing spiritual care. Only by adopting an open, nonjudgmental attitude toward patients and their families, the basis of trust can be established that is needed to communicate about one's deepest hopes and fears. It also implies being aware of one's own spirituality and being able to articulate this when asked for. As regards the frame of reference, it is important to have some basic knowledge of spiritual and religious traditions in other cultures.

In the second place, communicative skills are important. Spiritual care requires the ability to be listening rather than speaking, receptive rather than active, and asking open questions in order to help a patient or family member articulate what is most important to them. Many times, the spiritual questions people have are not issues to be solved, but rather questions to be answered by a hopeful presence (Nolan 2011). As for patients from other cultures, it might be important to work with people who are able to translate.

A third precondition is care for the caregivers. People who provide palliative care are often confronted with situations that have a great impact on their own spiritual resilience. It belongs to good professional practice to be able to monitor one's own well-being and resilience. Caregivers who are under stress, whose inner space is too much occupied with their own coping process, or who feel that they have signs of a beginning burnout should share their experience with colleagues or take a form of supervision (Sansó et al. 2015). Being able to give full resonance to the inner lives of patients and family members presupposes inner space in the caregiver above all. The collective spirituality of an interdisciplinary palliative care team may be a helpful resource here (Sinclair et al. 2006).

Since spiritual care is a developing field in palliative care, and in many respects still in its infancy, education in spiritual care is a fourth important precondition. Multidisciplinary education has a number of advantages here: professionals learn to understand each other's perspective and role, and what is learned by the team can also be taken home by the team. Chaplains and spiritual caregivers should be able to organize educational meetings. This enables them to share some of their expertise in the field, informing other disciplines about their approach and building a shared framework for reporting spiritual care in the multidisciplinary team.

According to a white paper on generalist palliative care competencies, professionals working in the field should be able to:

5a: Demonstrate the reflective capacity to consider the importance of spiritual and existential dimensions in their own lives;
5b: Integrate the patients' and families' spiritual, existential and religious needs in the care plan, respecting their choice not to focus on this aspect of care if they so wish;
5c: Provide opportunities for patients and families to express the spiritual and/or existential dimensions of their lives in a supportive and respectful manner;
5d: Be conscious of the boundaries that may need to be respected in terms of cultural taboos, values and choices (Gamondi et al. 2013).

The last precondition for providing good and effective spiritual care concerns the organizational dimension. All preconditions mentioned before should be guaranteed by the context of the organization, including having enough time for providing spiritual care and being able to develop oneself in this area (Keall et al. 2014). The importance attached to spiritual care should be visible in policy documents, the possibilities of education and supervision, and special initiatives, e.g., the appointment of a professional who is responsible for promoting the quality of this dimension.

11 Reporting and Referring

As in most aspects of palliative care, providing the best possible spiritual care largely depends on the quality of collaboration in a multidisciplinary team. Obstacles may be that chaplains refuse to share information with the rest of the team because they consider their work more confidential than the work of other caregivers. Another obstacle may be that the team struggles with the

question how to report spiritual issues in a way that is clear and recognizable. Both obstacles ask for good communication and close collaboration. Patients should be asked whether they agree with the chaplain sharing important information with the rest of the team. Integration of the chaplain in the multidisciplinary team and close collaboration help developing a shared language for reporting spiritual issues. Sometimes a shared model, e.g., the HOPE or FICA tool or ars moriendi model, can be a helpful tool to put spiritual issues in a shared framework (Blaber et al. 2015; Leget 2017).

Referral may be due to different causes. Firstly, sometimes patients who belong to a spiritual community or religious tradition prefer to be accompanied by a minister of this tradition. With respect to an issue as personal, intimate, and culturally determined as spirituality, speaking with someone who understands the emotional and spiritual depth of one's spiritual process by being part of the same community can be a great source of support.

Secondly, internal or external reasons may ask for a referral. If one feels there is too little chemistry or confidence, another caregiver may be better as a conversation partner. Also the feeling of not being able to meet the specific demands of a patient, having no time or space, or discovering a spiritual crisis that asks for special expertise are legitimate reasons to refer to another healthcare professional.

12 Conclusion

Spiritual care is a strongly developing interdisciplinary field of research and studies, both within and outside of palliative care. Although much research still needs to be done, in this contribution we presented some helpful elements of providing spiritual care based on both research and clinical experience. Although much support can and should be drawn from instruments, spiritual care cannot succeed unless one is able to connect to one's own inner life. From there spiritual care can be developed including bedside skills in which hearing, sight, speech, touch, and presence are integrated (Sinclair et al. 2012).

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Dignity in Palliative Care

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Megan Best

Contents

Abstract

Community demands for death with dignity developed in modern times as a result of the medicalization of death. Confusion has often surrounded the meaning of the term "dignity" at the end of life due to its association with both euthanasia and a peaceful, natural death. While it is recognized that dignity is both intrinsic and inviolable as a universal characteristic of all human beings, it is also experienced as an extrinsic characteristic which can be impacted by external factors. Modern views of dignity conserving care recognize that patient dignity is preserved when healthcare workers refrain from transgressing the patient's standards and values, or refrain from forcing the patient to transgress his or her standards and values.

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_29

In this chapter, models of dignity in dying patients are detailed, along with empirically developed approaches to dignity conserving care. The essence of dignity conserving care is found to be socially constructed, individually perceived, culturally influenced, relational, and embodied. It is impacted by the perceptions of both the patient and the palliative care staff. The experience of dying with dignity is dependent on the dying person knowing that their loved ones, carers, and strangers perceive them to be as fully human as they are, regardless of their frailty.

1 Introduction

The goal of helping patients to die with dignity has been identified as a summary of the basic tenets of palliative care, and is an increasing priority in healthcare generally. Dignity, then, is such an intrinsic element of palliative care that it needs to be understood if individual practices are to be judged according to whether they are consistent with best practice. Palliative care occurs within the biopsychosocial-spiritual model of the human being (Sulmasy 2002), as it recognizes the need to address care for all dimensions of the person – physical, psychosocial, and spiritual (World Health Organization 2002). By upholding the preservation of dignity as a goal of care, management of dying patients can be tailored in a holistic way to the individual's personal needs and values, especially at the end of life when individual vulnerability increases and one's control over the environment reduces.

This chapter will examine the historical rise of the community call for dignified end-of-life care, the ways dignity can be understood, and its associations with requests for hastened death. Measures of dignity are outlined as well as ways dignity-enhancing care can be implemented.

2 Background

The call to be mindful of patient dignity in healthcare at the end of life developed as a result of the medicalization of death. Attitudes toward death have changed considerably over the last millennium. Madan describes the difference as one of hopefulness or confidence arising from the conviction that life encompasses death, compared to hopelessness flowing from seeing death as the end of a good thing, namely life (Madan 1992). Up until the eleventh century, historians describe an attitude toward death which was not fearful, as death was a collective experience that was not necessarily the end of existence (for those who believed in an afterlife). It was the emergence of individualism that led to the idea that death was a personal tragedy.

The Enlightenment, an intellectual and philosophical movement in Europe during the eighteenth century, led to the empowering of reason along with increased questioning of the church. Enlightenment thinking saw the mind and body as separate. As a result, science claimed the physical body as its domain, and in order to escape the control of the church, downplayed all the other domains. Since then, science and medicine have focused almost entirely on the biological or the biosocial model of human beings, where what is real is only that which can be empirically proven. Humans became masters of their own fate, and doctors gained power over other human beings through a supposed ability to prolong life.

The subsequent "medicalization" of death led to a view of death as something which was a failure. This view is held widely by both healthcare and general populations (Smith et al. 2018). Many scholars have described the subsequent loss of meaning in life, and therefore in death, that has ensued. Human life has been invaded by technology, and so death is redefined as not a natural phenomenon, which may be seen as meaningful and dignified, but something mechanical, "the ultimate form of consumer resistance" (Illich 2010).

There is a risk that those approaching the end of life in modern western society may be either under- or over-managed. Ageing or dying persons may be relegated to an institution, apart from family and friends, where they experience multidimensional loneliness and lose their former independence and identity. Any expression of excitement or distress leads to the administration

of medications which, while relieving immediate symptoms, lead to further dependence on others and loss of self-esteem. Alternatively, those who are dying may be caught up in the acute hospital system, disempowered as patients, where they are dehumanized by technology and the timing of the end of life becomes a decision for doctors.

The latter situation led to the public criticism of medical end-of-life care and calls for euthanasia, to allow individuals to escape the "living death" of technically assisted existence. In the USA, the legal cases of Karen Quinlan (d. 1986) and Nancy Cruzan (d. 1990), both diagnosed with persistent vegetative state (PVS, also known as post-coma unresponsiveness or unresponsive wakefulness syndrome), led to prolonged debates in a blaze of publicity.

In April 1975, Quinlan stopped breathing after consuming barbiturates and/or benzodiazepines with alcohol while on a strict diet. She lapsed into a coma and required ventilation and nasogastric feeding to live. After 5 months, when her family realized that she would never recover, they decided to remove the ventilator and let Karen die. However, at this time the American Medical Association equated withdrawing a respirator in order to allow death to occur with euthanasia, and equated euthanasia with murder. After a long legal battle, in January 1976 Quinlan's parents were granted the right to discontinue life support. However, she was still alive in April 1976, by which time she had pressure sores extending to the bone. As disconnecting the ventilator was still viewed as a form of euthanasia by the medical staff, rather than just disconnecting the ventilator, Quinlan was weaned off. She was transferred to a nursing home where she lived for over 10 years before dying from pneumonia.

Cruzan's case led to a landmark decision by the US Supreme Court. Cruzan had a cardiac arrest following a car accident in 1983. She also experienced anoxic brain damage. She remained in PVS for 7 years, being kept alive by a feeding tube. Cruzan's parents sought legal permission to remove their daughter's feeding tube, and it went to the US Supreme Court before it was decided that there was sufficient evidence to believe that, had she been competent, Cruzan would have wanted the tube removed, and it was allowed by the courts.

In the United Kingdom, the case of Tony Bland (d. 1993) went through a similar process before a court order was granted allowing him to "die with dignity." As a result, he became the first patient in English legal history to be allowed to die by the courts through the withdrawal of life-prolonging treatment including food and water. While all three cases were complex in their own ways, they represent the failure of modern medicine to ask not only, "how can we prolong life?," but whether we should. And, as concern for death with dignity followed a pattern of neglect of the needs of the dying, it also illustrates how the phrase "dying with dignity" came to be associated with not only the push for legalized euthanasia, but also with the call for holistic care in the context of a natural death.

As time has progressed, rather than escaping the fear of death through the ever-increasing list of therapies available in western medicine, paradoxically, the fear of death has increased, and its discussion remains taboo. Personal spiritual and religious beliefs that could ease this fear are less common in western countries. The decrease in perinatal mortality and rise in hospitalization of the dying means that most members of the public have never witnessed a death or seen a corpse, and for many the mystery of death remains obscure and menacing. The ever-increasing diagnostic capabilities of medicine make death an overshadowing presence on the lives of adults, increasing with their years, and leading to regular health checks and dependence on medical specialists. Death in this context is commonly seen as a final indignity. Good palliative care recognizes this fear and acknowledges the existential distress that is experienced by dying people and their families.

3 What Is Dignity?

The Oxford English Dictionary defines dignity as the quality of being worthy or honorable (Brown 1993); however, this does not cover the extent of the idea of dignity in palliative care (Abiven

1991). The medical literature encompasses many interpretations of the word, difficulty in arriving at a final consensus possibly being due to the nature of the phenomenon. Qualitative research has illustrated that the concept of dignity in palliative care is broadly understood and influenced by culture and personal history, therefore the experience of dignity will be different for everyone. Moreover, dignity for any one individual is dynamic and can be perceived differently by the family and carers compared to the patient (Hemati et al. 2016). Long lists of factors that are thought to promote or undermine dignity are a good start, but have limited usefulness if dignity itself remains undefined. There runs a risk of conflating dignified palliative care with high quality palliative care, or simply, "a good death." While both include respect for patient dignity, neither is synonymous.

In an attempt to clarify the concept of dignity in healthcare, some authors have taken a philosophical approach. While it has been argued that dignity itself is a useless concept as it adds nothing new (if dignified palliative care just means high quality palliative care, recognizing the patient's autonomy, privacy, etc.), others have suggested that human dignity lies in the ability to reason. This thinking can be traced back to the eighteenth-century philosopher Immanuel Kant, who argued that the intrinsic worth, or dignity, of humans resides in their ability as rational agents to make their own decisions. This equates dignity with autonomy, and so a patient has dignity when he is she is able to live in accordance with his or her standards and values. Others have challenged this view, which raises the question of how these attributes relate to individuals with profound intellectual impairment who are unable to rationalize. Instead they propose that dignity is inherent for those who belong to the species *Homo sapiens*, as this is what gives one the ability to reason, even if they are unable to express it at a particular time (Pellegrino 2005). It is this view that confers value on all human lives regardless of individual characteristics. Certainly, the understanding of inherent human dignity which is universal and incontrovertible is that which is referred to in international human rights documents, such as the United Nations' *Universal Declaration of Human Rights* (UN General Assembly 1948).

However, if dignity is inherent for all human beings, then the concept of death without dignity is fallacious. Allmark finds it more helpful to consider the meaning of death with indignity (Allmark 2002). An indignity can be inflicted on someone and infers an affront. It would include actions such as withholding information and depriving a person of the opportunity to make self-determining decisions, or providing inadequate symptom control so that a person suffers great pain. While these actions would represent a failure to recognize the inherent dignity of some persons, it would not remove their dignity. It seems then, that the goal of healthcare professionals needs to be not so much aiming for death with dignity for their patients (as dignity is intrinsic and cannot be lost), but to avoid causing a death where the patient suffers from *indignity*. They can try to do this in two ways: The first is by not imposing indignities – for example, not taking choices away from people at the end of their lives. The second is by acting so as to minimize indignities, such as pain or humiliation. But there would never be cause to criticize people who suffer such indignities, nor hold them in contempt, because they are not in control of whether or not they suffer them.

Allmark (2002) also suggests that dignity may be seen as a continuum, where some people are able to live in such an exemplary way that they are viewed as possessing a high degree of dignity, so that they are able to experience a dignified death despite indignities inflicted on them (such as Jesus Christ or Mahatma Gandhi). This is, however, beyond the scope of this chapter.

Pullman manages the breadth of usage of the term by identifying two types of dignity (Pullman 2002). The intrinsic dignity due to each human person regardless of individual characteristics he refers to as "basic dignity." The sense of dignity that is more subjective, and transient in nature, he refers to as "personal dignity." This type of dignity can be either enhanced or diminished by external factors beyond the control of the individual, and it is this sense of dignity which is usually

the focus of dignity discussions in palliative care. It is the area in which the palliative care worker must strive to have an impact.

Proulx and Jacelon's review of the concept "dying with dignity" (Proulx and Jacelon 2004) confirmed this dichotomy, identifying both an "intrinsic, unconditional quality of human worth" and "the external qualities of physical comfort, meaningfulness, autonomy, usefulness, preparedness, and interpersonal connection." In a review of the Oregon *Death with Dignity Act*, they note that, for patients whose dignity is primarily experienced through independence and autonomy, euthanasia may be a welcome option, particularly in the context of a healthcare system which does not uphold individual patients' dignity in other ways. They express concern that societal pressure to be a "good patient" experiencing a "good death," and not waste limited health resources, may result in patients exercising their extrinsic dignity (autonomously choosing euthanasia) at the expense of their intrinsic dignity (in terms of the inalienable right to life). This would represent discrimination against the vulnerable who may feel they have a duty to die so as not to burden society.

In a study of patients with advanced cancer, Chochinov et al. (2002a) asked patients whether dignity was internally held and inviolable, or externally bestowed and able to be withdrawn. They found that outpatients were more likely to agree with the former definition while nearly two third of inpatients believed that they could be stripped of their dignity by others. The authors suggest that this may reflect the greater ability for self-determination in those living at home. It also suggests that those living in an institutionalized setting may be more vulnerable to loss of dignity.

Killmister's suggestion that patient dignity is preserved when healthcare workers refrain from transgressing the patient's standards and values, or refrain from forcing the patient to transgress his or her standards and values, provides a foundation for understanding what constitutes a violation of personal dignity (Killmister 2010). It is our standards and values that inform our decision-making, thereby shaping our lives and giving meaning and purpose to our existence. It helps us maintain a sense of who we are, or personhood. Historical, social, and cultural perspectives of the individual will shape our standards and values. Dignity will therefore lie closely with spirituality, those relationships which give meaning to our existence and underlie our means of coping with the existential challenges of life-threatening disease (Best et al. 2015). Chochinov has described loss of the sense of dignity as a possible symptom of existential or spiritual distress (Chochinov 2006). The Enlightenment's exclusion of non-physical from science, as explained above, is one of the reasons why this dimension of care has been so long neglected in western medicine (Cassell 1982), contributing to considerable suffering in the medical context.

Killmister suggests that these standards and values may not be particularly distinguished but include our moral codes, religious commitments, cultural mores, sense of etiquette, and ideas about appropriate interactions with other people. This explains why we may feel shame at having our bodies exposed in medical procedures, or by experiencing loss of bowel function in public. The reason why being left semi-naked on a hospital trolley is experienced as humiliation is because it is a violation of dignity for the patient who has standards of public decency that they strive to maintain in their daily lives. Dignity is known to correlate with one's appearance and how one wants to be seen. It reminds us that dignity is embodied, and that the experience of dying is associated with altered, deteriorating bodies, the limits of which will dictate when life must end. Street and Kissane (2001) listed the sufferings of the body in illness associated with physical changes such as amputation, stomas, fistulas, bedsores, and ulcers, as well as physiological dysfunctions such as weakness and incontinence, so that the body may become a focus for shame, humiliation, and disgust. As all these factors can be impacted through the course of illness, the patient's sense of dignity can be challenged repeatedly throughout the trajectory of illness (van Gennip et al. 2015) and will thus need to be considered at all stages of palliative care.

While patient standards and values cannot be allowed to trump all other considerations in the performance of healthcare, Killmister's definition is the beginning of a more coherent understanding of dignity. Many authors agree that that the concept of dying with dignity is dependent on the dying person knowing that their loved ones, carers, and strangers perceive them to be as fully human as they are, regardless of their fragility. Moody perceived this insistent claim to dignity to reflect the part of human beings that is truly transcendent, or more than their physical body or social role.

4 Quantitative Associations with Loss of Dignity

Further understanding of what impacts dignity can be obtained by considering those factors with which it has been empirically associated. Wilson and colleagues found that burden to others was correlated with loss of dignity ($r = 0.49$, $p \leq 0.01$) in a group of 69 Canadian patients with advanced cancer (Wilson et al. 2005). In a study of 189 Canadian patients with end-stage cancer, Chochinov and colleagues found that existential variables, including dignity, had the most influence on the will to live (Chochinov et al. 2005). In both studies, physical sources of distress were less influential.

5 Carers' Attitudes to Dignity at the End of Life

Proulx and Jacelon (2004) found that healthcare providers and families of dying patients can be reluctant to accept that a dying individual's priority may be spiritual guidance rather than technologically advanced medical care, when aiming for dying with dignity. Holstein (1997) reported that physicians may recommend continuing active treatment to avoid peer criticism, and the family may agree to avoid blame or guilt, despite agreement that patient autonomy is important. Steinhauser and colleagues also reported on discrepancies between patient's views and carer's views on what is important at the end of life (Steinhauser et al. 2000). This suggests that the dignity-protecting needs of vulnerable patients are at risk of being misinterpreted or ignored by those caring for them. Nurses are reported to be more in tune with patient preferences.

A study of over 1000 American physicians found that 90% thought that the concept of human dignity was relevant to their practice, although there was not consistent understanding of what the word dignity meant (Antiel et al. 2012). Physicians who understood the word dignity as "basic dignity" (defined above) were significantly more likely to judge that the life of a patient in a case history of an end-of-life scenario was worth living, compared to those who conceive dignity as "personal dignity," or as a form of autonomy. This suggests that the physician's understanding of human dignity may impact their understanding of ethics in end-of-life care.

6 Measures of Dignity

6.1 The Patient Dignity Inventory (PDI)

Based on a qualitative study focusing on how dying cancer patients in Canada understand and define dignity, Chochinov and colleagues developed an empirical model of dignity (Chochinov et al. 2002a). Themes and subthemes from the model were used to devise 22 items, and terminally ill cancer patients were asked how much they thought that these items could influence their sense of dignity. The 22-item PDI prototype was later revised and became the 25-item PDI, a measurement instrument which can be used by clinicians to detect end-of-life dignity-related distress, which was validated in a cohort of Canadian palliative care patients (Chochinov et al. 2008). It is measured as five factors: symptom distress, existential distress, dependency, peace of mind, and social support. A study from the Netherlands using the PDI found that communication and care-related aspects were also important for the sense of dignity in the patient cohort (Albers et al. 2011).

7 Models of Dignity

7.1 Chochinov's Dignity Model

Chochinov and colleagues developed the "Dignity Model" of palliative care to understand how patients face advancing terminal illness and to inform dignity conserving care (Chochinov et al. 2002a). It was based on qualitative interviews and surveys with 50 terminally ill patients, who were asked how they personally understood and defined the term *dignity*, and what experiences supported or undermined their sense of dignity. Given the association between loss of dignity and death-hastening decisions, patients were also asked about how they thought dignity may impact end-of-life decision-making. Three domains that can impact on personal dignity (positively or negatively) were identified in the analysis: (1) illness-related concerns, (2) dignity conserving repertoire, and (3) social dignity inventory.

7.1.1 Illness-Related Concerns

This domain includes issues related to the illness that impact on the person's level of independence and symptom burden, and thus threaten or actually impact their sense of dignity. It includes (a) level of independence (the ability to remain cognitively alert and perform activities of daily living) and (b) symptom distress, which could be physical or psychological. Physical distress related to symptoms of the underlying illness, and psychological distress could refer to medical uncertainty about disease management or progression, or death anxiety associated with one's imminent death. All could threaten personal dignity.

7.1.2 Dignity Conserving Repertoire

This domain includes "dignity conserving perspectives," or promoting dignity by the way you view a situation, and "dignity conserving practices," or personal actions that can support one's sense of dignity.

Dignity conserving perspectives refer to established personal characteristics and values, such as (a) the sense of continuity of self (feeling you are still being treated with respect as you were before you got sick), (b) personal role preservation (still being able to function in a social role despite illness), (c) leaving a legacy (through one's accomplishments or connections), (d) maintenance of pride (maintaining self-respect despite diminishing independence), (e) hopefulness (associated with seeing life as meaningful and purposeful), (f) personal autonomy (the ability to maintain control over life circumstances), (g) acceptance (coming to terms with changing life circumstances), and (h) resilience (the mental determination to rise above the illness experience to optimize quality of life).

Dignity conserving practices refers to the techniques that patients can use to preserve personal dignity. These include: (a) living in the moment (rather than worrying about the future), (b) maintaining normalcy (carrying on with usual routines while going through the illness experience), and (c) seeking spiritual comfort (finding comfort in one's spiritual beliefs).

7.1.3 Social Dignity Inventory

This domain refers to relationship dynamics which can impact one's sense of dignity. It includes (a) privacy boundaries (the ability to protect one's personal environment from intrusion), (b) social support (having a supportive community of friends, family, or carers), (c) care tenor (the attitude taken by those interacting with the patient), (d) burden to others (whether feeling is actual or anticipated), (e) aftermath concerns (fears associated with the impact of death on those left behind).

This conceptual model of dignity suggests that where illness-related concerns and the social dignity inventory (both potentially having a deleterious effect on dignity) were moderated by a positive dignity conserving repertoire (including dignity conserving perspectives and/or dignity conserving practices), the patient could maintain a sense of dignity. The reverse, where a limited dignity conserving repertoire exists, puts the patient at risk of a diminished sense of dignity. Furthermore, this model proposes that dignity in palliative care is an interactive process between

the dying and their carers, a point suggested in an analysis of dignity by Johnson (1998). It therefore provides guidance for providing dignity conserving care, listing specific practices that could preserve patient dignity (such as by adopting a shared decision-making model), and/or act as interventions for patients with an impaired sense of dignity.

Chochinov's dignity model is also recommended by the authors in view of literature describing patients' preferences of hastened death when experiencing depression or hopelessness (Breitbart et al. 2000). As loss of dignity can be associated with depression, hopelessness, and a desire for hastened death, and dignity can influence the will to live (Chochinov et al. 2005), it is important for palliative care workers to understand the importance of dignity in the lives of dying patients.

8 Dignity Conserving Care

It is therefore obvious that, even if one has a general understanding of what constitutes dignity conserving care, and values it in the context of the dying patient, in order to provide it, one will need to take the time to ask, listen, and understand what it means for any particular patient. The more healthcare workers affirm the individual's value as a person, the more likely it will be that the person will perceive their dignity to be upheld. Respecting the dignity of the patient results in the reduction of her/his suffering and prepares her/him for a comfortable death (Hemati et al. 2016).

Many authors have noted that, once dignity is the goal of care at the end of life, management options will expand beyond symptom control to include physical, psychological, social, spiritual, and existential aspects of the patient's experience, which, as noted above, is consistent with the WHO definition of palliative care (World Health Organization 2002). In a review of dignity conserving care at the end of life, Ostlund and colleagues reported the evidence to support care actions in a broad spectrum of domains (Östlund et al. 2012).

8.1 A, B, C, D of Dignity Conserving Care

Chochinov developed a mnemonic to support dignity conserving care (Chochinov 2007):

(A) *Attitude:* Healthcare providers need to examine their approach to patients, because it is possible that they are based on preconceptions that do not reflect the reality for a particular patient. Chochinov gives the example of assumption of poor quality of life for a patient with chronic disability which may lead the health worker to withhold life sustaining choices. As the way they are viewed by healthcare workers impacts on a patient's view of him or herself, healthcare providers need to be aware of the attitudes and assumptions toward those for which they care. Trying to imagine what it would be like to be in the patient's position and self-reflection are encouraged.

(B) *Behavior:* Awareness or change of one's attitude can lead to behavioral change. The understanding that one's attitudes play an important role in mediating patient dignity should lead to a practice of treating all patients with kindness and respect. This would include actions such as treating all patient contact professionally (not avoiding those patients who are dying) and maintaining courtesy during physical examinations by recognizing the intimacy of the situation and asking permission to touch the patient. Small acts of kindness such as getting a patient a glass of water conveys the message that the person is worthy of this attention.

(C) *Compassion:* Attitude and behavior can be examined cognitively, but compassion will engage the emotions. Compassion refers to "a deep awareness of the suffering of another coupled with the wish to relieve it." Chochinov recognizes that compassion may not be instinctive and may require time and experience to fully develop, through growing understanding of human nature. It may be cultivated by exploring the medical humanities, the arts, or one's own experiences of illness and suffering. It will be conveyed to

the patient through some form of communication, a look or a touch that acknowledges the person, not just the illness.

(D) *Dialogue:* As communication of information is such an important part of healthcare, dignity conserving care requires that dialogue acknowledges the personhood of the patient and the emotional impact of their experience of illness. Dialogue can be used to get to know more about what is important to the patient, so that care can be tailored to their individual needs. Asking about an individual's values and beliefs allows the healthcare provider to build trust, honesty, and openness in the therapeutic relationship.

8.2 The Dignity Care Pathway

The Dignity Care Pathway (DCP) is a community nursing intervention based on the Chochinov theoretical model of dignity care. It was developed to support nurses caring for people at the end of life, and it was found to have high acceptability and feasibility in a trial in rural Scotland (Johnston et al. 2012). The community nurse makes a clinical judgment on when to apply the pathway. The DCP has three components: (1) The Patient Dignity Inventory (PDI, see above) is used to assess possible sources of dignity-related distress; (2) Reflective questions are used to explore the identified issues and the patient's preferences on how to address them; (3) Care actions are the implementation of the patient's wishes regarding dignity conserving care. With the patient's permission, they may be shared with the family. The goal is to give the patient a voice in their own care as a way of treating them as equals, respecting them, and acknowledging their value and worth. The PDI is then used to evaluate the interventions. If new issues arise, the pathway is recommenced. A manual has been produced to support the use of the DCP.

8.3 Dignity Therapy

This is the name given to a therapeutic intervention developed by Chochinov et al. (2005) to treat depression and spiritual suffering in palliative care patients. It is a form of life review and was designed to involve two sessions of 1 h or less each, where the patient has the opportunity to talk about their life to a staff member in a recorded interview which is then transcribed, edited, and returned to the patient. It would therefore assist in promoting the dignity conserving perspective of leaving a legacy (above). A recent systematic review of 12 quantitative studies trialing Dignity Therapy (DT) found that DT is highly acceptable to patients, who report high levels of satisfaction and benefits for themselves and their families. Families also report finding it helpful in bereavement (McClement et al. 2008). In all the studies examined in the review, the feasibility of DT was challenged due to the difficulties of recruitment and retention of seriously ill patients in longitudinal research. Also, DT is labor intensive for both the patient and the therapist, with one study reporting that four to six sessions were required for completion of therapy, with over 15 h devoted to each patient, plus significant costs for the interview transcription (Hall et al. 2012). Efficacy was demonstrated in single group studies, including improved sense of dignity; however, no randomized controlled trials have yet shown a significant impact for DT. The authors suggest that this may be due to technical errors, such as recruitment issues, measuring the wrong outcomes, or ceiling/floor effects. More research needs to be done to clarify the underlying mechanism of DT's impact.

9 Future Directions

As definitions of dignity in palliative care become clearer and our understanding of its breadth improves, we have come to appreciate how conceptions of dignity are socially constructed, individually perceived, culturally influenced, relational, and embodied. For example, a study of Japanese patients found that participants did not want dignity therapy and viewed a good death as an oblivious death (Akechi et al. 2012). It will therefore be important to investigate the factors that impact patient dignity across a wide range of

cultures and illnesses to ensure that appropriate dignity conserving care is offered in each context. It is possible that particular diseases may be associated with risks for loss of dignity that are not present in all situations. Vulnerable populations such as patients suffering from dementia may also be at risk in unique ways and require study. More work also needs to be done to fully understand the discrepancies between patient's and carer's views of dignity, in order to minimize risks to dignity for those unable to express their own care preferences.

Dignity therapy has high patient and family acceptance, but is labor and resource intensive. Research is required to identify which patients are most likely to benefit from specialist therapy, and which would be adequately managed with overall dignity conserving care, in order to clarify referral criteria (Lindqvist et al. 2015).

10 Conclusion

Evidence suggests that threats to preservation of dignity at the end of life can be cultural, institutional, and individual. Professional organizations have advocated that increased public discussion about death and dying is needed to improve understanding of normal end-of-life care. Cultural acceptance of the terminal stages of life which lead naturally and inevitably to death is required to ease the fear which is prevalent in western societies, and encourage more open conversations about end-of-life care preferences. There are recommendations in the literature that institutions need to consider the need to ensure proportionate treatment for patients, and to promote the importance of a dignified death to staff members who care for the dying. Healthcare workers are in the position to promote dignity in dying by encouraging patients to articulate their preferences and learning to listen to what they say. There are as many descriptions of a dignified death as there are dying patients. Palliative care workers need to be open to understanding what matters to each patient in their care if they are to succeed in supporting them in a dignified death.

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Creative Art Making in Palliative Care

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_38

Abstract

This chapter has an intentionally broad title to convey the breadth of ways that arts (with an emphasis on visual arts but also performative, poetic, tactile, and narrative art forms) contribute to whole-person wellness, hope, and engagement, across a range of stages encountered in palliative care services. This chapter looks at participatory arts, community and creative art facilitation, and art therapy. While there is considerable overlap in the utility of art and its benefits, such as creative enabling and expression for the patient, the range of approaches to art in palliative care herald from different disciplines, with different objectives, and are usually practised by people with distinctive professional backgrounds. It will also be clear that aspects of art facilitation in palliative care overlap substantially with approaches found in mental healthcare, dementia care, aged care, rehabilitation, and wellness initiatives in the general population. Specific to palliative care are the needs of the individual patient. Arts in palliative care now cross a range of settings, from hospital or hospice to residential care homes and community settings, variously with a dedicated studio space or a relatively mobile setup provided by the practitioner in any venue, even at the bedside. There is also some degree of nexus between arts in palliative care discussed here and psychotherapy and psychoanalysis, music engagement, "social clubs," and initiatives for art appreciation offered by art organizations, galleries, or museums and community-run art-making courses. However, this chapter focuses on the art experience tailored to people with palliative care needs.

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1 Introduction

Serious illness brings with it various crises of selfhood; changing capacities and identity; adapting and scrutinizing expectations and long-term plans; undermining the sense of belonging to the community or changing communities; relaxing control of various aspects of one's life, organizational, physical, emotional, and temporal; and processing the feelings associated with approaching the end of life and death – its meanings and ramifications. These estrangements from the familiar all threaten the wholeness and integrity of humanness of the individual. Palliative care is uniquely positioned in medical disciplines to embrace this whole-person narrative and utilize nonmedical interventions that will help nurture wholeness and living fully until death.

1.1 Terminology

This chapter divides the delivery of arts in palliative care into two broad approaches. The first approach may be described as **art facilitation** which includes individual or group participatory art making (sometimes also called therapeutic arts), and also community arts, in which the facilitator is primarily an artist by training and experience, and the explicit objective for participants is creativity and expression along the path to making art. In regard to art facilitation, we have drawn on our experiences and learnings from a participatory art program delivered in Sydney, Australia, by HammondCare (a provider of aged care, rehabilitation and palliative care services) and the University of New South Wales. The program was based on the "Arts on Prescription" model originally developed in the UK (Rigby 2004, pp. 25–28). Our "Arts on Prescription" initially targeted older people with unmet health and wellness needs, including recent bereavement, living in the community, and, later, included a "home delivered" art program for carers and people living with dementia. Recently, we have extended the model further to the inpatient setting through its deployment into a cancer rehabilitation ward.

Art facilitators include artists who may or may not have training in a range of artistic contexts, e.g., people who may have trained as teachers of children or adults but with no formal experience within healthcare settings. This category best describes the painters, ceramicists, actors, musicians, and media artists who facilitated patient art in the HammondCare "Arts on Prescription" program (HammondCare 2016). For patients and the artists themselves, the authenticity of their artistic background and use of genuine quality art materials (such as good brushes, paints, clay, and paper stock) were integral to providing a real art experience, that would not be misconstrued as mere entertainment, and one that would ensure that legacy artworks would be of high quality and longevity.

Community artists are grouped here with art facilitators. Community artists often work in an urban environment with community groups, especially marginalized and minority groups, in order to give voice to their concerns collectively through making group artworks and installations in public places (Hartley et al. 2008, pp. 22–23). In Melbourne, Australia, for example, this includes facilitation of hip-hop music writing, dance groups, mural painters, and textile makers from indigenous and migrant groups, choirs for older people, and situating art studios in youth centers to enable marginalized, disadvantaged, and minority groups to build a community and express themselves, e.g., Footscray Community Arts Centre (2013).

Art facilitators and community artists could provide programs in palliative care settings even though they may not have a specific background in palliative care. Drawing on our experience with "Arts on Prescription," we suggest that artists are selected based on their skill and passion as artists and their ability to work with people, in individual and small group settings. Training in the specific needs of palliative care patients can be provided by training in a classroom setting and/or through mentoring offered to the artist by other palliative care team members.

The second broad approach to be discussed is **art therapy**, which is an extension that has grown out of psychotherapy as a tool for psychological exploration, communication, and developing the relationship with a therapist (sometimes a psychoanalytical relationship in which images are interpreted), where the practitioner is primarily an art therapist or psychologist by profession, and the artistic by-product is of secondary importance to the inner journey. The artifact can remain confidential in many art therapy situations, serving rather as the visual vehicle for relating emotions and uncovering subconscious themes. This is one of the greatest distinctions between art facilitation and art therapy: the purpose of the art making is to evoke private, safe conversation but not to express or share. "The current definition from the British Association of Art Therapists (BAAT) is as follows: Art Therapy is a form of psychotherapy that uses art media as its primary mode of communication" (Case and Dalley 2014, p. 1). The art therapist can work on a one-to-one basis and also with groups of patients.

Palliative care and supporting people who are aging is an important area for art therapists (Case and Dalley 2014, p. 11; Pratt and Wood 1998):

> Old people often feel lonely and isolated, and therapeutic work helps acceptance of old age and infirmity by focusing on the past, recollecting significant events that happened a long time ago. For those who are terminally ill, art therapy enables an experience of working towards acceptance of death. For younger patients and children, who have life-threatening illnesses such as cancer or AIDS, using art helps to express uncertainties, fears and anxieties about the future. (Case and Dalley 2014, p. 11)

People who deliver arts in palliative care programs may variously be referred to as arts therapists, community artists, and other art practitioners with a range of titles, including art facilitators, creative therapists, art teachers, art group leaders, or creative therapists (Hartley et al. 2008, pp. 17, 22) and even sponsored artists-in-residence. Many artists and musicians would argue that *art making* is therapeutic in its own right – through immersion, concentration, and creativity – that "can take you onto another level of thinking, existing and philosophising" (Hartley et al. 2008, p. 133).

This chapter focuses on the art experience tailored to people with palliative care needs. The emphasis will be on art facilitation, rather than the specifics of art therapy, a specialist area well discussed by others. In keeping with our broad approach, we will simply use the term "artist" where we do not see any necessity to differentiate between art facilitator and art therapist in the text and reserve the specific terms for situations where the difference is important or where other writers have specifically referred to one or other group. Some of the art facilitators in our HammondCare programs are also trained art therapists and have shown themselves able to work in either role.

2 The Purpose of Art

Alain de Botton and John Armstrong in *Art as Therapy* (2013) prioritize seven functions of art (primarily visual art, but the functions apply equally well to sculptural and other arts) that support human *wholeness*: remembering, hope, sorrow, rebalancing, self-understanding, growth, and appreciation.

Reinterpreted through the lens of palliative care, some of these functions adopt greater importance, such as:

- Remembering or encapsulating important moments, creating and sharing meaningful experiences to cherish with loved ones and to create a legacy
- Hope, exploring positive and thankful expressions that resolve and heal, manifest in aesthetics of beauty, focusing on values and "the good" rather than pathology, giving form to spirituality and philosophy
- Rebalancing – examining priorities and adjustment of horizons and attitudes
- Self-understanding and growth – reflection, contemplation, developing one's "best self" irrespective of circumstance, learning, passing on ideas
- Appreciation – gratitude, immersive focus through art and diversion from pain and disease

The functions perhaps of greatest relevance in healthcare and in palliative care specifically include the potential of art making to:

- Enhance identity
- Empower with new skills and an opportunity for discovery
- Give the patient control and choice
- Create a safe community of belonging and relatable experiences for the patient
- Think through existential, psychosocial, and emotional issues
- Give expression or voice (even in a nonverbal sense) to anxieties, tensions, gratitude, and growth
- Enhance social interaction and relationship formation

Part of integrating arts in palliative whole-person care involves recognizing the appropriate degree of activity and timing that will complement medical and other allied health treatment and identifying who can facilitate such experiences, ranging from art therapists to artists and

skilled volunteers or other skilled staff and family. The objective is always in supporting the expression and well-being of the patient.

For staff navigating a complex time in the patient's treatment, and for families experiencing an important part of their life together, the arts are an instrument of motivation and experience (Hartley et al. 2008, p. 13), an important psychological therapy. Palliative care occurs in a wide range of community settings, e.g., care homes and GP surgeries, and in the community. "Unlike much healthcare, which has taken place in large hospitals with an emphasis on biomedical science in medical treatments and nursing care, palliative care incorporates strong elements of *spiritual care* and *social work* and *welfare practice* along with biomedical science": an opportunity to interact with physical and mental deterioration, death, pain, and loss (Hartley et al. 2008, p. 13).

Payne and Hartley conclude:

> Creative work is a vital human activity that seeks to help people live until the moment that they die . . . Art and creative work enhances psychological and social stability, enriches human life and enables people to experience *self-fulfilment*. Art also supports patients and families to find solace and relief from distress and difficulty . . . The arts can be an instrument of psychological therapy . . .The arts facilitate communication where it is physically, socially or psychologically difficult. Participation and *inclusion* through creative work can enable patients and their families to *repair relationships* among themselves when facing the stress of an advanced and final illness. (Ch.15 by Payne and Hartley in Hartley et al. 2008, p. 186, emphasis added)

2.1 Art's Contribution to Individual Wholeness

McNiff (2004, p. 3) states that in the past, "Healing belonged to the 'soft' realm of spirituality, whereas clinical treatment aspired to a more technical and controlled realm of expertise. Our culture has lost the ancient insight of Socrates, who chided Charmides for trying to heal the body without first engaging the soul. 'Curing the soul', he said, 'is the first and essential thing.'" Today, people who suffer from illness want to be involved in their recovery, to contribute to the healing process, and not just to passively receive treatments administered by others. Participatory arts may constitute a form of active involvement in healing action.

2.1.1 Identity and Personhood

An important aspect of creative fabrication is weaving together and retelling narrative. It is important to give expression to each individual's story, whether a life story, a recount of significant events, viewpoints, or a message to family and friends. Sometimes it can be difficult to put these ideas into conversations; however the abstraction of poetry, song, painting, or assembled objects can liberate the message. In some instances, such as the participatory painting classes, patients are equipped with materials and techniques that enable them to directly create their own expression. In other instances, the role of the artist is as facilitator who helps put snapshots and ideas into an artistic form, e.g., to write songs and poems and create a collage or even a play script. We have found this partnership method can be especially effective for a person with dementia who relates experiences and moments nonchronologically or nonverbally. The skilled artist can help build an artifact that will serve as a legacy for family and friends (Hartley et al. 2008; Pratt et al. 1998, Loc.879; Connell 1992).

"Death, dying and bereavement are an important part of life, and while we all know that we will face them, we often do not think through our responses to these powerful elements of life in advance" (Hartley et al. 2008, p. 13). The arts are a mechanism for facilitating a response to current experience and giving it meaning. Stanworth (2003) says the arts create possibilities for motivation and growth, for coping and change, and for self-actualization and self-realization. For patients unaccustomed to the language of spiritual or reflective thought or unable to analyze their feelings, creative arts may help them express these ideas (such as hope, joy, or distress).

Arts also offer possibilities to make sense of situations, to create something of value, and to leave something behind – a legacy not only for patients but also for their families and carers and the inherently valuable role of such legacies as part of human experience. When great attention

is being given to the body, "the many other facets that make a person whole can feel neglected leading to a sense of *disorientation, disassociation and a loss of identity*" (Hartley et al. 2008, p. 141), and illness can permeate and consume one's whole being. Therefore, when people are nearing death, it is essential that people feel understood and recognized in order to feel alive and present.

Themes of identity re-formation that frequently appear in therapeutic arts include the patient's experience of their ill or failing body, in engaging with materials and linking bodily experiences with art making. This approach has also been utilized by art therapists working with psychotic clients and people with eating disorders (Levens 1995). Erskine and Judd (1994) articulate this *interrelationship of body and mind*. The symbolic capacity of art materials enables wordless layers of individual experience and self-image to be rendered in concrete form, which can be therapeutically powerful.

2.1.2 Diversity

As a means of communication alternate to language, engagement with arts can help palliative care services respond to diversity – to people with dementia, people with different language backgrounds and cultural experiences, people from varying educational and socioeconomic experiences, or people limited by intellectual or physical disabilities. Thus, the arts may help people with learning disabilities, cognitive impairments, dementia, or speaking difficulties to be heard. "Art, craft and music can help people express spiritual ideas, metaphors and preferences in ways that reflect different cultural traditions, and expand the arts in society" (Hartley et al. 2008, p. 17). Integrating culturally relevant and meaningful objects and images in art overcomes diversity, as does emphasis on the creative experience over and above the final artifact.

2.1.3 Nonjudgment

That the art product or artisanship is not a subject for criticism and that the creative environment is nonjudgmental and exploratory is central to this emancipation from the outcome. For many participants, they are learning a new artistic skill that they have never before utilized, which is both intriguing and liberating. Social interaction in a group setting should be fun and encouraging, not competitive or critical. Participants are often extending their experience.

2.1.4 Control

Virginia Hearth (Chap.11 in Hartley et al. 2008) particularly emphasizes that the arts can help people feel more in control, by gaining control of materials and ideas as part of the creative experience. For people who have lost control of many aspects of their lives and their own care and independence, the importance of making choices and having control is especially poignant and reassuring.

Art making is "tangible evidence of [a patient's] vitality and capacity to control their bodies" (Pratt et al. 1998, Loc.886).

2.1.5 Processing Illness, Dying, and Grief

The creative, abstract, and metaphoric side of human experience is largely ignored in a medical treatment model; however arts can help the patient develop their own understanding of their experience. Coming to terms with isolation caused by illness and an increased sense of autonomy and confidence, which consequently strengthens the patients' ability to cope with illness, are potential areas of "processing" that are supported by art making (Pratt et al. 1998, Loc.865).

Beyond self-fulfillment for the patient, arts are intended to contribute to an overall healthcare service for patients and their families and may also contribute to the community's engagement with death, dying, and bereavement. Therefore, the needs of the patients and their families should determine the arts selected and how they fit into the patient's overall care plan. The choice of art medium aims to enable patients to reach their creative best.

2.2 The Patient Experience

The arts can elicit strong reactions, and developing an understanding of these responses is part of understanding the whole patient.

Both the intellectual problem-solving and the emotional process adjustment can be facilitated by arts that offer time and space to reflect on, and adjust to, bad news or powerful feelings (Pratt et al. 1998, Loc.1123).

Patients in palliative care and people undergoing cancer rehabilitation share a traumatic experience; however they do not constitute a homogeneous population. Among them there may be patients with a psychiatric history (with revived vulnerability); patients who may have developed a dysfunctional coping mechanism, e.g., substance abuse; patients experiencing a temporary circumstantial stage of anxiety or depression; and others who cope in a mature way who ask for the help they need (Pratt et al. 1998, Loc.3777) – focusing on the inner *psychic* reality.

Palliative care outpatients and cancer patients may not be in pain but nevertheless "often the memory of the pain is still very alive, or the effects are visible in their body. They may be suffering from side effects of surgery, or radiotherapy, or chemotherapy, or bone marrow transplant. They may suffer from fatigue, weakness, migraine, swollen arms, [and difficulties] walking, talking, eating, [and] impairments in any area of functioning. The *body* becomes suddenly very important in the therapeutic relationship" (Pratt et al. 1998, Loc.3792).

Physical needs can include relaxation and soothing experiences, finding relief in relaxing forms of art practice, guided by principles of self-hypnosis and visualization, or as a form of cathartic expression (taking negative feelings out on the paper, making a mess, throwing out the paper, etc.) (Pratt et al. 1998, Loc.3802). Patients can use visual arts to represent pain, e.g., shapes and colors that symbolize, express, and contain pain. "In treating physical injuries, we know that symptoms, however uncomfortable, often function as messengers. They have stories to tell about how we live our lives and how sensitive we are to the body's needs" (McNiff 2004, p. 112).

According to McNiff (2004, Loc.89), art heals by accepting the pain and doing something (fruitful, productive) with it, i.e., a useful transformative process.

2.3 Expressing Fears and Finding Meaning

The arts offer us a way of making sense of the world and help us to define who we are and who we have been: "Our mind works in pictures, not words, and we grapple to express the inexpressible"(Waller and Sibbet 2005, p. 4). Throughout history artists, poets, writers, musicians, playwrights, dancers, and puppeteers have used *metaphor* to reveal wisdom through their creativity. Death has always been an inspiration for artistic imagination: a way to confront mortality, fears, and taboos. The arts are useful for confronting terminal illness, death, and bereavement through the use of metaphor and euphemisms, e.g., focusing on beginnings and endings, journeys and change, and seasons or transforming metamorphosing creatures like butterflies (Hartley et al. 2008, p. 142).

Metaphors allow people to step away from their reality and view it as a "witness" and also to look beyond the present to envisage the continuation of life without them.

"The images of ill health, pain, suffering, ageing, death and dying are some of the most poignant we retain and probably the most easily distorted" (Pratt et al. 1998, Loc.2239). Image making is a method to open and engage the imagination, enabling pictorial language and communication – a code of understanding, belonging only to the person who has created the image.

2.4 Art Modality and Materiality of the Medium

Interacting *with* the art media kindles creativity. Getting dirty hands, feeling the squelch and coldness of clay, the freewill of paint on wet paper, malleability, tactility, colors, textures, scratching, scraping, layering, adapting spontaneously to "accidents," and etching repeatedly are all part of the inspiration drawn directly from the chosen medium itself. Art making is somatic, experiential, physical, and sensual:

> I like getting messy! And experimenting! — R. (Cancer rehabilitation ward patient)

A function of the artist is to enable an experience of empowerment through the art materials so that the patient becomes "the expert" in telling their own story (Pratt et al. 1998, Loc. 916). Connell (1992) notes that capacity to contain *layers of meaning* (which carry the experiences, thoughts, and concerns of its creator) is characteristic of art (and music).

Interacting *about* the media enables communication between artist and patient – even more prescient in art therapy when the therapist-patient relationship is instrumental. Different art media can motivate or "jumpstart" hesitant patients. The materials and projects selected should facilitate an "achievable beginning, and lay the foundation for future development" (Hartley et al. 2008, p. 85), taking into account the constraints of the individual's strength and disease.

"There must be a large enough range of art materials from which the client can choose, as each medium lends itself to certain kinds of emotional communications" (Pratt et al. 1998, Loc.255). Case and Dalley (2014, p. 107) suggest a range of materials "from paint, paper and crayons to materials for three-dimensional modeling such as clay, plasticine, 'model magic' and 'junk' for making models and sculptures. The materials in art therapy can be used in many different ways to indicate states of mind, profound feelings, thoughts and ideas." Over time, patients usually progress from "safe" familiar materials to more adventurous ones.

2.4.1 Painting

Appropriately pitched projects are intended to give satisfaction and expression, which is valued over technique or mastery for those art forms with a steep learning curve, as well as accommodation of techniques that "unfold" themselves and include some spontaneity. For example, eliminating the need for sketching that many people find difficult and daunting, participants can paint directly onto the canvas or textured paper "wet on wet" which allows watercolor paints to run, blend, and shade, influenced by the texture of the paper. Again, there is no "right or wrong" implied, liberating the maker. Teaching general techniques such as different hue intensities to differentiate foreground and background, or the two-thirds sky "rule," scaling foreground, and important elements larger to create a sense of perspective without setting up perspective lines formally can be "shortcuts" that move the participant forward and equip people with creative tools and an appetite for exploration (Hartley et al. 2008, pp. 91–93).

Quality art materials are used in respect to the patient, to ensure that paintings do not distort while drying, and reinforcing the authenticity of the art experience, e.g., 300gsm artist-quality watercolor stock and artist-grade paints that will not fade.

A group painting – produced by a number of painters participating in the HammondCare "Arts on Prescription" program for older people with health and wellness needs – created around a single giant canvas, unified by a single theme and coherent color scheme, now hangs proudly in a medical center reception for the community to appreciate. A similar endeavor could be pursued in a palliative care setting, leaving a "legacy" for subsequent patients.

Painting is the genre that patients are most likely to have experienced before, sometimes with a frustrating school experience or notion that they cannot draw or depict lifelike images. In this regard, alternate media may be helpful; however exploring techniques and styles that do not superimpose precise expectations also facilitates greater freedom. Learning new skills allows even the very unwell patient to experience themselves in a different way (Hartley et al. 2008, p. 93), to feel enabled, capable, and excited by personal growth, influencing materials and making something aesthetically beautiful. Artworks also allow the friends and family to see the patient in a new way, expressing choice, showing their personality, and challenging limitations (Kennett et al. 2004, p. 254). Through artwork patients may also experience their environment more fully, noticing details, excited by color, observing nature, seeing afresh, more present in the moment, and actively involved.

2.4.2 Printmaking

Printmaking using lino cuts and multiple impressions of textured painted objects (such as feathers or leaves) and multiple color permutations and layers was a popular medium in HammondCare's cancer rehabilitation ward because prints could be made, dried, and returned to patients or displayed on the day of their making. Prints adapt well not only to wall mounting but also to cards and gifts that let participants share their art with friends and family. Printing en masse means that a group can literally cover a wall with joyous pictures and transform a space. Our artist recounts a patient's wish to illuminate a room with light and joy. The class together made prints of beaming flowers that filled the family room wall and collectively brought the patient's dream to fruition:

> "I want to adorn my walls with flowers: I want to wake up to beauty instead of a bare white wall."—L. (Cancer rehabilitation ward patient)

According to Hartley et al. (2008, p. 98), the most popular art forms with patients are mosaics, painting or printing on silk, and painting on glass or porcelain, inspired by seasonal interests. Once again silk painting, printing, or dying can be completed in a single day and suits people with limited mobility.

2.4.3 Pottery and Modeling Clay

Lynn Harmer, in "Pottery and Painting" (Hartley et al. 2008, p. 88), writes of clay's soft and receptive nature. It has a pressure-releasing tactile quality and almost hypnotic repetitious cycle of rolling, pinching, coiling, spinning, or smoothing that gradually evolves the three-dimensional object. Similarly repetitive brushstrokes or pastel marks can have this immersive and meditative quality.

Harmer describes a process in which patients are invited to decorate their pottery "usually in the form of a glaze; this makes it endure longer, making it stronger and more waterproof" (Hartley et al. 2008, p. 91). Brush-on glazes can be applied in a similar fashion to paint, and clay and earthenware glazes are more conveniently fired. Additional ornaments and textures may be applied within a scope and style that is rewarding.

Much consideration is given to equipment and resources, e.g., choosing clay that is responsive and tolerant, extremely reliable and resilient, and using earthenware glazes as they have a lower melting point and therefore fire at a lower temperature than other types, resulting in faster and more affordable firings so that work can be returned to patients and families promptly with pleasing results (Hartley et al. 2008, p. 97).

2.4.4 Dramatic Art

McNiff (2004, pp. 70–72) observes that patients instinctively tell stories in response to their art. These responses can grow to encompass "poetry, drama, movement, voice, and other expressions that emerge naturally when looking at images, contemplating them deeply, and letting them act upon our thoughts and feelings . . . Images generate stories, imaginal dialogue, and other forms of artistic expression, but they also act directly on our bodies, minds, and senses."

In other words, sometimes the movement, performative narration, or dramatic interpretation arises from the initial image-making act and the attempt to further convey its nuances and meanings for the creator to the artist or audience.

Like poetry, sometimes patients do not have the time or techniques to develop their own play script, so the artist "expert" can support the patient by crafting their ideas into a dramatic form. Patients can also engage in improvisation – a more direct explication of their experiences and thoughts.

Through performance art, the patient is given the opportunity to move with the image. People who respond to their art through performance experience release from debilitating self-consciousness (McNiff 1992, p. 120). "Theater offers clearly defined structures—preparatory procedures, beginnings, endings. The audience has a contributing role in making the performance an 'event' to be witnessed" (McNiff 1992, p. 120).

2.4.5 Poetry

In poetry, perhaps due to its concise yet distilled and saturated form, often metaphoric and symbolic language evocative of thoughts, feelings,

and experiences that are difficult to voice literally, there is a long history of so-called death poems. These range from John Donne's *Holy Sonnets* of the seventeenth century, said to be one of the English language's finest metaphysical meditations (or *Divine Meditations*) on the nature of death and dying and the journey of the soul, and similarly ancient Japanese death poems written in the dying hours or moments of Zen monks (Hoffmann 1985), to MacLeod's (2014) collection of poems, *The Unknown Sea: An anthology of poems on living and dying*, drawing on sources as disparate as Shakespeare to contemporary poets. Poetry may use familiar language, but it operates through imagery and abstraction that seems to condense intangible and elusive experiences into an economy of well-sounding text.

This economy of words also makes it plausible to record, or have someone else transcribe, poetry if the need arises. Hartley et al. (2008, p. 122) describe a blind and bedbound patient (Paul) who felt very isolated and desperate to have his voice heard. He recorded ideas about his body image and sense of self in poetry that was subsequently published on the Rosetta Life website (2007) through which he connected with other patients in different locations, which eased his feeling of being alone, and he was delighted by the positive response to his work.

In other instances, poets, rap singers (rhythmical lyric poets), and wordsmiths transform the stories related by patient conversations into poetry, song, drama, or puppet theater that can be performed to friends and family.

Describing their experience in a cancer hospital, Pratt et al. (1998, Loc.1902) state, "Much poetry and prose is written or quoted, so that *hope and understanding can be shared* even when the worst fears and losses are depicted." The therapeutic aim is for patients' greater openness toward themselves and to a better understanding of their situation. Pratt et al. (1998, Loc.1954) read poetry to patients for whom "it seems undeniable that the event is nearly always a source of psychological nourishment for both the patient and therapist." They describe choosing poetry that was familiar or relevant to the patient from an anthology in order to read aloud.

Poetry has catalytic, expressive, and transformative therapeutic potential. Allen Ginsberg and Carter (2001) affirms this: "The only thing that can save the world is the reclaiming of the awareness of the world. That is what poetry does" (p. 273). Transformation, here, refers to awakening a deep sense of authenticity, nourishing inner growth and expanded consciousness, exploring meaning, asking existential questions about death and identity, and openness to the spiritual dimension to life. "Poetic language, rich with metaphor, image and symbol, makes it possible for us to express the diverse, paradoxical, vibrant organisms we are – human beings that grow and struggle, sometimes get ill and heal, live and die, sorrow and sing" (Rappaport et al. 2014, p. 118).

Some of the participants in HammondCare's "Arts on Prescription" cancer rehabilitation program used poetry they composed to accompany paintings and prints they made, evoking inner qualities of atmosphere, emotions, and imagery.

2.4.6 Mixed Media and Collage

Objects from the patient's own environment may be incorporated into mixed media pieces, to convey perhaps some intimate symbolic meaning (Pratt et al. 1998, Loc.255): trinkets, keepsakes, reminders, icons of meaning, and memories relevant to the participant. The tactile and textural qualities of mixed media can be especially appropriate for people with dementia or people with visual impairment.

2.4.7 Digital Media: Film, Photography

Closely and "timefully" examining an object or an environment removes the viewer from focused activities that usurp thoughts and perceptions and, in turn, creates the opportunity to perceive experiences with greater mindfulness (McNiff 2004, p. 57). Through photography, people become more aware of their environments. Walking with a camera searching for images leads to a different kind of observation and concentration. Capturing that image gives the photographic stills camera or video camera a unique ability to hold moments of perception.

Beauty and aesthetic reverie are found in all the world's ancient and traditional cultures.

Appreciating beauty has a vital place in the process of meditation, stress reduction, relaxation, and an overall integration of body, mind, and spirit.

2.5 Art as Mindfulness Meditation

Mindfulness is a practice of bringing awareness to the present moment with an attitude of acceptance and nonjudgment. "Mindfulness and the arts can play an important role in psycho-spiritual growth and the evolution of human consciousness" (Rappaport et al. 2014, p. 2; Loc.15).

Mindfulness practices are found in most major wisdom traditions (including Old Testament Jewish prophets and desert aesthetes), but the clearest contemporary expression owes much to Buddhist thinking. Various secular contexts have adopted the practices of ancient mindfulness, e.g., psychotherapy, education, and work environments, and there exist numerous "techniques" available for practicing mindfulness and meditation in clinical settings (Rappaport et al. 2014, p. 2; Fjorback et al. 2011).

Over the past 40 years, neuroanatomy and physiology of internal composure have been found to impact brain science, e.g., the autonomic nervous system, polyvagal theory and the stress response, human brain evolution, hemispheric lateralization, attachment theory, pleasure and pain, trauma and PTSD, addiction, self-awareness, empathy, memory, and emotion (Rappaport et al. 2014, Loc.18). This has produced a growing body of clinical evidence demonstrating efficacy in reducing stress, decreasing depression and anxiety, improving quality of life, enhancing well-being, improving immune function, lowering blood pressure, and providing other benefits. Thus mindfulness can be viewed as an *integrative approach* for clinicians and patients. Practicing arts, especially tailored art practices that focus on attentiveness, concentration, repetitious gestures, and immersion (Rappaport et al. 2014, Loc.27), is a way to avail the benefits of mindfulness in a palliative care setting.

Early influences of mindfulness in psychoanalysis include the work of Sigmund Freud, Wilfred Bion, Karen Horney, and Erich Fromm, subsequently developed into contemporary approaches including mindfulness-based cognitive therapy, dialectical behavior therapy, and acceptance and commitment therapy. Kabat-Zinn's (1990) mindfulness-based stress reduction (MBSR) program has been especially influential. Caroline Peterson integrated art therapy with Kabat-Zinn's model to create an 8-week program – mindfulness-based art therapy (MBAT), which has demonstrated a positive impact on people living with cancer (Monti et al. 2006).

Meninger, Pennington (1982), and Keating (2009) developed the Centering Prayer method that is based on ancient practices by the Desert Fathers and Mothers of the Fourth and Fifth Centuries, and inspiration from Thomas Merton (1961). Blanton (2011) compares the Centering Prayer with contemporary mindfulness and discusses its application to psychotherapy. There are also some similarities to be found in the Jewish contemplative Kabbalistic meditation practices. The mystical branch of Islam is Sufism. The poet saint Rumi, born in 1207, founded the Mevlevi Order of Sufism and is often quoted to inspire states of awareness, mindfulness, compassion, and the divine. Mirdal (2010) describes "acceptance and acknowledgment of positive and negative experiences, unlearning old habits and looking at the world with new eyes" (p. 1206), breathing and walking meditation, intentions, and cultivating insight and compassion. Integrating Sufism and Rumi's philosophy and poetry with mindfulness-based approaches to psychotherapy may be a way of providing a culturally relevant service for patients with a Muslim background.

Mindfulness-based cognitive therapy (MBCT) and dialectical behavior therapy (DBT), developed by Marsha Linehan (1993), incorporate mindfulness along with interpersonal effectiveness, emotion regulation, and distress tolerance. The roots of mindfulness and the art therapies can also be found in arts in rituals to enhance spiritual and religious practices, intended to promote healing and transformation. "Artists engaging in the process of art-making can be absorbed into a state of flow," i.e., immersed in the process, and quieting of the mind (Csikszentmihalyi 1990;

Rappaport et al. 2014, p. 10). Rappaport et al. states that the "creative process is the healing agent" (2014, p. 20).

According to Carlson (Carlson et al. 2012), the diagnosis and treatment of cancer is associated with both physical and psychological distress which can have a negative effect on memory, behavioral inhibition, negative emotions, hypervigilance, and disruptive ruminative thinking (Britton 2005). Relaxational and stress-reducing art practices are therefore appropriate interventions in cancer care (Bultz and Carson 2006). Monti et al. (2006), in a National Institutes of Health randomized clinical trial of mindfulness-based art therapy with cancer patients, showed significant reductions in psychological distress and increases in health-related quality-of-life post-intervention for the experimental group. Reflection helps to deepen awareness within oneself and experience the benefits of expressive therapy.

Dannecker et al. (2008) suggest that art therapy can help to deepen observation of the pain experience and uncover its symbolic aspect "Most patients with chronic pain report that the suffering from pain significantly decreases while they engage in the creative process of art therapy" (Dannecker et al. 2008, pp. 288–289). Jürgen Fritsche describes seven stages in the Mind-Body Awareness in Art Therapy model (echoing Elisabeth Kübler-Ross' thinking) used with people experiencing chronic pain:

- Examination,
- Expression,
- Expansion,
- Energetic Release,
- Redirection,
- Recognition, and
- Relief (Rappaport et al. 2014, p. 61).

He suggests that this approach can be integrated into various disciplines by medical doctors, psychologists, physiotherapists, Feldenkrais therapists, art therapist, nurses, and other clinical disciplines.

Dance/movement therapy can facilitate the movement from mindfulness to *embodiment* by helping a patient to "kinesthetically engage with sensations, images, emotions and memories, leading to improved physical, mental and emotional well-being" (Rappaport et al. 2014, p. 73). Both mirroring and rhythmic variation are two fundamental techniques for cultivating embodiment in dance/movement therapy (Levy 1992).

2.6 Constraints in the Palliative Care Context

We have found that patients receiving palliative care and cancer rehabilitation services are receptive to learning new skills and trying art projects with an achievable outcome fine-tuned for this context by our artist. "Because patients in palliative care have limited time left to them in their lives, and an important principle in palliative care is 'to live until the moment that you die', doing something worthwhile in that time is important" (Hartley et al. 2008, p. 85). Art activities need to accommodate some limitations in order to maximize the quality of process and satisfaction it produces.

Many palliative care patients have limited energy for active pursuits, household chores, or their former pastimes. However, many forms of art practice can be approached on an appropriate scale and degree of effort to still achieve satisfying results. For many people, too, it is a first foray into a new art technique, such as painting or working with clay. The therapist or facilitator must work within the capacity of the patient's artistic development.

It is important to work within the physical limitations of the patient: conducting shorter sessions when the patient is tired or nauseated, disposing of leftover materials to avoid cross infections between patients, and using materials that are textured or have tactile properties for people with sight impairment (Pratt et al. 1998, Loc.847; Connell 1992).

One way to amplify the effects of individual effort is to make a collective (group) artwork, and another is to integrate different arts and skills into one project – either from multiple contributors or built up over several sessions.

Principally, the artist works within a timeframe that will allow the patient to develop their work in the presence of tiredness and any other symptoms that may limit their activity. The artist shows participants foundational techniques that will be useful for making other things, thus suggesting a creative future. Staff work hand in hand through the creative process and can collaborate or support as needed without usurping artistic control or making choices on behalf of the patient. Directed by the patient, for example, the artist can expedite technical or physically challenging steps. Projects are typically designed in incremental steps, and a whole session is designed to fit within a reasonable attention span for people who may be tired or frail.

Feelings of envy and disempowerment caused by the power differential between a healthy "expert" artist and physically weak or restricted patient may compound existing feelings of loss for the patient. This may be a challenge in the artist's encounter with the patient (Pratt et al. 1998, Loc.903).

3 Participatory Arts and Art Facilitation

3.1 Community, Integration, and Belonging

The HammondCare "Arts on Prescription" programs have shown the individual and family satisfaction gained through learning new skills, creating artifacts, experiencing facilitation by an expert artist, and creating works culminating in a form of acknowledgment, such as a collated collection, exhibition, publication, or performance. These forms of affirmation reinforce worth, contribution, and belonging, especially at a time when former capacities may be impacted by disease. A bespoke palliative care art program provides a respectful and "safe" environment in which patients can explore new expression without concern about technical experience. Outcomes from the HammondCare experiences have included paintings that now hang on the walls of a community medical center, participant stories with accompanying illustrations in an adult coloring book, legacies for families to keep, several exhibitions open to the public, and recognition by the broader community that perforates institutional boundaries.

Participatory arts, such as painting, printmaking, ceramics, drawing, photography, video making, movement, and music, provide a setting for agency, social interaction, enablement, self-discovery, learning, affirmation, and sharing in addition to the functions above. Some participatory arts may be most suitable earlier in the palliative care trajectory because they require movement and expending energy. Participatory arts can provide a positive counterpoint to the change and emotions associated with diagnosis. Participatory arts often occur in a group setting, though individual participation or participation in community-run art programs may also serve as therapeutic diversion and empowerment.

People receiving palliative care services or with a terminal diagnosis can find themselves isolated geographically and socially from their community groups and social circles, both due to their change in availability and capacity and because those around are not sure how to respond, similar to the experience of people with dementia. People can feel marginalized and emotionally isolated in their battle with disease, treatment, and time-consuming medical appointments or hospitalization. The group in which art is practiced can restore a degree of belonging and connection with people encountering similar concerns and circumstances and simply for companionship and normal interaction.

Art making is not perceived as an activity that has to be perfected, and there is a sense in which participants are sharing the learning experience, jovially comparing, laughing, telling their stories, and sharing feelings with nonmedical staff, with people who may understand from their own experience. The artifact is a vehicle for communication and expression in the group. Eventually the work may end as part of a bigger picture (an installation or exhibition):

> Groups provide a safe and supportive environment where staff and patients offer cooperation and

> camaraderie. It feels as if everyone enjoys each other's creative journey, and there is a very strong feeling that we are all sharing the same experience (Hartley et al. 2008, p. 95).

Kennett et al. (2004, p. 256) report patient feedback including: "enjoyment, lifting of mood, calming anxiety, relief of boredom, pride, achievement and pleasure at being able to make a gift for a relative or friend." As with music engagement, participatory arts often lead to increased personal attention and conversations about the music or art itself.

Members of a group "develop a shared experience, so that people feel they are trying something new in the knowledge that they are supported and encouraged by those around them . . . Symptoms, fears, worries and feelings of isolation are aired in discussion, as well as feelings of joy and relief when something positive is achieved" (Hartley et al. 2008, p. 114).

3.2 Participatory Arts for People with Dementia

In many ways, the needs of people living with dementia are similar to those of people confronting a life-changing physical illness: e.g.,isolation, challenges to identity, belonging, reduced capacity, changes, and losses, which are then compounded for people who require both palliative and dementia support. Many palliative care patients are elderly. It is also common to have complex comorbidities or for people in palliative care to have cognitive impairment for different reasons.

Our "Arts on Prescription" At Home project (a small pilot project) was targeting dyads – the carer and the person with dementia. The aim was to address the health and well-being needs of carers (and enhance the dyadic relationship). The carer and the person with dementia both made art (not necessarily the same project). Via individual interviews after the pilot, carers reported that they enjoyed the company of the artist, they also had something to share with their families, and they found it relaxing. It provided new dyadic interactions around a non-care shared creative experience, and some learned new ways of interacting with their loved one by watching how the artist interacted. Some carers also reported a sense of achievement and pride in their work and noted positive outcomes for their loved one, such as smiling, engaging with the artist, and ceasing repetitive behaviors while engaged with the artistic endeavor.

The creative arts can reach even the most cognitively impaired people because expression through the arts depends on something other than the intellect:

> Creativity comes from somewhere beyond the intellect; it flows from an intuitive non-rational place in the body and mind, so we can tap into the creativity of everyone, no matter how much their logic or sequential memory has been disturbed. The creative arts have the power to stir feeling and memory when a person seems to have lost contact with chronological time. The arts seem to reach below the conscious level of experience and move underground towards a hidden depth memory, accessing the feelings stowed away. (Hayes et al. 2011, p. 15)

It is also important to create opportunities for people with dementia to express their feelings in the present moment. Life can seem "full of loss and confusion, fear and frustration in states of dementia and it seems vital that such feelings are acknowledged and listened to" (Hayes et al. 2011, p. 16). Expression through arts and music can be effective when words are difficult to find, and improvisation or art generated in the present need not rely on cogent and sequential memories (Beilharz 2017).

Piecing together fragments and creating images has an important role in dementia when personhood seems to be disintegrating. Creative artifacts can encapsulate personality and emotions and can surprise and impress friends and loved ones. Hayes et al. (2011, pp. 32–33) suggest that brightening homes, day centers, and hospitals with art, with color, expressing hope and love, together with the opportunity for storytelling that arises in singing, dancing, and art making are important for the person with dementia. "In making a story about someone's life we celebrate the *spirit* of the person; we show that they matter, that they are important" (Hayes et al. 2011, p. 94).

Story making can utilize fabrics, paints, poetry, or writing. A person with dementia may be able to make substantial or partial amounts of their story with some degree of assistance putting it together (Craig and Killick 2012, p. 65). Mixed media collage is popular for story making because it is inclusive and works well as collaborative team effort. Oliver Sacks in *Musicophilia* (2007) writes about the benefits of music in the context of identity because dementia is most tragically often associated with a disintegration of identity. When people no longer hold their own stories, loved ones and the community take over this role of telling a person's story (Swinton 2012):

> In dementia we lose our sense of clock time. We can no longer locate ourselves on the sequential time line of our human life. We are no longer part of a chronological system. Our sequential thinking is damaged and we can no longer easily participate in conversation relating to shared events. Participation in life seems threatened because we cannot orient ourselves in time. (Hayes et al. 2011, p. 47)

John Swinton refers to this new nonlinear, slower time as "dementia time." Locating moments from patients' lives in time and gathering memories gives a sense of identity and value. Disoriented chronological time, spatial perception, as well as a number of sensory changes (visual, olfactory, touch, hearing, and taste) can affect people with dementia.

Hayes et al. (2011, p. 48) believe that in cultivating a greater awareness of our physical self and the movements, we become more sensitive toward the people we move around and who we touch. "Gentle, sensitive movements in relation to others convey a message of love, respect and acceptance." Touch is useful for connecting with people living with dementia when listening to music. Touch can also be harnessed in art through the use of tactile clays (Craig and Killick 2012, p. 72), interesting textures in collage and mixed media or textile work, or may even draw on old habitual memories such as the craft of knitting, or crochet, if it has been a part of a person's past. Claire Craig gives special status to hard and heavy substances – stone, wood, metal, and glass. "Stone, wood, metal and glass are solid and possess an air of permanence which means they will remain long after other organic materials such as fabric and paper have faded and decayed. This has been important for some people for whom the idea of leaving a mark, a legacy for future generations has mattered, something to say, 'I was here'" (Craig and Killick 2012, p. 78): these materials carry weight, suggesting strength and gravitas. Manipulating materials – shaping, moving, and positioning – demands engagement, placing the patient in control.

"Working with textiles is also inherently sociable and the act of taking part in rag-rugging or quilting where everyone sits and works together has inspired feelings of connectedness, fun and friendship, prompting participants to share stories whilst also promoting a sense of shared ownership in the final piece" (Craig and Killick 2012, p. 85). Crafting or art making begins with exploring the materials – yarns, silk scarves, raw wool fibers, and fleece squares – which embody a strong expressive quality. The artifact is then a tangible reminder of the textured journey traveled together (Craig and Killick 2012, p. 89).

Photographs provide an enduring tangible record, a prompt for memory, and potential recollection aid. John Berger (1992, p. 192) said, "The thrill found in a photograph comes from the onrush of memory." Photographs have been used extensively with people with dementia as a prompt for reminiscence and supporting communication while taking into account associated visual loss (from such causes as macular degeneration or glaucoma, etc.). The camera is a tool for exploration and experimentation with a focus on the present, offering an outlet for self-expression (Craig and Killick 2012, pp. 98, 100). Images are objects loaded with emotion.

"Our traditional view of dementia is one that focuses on *loss*" (loss of nerve cells, memory, and impairments in various types of cognition) measured by what people living with dementia *cannot do* (e.g., Folstein Mini-Mental Status Exam) (Lee and Adams 2011, Loc.92). Reducing a person to the sum of discrete tasks distracts from the many complex and integrative skills that continue even into advanced illness, not least

emotional responses. Power (2010) proposes that dementia is a shift in perception of the world that, in turn, can be better understood by shifting the therapist's understanding of personhood in terms of experience, not deficits.

Lee and Adams (2011, Loc.119; 133) define creativity as "a spirit that is ignited when the mind is fully engaged in the genesis of new thoughts. There is an inherent joy in beholding something that you have conceived in your own way." Engaging in creative arts can activate pathways that release thoughts and words previously held captive by limitations of language and conventional communication. Instead, connection can be made through art, music, visual stimulus, tactile sensation, humor, or strong emotion.

In the therapeutic creative space, there are no rules and regulations and no "right answer." This emancipation embraces an infinite array of approaches and outcomes. Lee and Adams (2011, p. 5) assert, "Creativity has a strong value within person-centred care because it enables the strengthening and expression of personhood while also providing opportunities for enriched relationships." According to Kasayka (2002, p. 9), the core functions of the expressive arts are "the reclamation, the regeneration and the celebration of the human spirit," i.e., the same primary goals as person-centered care.

Craig and Killick (2012, p. 39) advocate the suitability of spontaneous and intuitive arts, such as dance: "an ordinary and fundamental human activity hidden by a culture that has little regard for spontaneous movement as an expression of who we are and how we feel, in favour of more intellectual means," the "body's response to everything we do and see" (Coaten 2009), and "a different, non-verbal way of communicating" (Coaten 2008, pp. 19–22). Oliver Sacks (in *Musicophilia)* says: "When we dance together bonding is deeper. Moving together helps to regain a sense of physical identity" (2007). Furthermore, when people dance together, they share an experience and an equality that overcomes any clinician-to-patient differential.

3.3 Sharing Art and the Exhibition

Creative work and its exhibition may provide a context for integrating family and carers into the experiences of the patient in palliative care and a way of enabling communication among patients, between patients and professionals, and between patients and their families and social networks. According to Hartley et al. (2008, pp. 16, 19), exhibiting has a huge influence on the environment and how people then experience the work, e.g., presented, mounted, or hung, with a program or title, perhaps an opening event, family and community audience.

Not only does art brighten and stimulate the hospice or care environment, it also highlights the place of creative art group work within a hospice day care setting as an enhancement to emotional stability, personal enrichment, and *self-fulfillment* (Kennett 2001).

An "open studio" or exhibition generates a goal and a future horizon. Although some people may choose not to display the work they have created, painting, music, dance, poetry, and sculpture are created to be witnessed, and patients usually respond with pride, excitement, and satisfaction when others can appreciate their creations. It allows people to be acknowledged as capable, to experience a seal of validation:

> Although the expression and motivation of the artist who produces the art is central and the process of creating will have been integral to their own lives and experiences, the product created is then given over to the public who are entertained, moved, inspired or disturbed from their own personal perspective. Such responses give the artistic product value and can have an important part to play in the success of both the product and those who created it. (Hartley et al. 2008, p. 53)

4 Art Therapy

Individual or group psychotherapy is a more specialized provision needed by fewer patients. This process uses the creation of an art object, and the process of achieving it, to engage the patient or

family member in interactions with the therapist in order to resolve psychological and emotional difficulties, i.e., "art activity is a conscious process which gives concrete form to feelings, which are often unconscious" (Case and Dalley 2014, p. 86).

"The art therapist's attention to emotional detail opens up the possibility for the patient to explore on a deep level within themselves" (Jansen 1995; Wood 1990; Connell 1992). Art therapy is psychoanalytically oriented, "recognising the fundamental importance of the unconscious as expressed in the patient's dreams, day dreams and fantasies … Spontaneous graphic art becomes a form of symbolic speech which may serve as a substitute for words or as a stimulus which leads to an increase of verbalisation in the course of therapy" (Case and Dalley 2014, p. 2). The therapy is not directed by the therapist but rather follows the patient's lead (McNiff 1992) in the palliative care setting, often in order to express powerful, difficult emotions concerning their illness, treatment, mortality, and life. The process works through distress in order to normalize living with dying, which may address some of the psychological trauma of the realities of terminal illness (Beilharz 2017). The therapist creates a reflective space for the clients. The focus is on image or artifact making, alongside the process and relationship with the therapist, referred to as the "triangular relationship" (Schaverien 1998).

Art therapy, like participatory arts, can take place in a group setting, though the boundaries reflect the art therapy *milieu*. The therapy group should be contained and safe, though often open to carers and families who may wish to join in and explore some of their feelings, relationships, and memories that come up through image making:

> The nature of group work is inspiring as the clients can help each other along with image making and themes that can come up; a sense of belonging; and feeling that 'I'm not the only one' … The focus is on creating images, an empathetic environment and respect for each other and each other's image making … As with individual sessions, whatever is made in the group is confidential and the therapy is private. (Samantha Dobbs 'Art Therapy' in Hartley et al. 2008, pp. 131–132)

There is some difference of opinion in the art therapy (and psychotherapy, psychoanalysis) profession as to whether the role of the therapist extends to interpreting the images made by the patient. While some believe that interpreting an image "fixes" and seals it, or imposes meanings that do not necessarily concur with the patient's own, despite a long epistemology of symbols and archetypes in the Jungian tradition, others such as Susan Bach and Greg Furth in the field of terminal illness have endeavored to develop frameworks for "reading" pictures. McNiff (2004, pp. 69–70) is very critical of reductionist approaches in psychology that link colors, forms, and compositions to the particular pathologies of the people creating them. In his view, these systems of art diagnosis are built on narrow and typically idiosyncratic psychological theories. McNiff is particularly concerned by the literalism of such connections and the danger in drawing simple constructs from complex experiences (such as black connoting depression, red connoting anger, large eyes revealing paranoia, etc.), all of which may be further mediated or clouded by the patient's potentially limited artistic skill. Ultimately, he asks whether these reductionist analytical practices are beneficial either for art or for healing.

Art therapy can be helpful to develop awareness of Kübler-Ross's (1970) stages of death and dying: grief, anger, acceptance, shock, depression, bargaining, and denial. Patients may go through these stages *at any time and in no particular order.*

The issue of *control* is often present and powerful. In palliative care or after a particularly lengthy period of medical treatment, clients often feel that they have no control over their illness and their treatment or feel that they are on a "conveyor belt" of sequential highly standardized treatments. This leaves no room for the patient's proactivity or flexibility. The patient may also have lack of control over their bodily functions, which contributes to their *powerlessness* (Pratt and Wood 1998). In the midst of a medical model of care, it is not unusual for the disease rather than the patient to be the focus of care, rather than the patient's emotional and psychological concerns.

In the making of a picture or artwork previously unacknowledged, feelings can be *given form* and reflected upon and then discussed with the art therapist. "The artwork is a container for a rich breadth of issues, which may be contradictory, contentious or even bizarre and which may be difficult for them to articulate in any other way" (Pratt et al. 1998, Loc.210). Images developed and "worked through" in the therapeutic process form a useful lasting record for continuing exploration, reflection, and comparison. It has also been demonstrated that patients who are suffering emotionally and spiritually often have a lower threshold for physical pain, and so art therapy has an important role on a physical level (Corbett et al. 2017; Craig et al. 2013).

"Arts therapists are, at present, the only group of artists who are recognised as a profession to practise within healthcare [in the UK]" (Hartley et al. 2008, p. 22). In Australia, art therapists generally hold a degree in art therapy, psychotherapy, or psychology, as well as some personal art practice.

5 Challenges Facing Creative Arts in Palliative Care

5.1 Funding

In the UK, hospices that provide palliative care are often small independent charities involving local community support. Their independence often provides the flexible and supportive environment that can accommodate creative arts into palliative care within the scope of resourcing constraints that obviously favor essential medical services (Hartley et al. 2008, p. 11). Similarly in Australia, many people receive palliative care and supportive services in nonprofit private hospitals, or community services in the home, the latter currently governed under a system of consumer-directed care packages, in which complementary and whole-person therapies compete for attention with medical and convenience services (housecleaning, transport to appointments, etc.). HammondCare is trialling music engagement as a complementary therapy offered to patients through consumer-directed care packages. This envisages a future with creative arts and music available under national medical schemes and home care services, i.e., acknowledging its value and availing its accessibility as an integral part of every person's health consultation.

Many people say they would like to die in their own homes, but a high proportion are admitted to hospitals and die there. This situation is further exaggerated in regional areas where there fewer specialist palliative care or hospice services are available. "Art and creative work are a vital human activity" (Shaw 1999) for good life quality, emotional stability, personal enrichment, and self-fulfillment and can offer a diversion from depression or difficulty. According to Hartley et al., if "palliative care is about living life to the full, then that life will include the arts" (Hartley et al. 2008, p. 12). This points to the need for complementary palliative care services including creative arts in both home settings and acute hospitals.

5.2 Patient Confidence

When people join an art group, they may feel self-conscious or apprehensive but group participation, fueled by curiosity for what others create and the range of outcomes from a single medium, usually quickly dissipates any fears. The artwork speaks for itself as an object or image emerges, and enjoyment and confidence grow proportionally. Work by past patients, in all its diversity and variety, can also help overcome a beginner's inertia. Most people delight in the discovery of what they can make.

Our artist collected the following comments from participants in HammondCare's "Art on Prescription" for people receiving cancer rehabilitation, who overcame their initial hesitations:

> "I have never printed before. I never thought I could." — M.
>
> "I don't think I am creative. I have never done it before! Maybe one day I'll give it a go, when I'm not busy. I have things on today: [making excuses] I think a visitor is coming . . . My wife said she might call me . . . No, I think I won't be good at that [trying art]: I'm too awkward, others are better than me. *Then P had a go.*"I love this. I can do this! Can I do more?" — P.

"Look at me! My eyesight is blurry. I have no feeling in my fingers and toes. I am confined to a wheelchair. I have tubes coming out of my neck. And to top it off, I am a banker! . . . Okay: I will give it a go!" — L.

"Art has given me a fun time during a slow recovery." — N.

"You swept away my sadness." — E.

6 Evaluation

Hartley's survey of the *Journal of Medical Humanities* observes that the main focus of arts and humanities evaluation is on how arts in palliative care reflect medical and healthcare experiences. "The contribution of the arts to *treatment* is largely absent" (Hartley et al. 2008, p. 66). An important ideology in palliative care is *holism*; therefore creative expression, self-fulfillment, and other psychosocial objectives are relevant in evaluating arts in palliative care and healthcare needs. Hartley proposes that analysis of trends, observation of behaviors and responses, surveying attitudes toward artwork, comparison with other treatments received, preferences for activities, and perceptible impacts are all relevant hermeneutics. Respondents typically include patients, staff, carers, and family. A number of standardized methods can be applied in the context of arts in palliative care, e.g., the Hospital Anxiety and Depression Scale (HADS), Quality of Death and Dying questionnaire (Downey et al. 2010), spirituality measures, etc. (Hartley et al. 2008, pp. 72–80).

Gilroy and Lee (1995) reviewed the art therapy research in the UK and found it to be focused mainly on issues relating to the professional development of art therapy or to the exploration of clinical practice using case study-based research (Pratt et al. 1998, Loc.372).

Both formative and summative evaluation of programs is important because participatory creative arts will be a new area of application for the majority of palliative care services. An evaluation framework alongside the program not only helps practitioners to learn about the application of the arts in palliative care but also contributes to increasing the knowledge base.

In addition to understanding the efficacy of art making for the patient, evaluation of impact and measurement of effect is important to demonstrate the worth of art interventions to colleagues and funders (see sect. 5). The limited evidence in this field makes it difficult for hospital administrators to justify investment in art programs when faced with resourcing constraints and other "evidence-based" interventions which demand funding.

7 Summary of Key Points

Creative art making offers opportunities to support the person processing a life-changing or terminal diagnosis and receiving palliative care which are not otherwise met through medical care alone. In aiming to provide good whole-person care, there are areas of psychosocial isolation, spiritual or existential anxiety, and deep emotional feelings that may be difficult to express and discover through verbal communication alone or which may seem awkward to voice explicitly. The nonverbal modalities of creative arts allow some of these concerns to be expressed and explored and therein may be relieved, through a variety of art media. The choice of medium can be suited to the interests, frailty, sensory capacity, tactility, and curiosity of the patient.

People find satisfaction in being positively productive and creative, in learning new skills, and in demonstrating abilities to loved ones, staff, and even community engagement through exhibition and leaving a legacy. As artwork is usually more abstract than natural language, sensitive ideas can be veiled or expressed to the degree that a person finds comfortable. For patients who are unable to speak due to physical, medical, cognitive, or other constraints, expressing ideas and emotions through art may provide a way to be heard and a way to express emotions. Illness can affect many aspects of identity and personhood, which may be redeemed to some extent through expression and creativity. Joy and mindful immersion may be experienced through the concentration required in making art. That focus often serves to take attention away from persistent thoughts about

medication, disease, or pain. Pursuing an art form deeply and repetitively is often relaxing.

Through art facilitation in groups, people meet others and even make friends with those who face similar difficulties, finding comfort in not being alone, and also find a safe environment in which they can interact socially and in which their artistic experiments will not be judged. People working into the creative arts in the palliative care space may come from various backgrounds, ranging from professional and community artists working as facilitators, focused on the creative process and artistic fruits, to people from a psychotherapy or art therapy background who use the art-making process to help patients explore their inner world. In the latter scenario, the artifacts often remain confidential and the objective is to reveal psychological concerns, bringing subconscious themes into consciousness for the patient, and to allow them to work through these thoughts with the therapist. Making art can also work in tandem with a cognitive behavior therapy or dialectical behavior therapy model or pastoral care.

Creative arts in palliative care focus on life quality, meaning making, and personal fulfillment in living life fully until the very end.

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Music Engagement and Therapeutic Music

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_39

Abstract

This chapter outlines the role of music in well-being for people near the end of life. Written for the care professional or member of a multidisciplinary team, this chapter assumes that music engagement and a therapeutic approach to music in palliative care is relevant and accessible for all healthcare professionals, not only specialists or music therapy experts. The information provided here looks at the potential impact of music on pain, agitation, and diversion and for supporting emotional and spiritual life quality. Music is especially useful as a relational tool supporting whole-person care and a good end-of-life experience for the patient and their family and friends. This knowledge can be utilized to provide music, to facilitate therapeutic musicians interacting with a patient, and to increase awareness among staff and patients, and patients' families regarding the benefits of music in care, in particular, supporting emotional, psychosocial, spiritual, and physical needs not otherwise supported by medical care. Therapeutic music is presented from a historic, scientific, and holistic perspective, including considerations that will assist in cultural sensitivity.

1 Introduction

Knowledge of the potential application of therapeutic music in palliative care is relevant for the care professional. Firstly, whole-person care is everyone's concern. An appreciation for the evidence-based benefits of music and well-being will help care professionals balance the emotional and psychosocial aspects of well-being that cannot be nourished by medical care, as well as physical symptoms such as pain, loss of appetite, and sleeplessness that can also be improved with appropriate music intervention.

Some of the practical information in this chapter will equip care professionals, irrespective of musical or technological experience, in using or suggesting music as part of palliative care services. In addition, the care professional may need to represent the needs of the patient and advocate for the family when liaising with music therapists, thanatologists (bedside musicians providing a quality end-of-life service), therapeutic musicians, and volunteers involved in music services. In a diverse society, sensitivity to the cultural or spiritual needs of patients and families is core to cultural competency.

It may surprise some people that emotionally impactful music surpasses merely providing joy and relaxation but may also reduce pain and agitation and support appetite, diversion, relational care, and spiritual care.

David Aldridge notes that, "within the past decade music therapists have developed their work with people who have life-threatening illnesses and with those who are dying" (Aldridge 1999). This chapter serves to ensure that medical and care professionals are aware of the advances and scientific corroboration of ideas so that this information reaches patients and their families. Palliative care is also a specialization in which quality of life and meaningful experience supersede the approaches found in other areas of therapy, such as curative, targeted, and physician-directed goal-oriented programs, in favor of patient-initiated choice and focus on inner

psychosocial and spiritual wellness, more than physical goals. Aldridge describes this situation as working collaboratively and creatively: enhancing "the quality of living can help patients make sense of dying . . . [integrating] the physical, psychological, social and spiritual dimensions of their being" (Aldridge 1999).

The contemporary disciplines of music therapy and therapeutic music emerged from a confluence of occupational therapy, general psychology, psychotherapy, special education, music education, anthropology, and medicine, with a variety of goals ranging from artistic, scientific, psychosocial, behavioral, psychotherapeutic to rehabilitative (Wigram et al. 2002, p. 30). To this list may be added the work of pastoral carers and social workers who use music for awareness, insight, spiritual and emotional expression or exploration, facilitation, and "auxiliary" ways (Bruscia 1998). Supportive interventions include intentional distraction and provision of coping skills, and comprehensive resonance therapy includes entrainment and guided imagery with the objective of resolving pain (Wigram et al. 2002, p. 33).

The language of "constructionism" (participant engagement and meaning-making) has found its way into the therapeutic activity of creating "meaningful experiences." These ineffable and ephemeral experiences constructed with music are nonetheless important, especially for friends and family members of the dying person, who will cherish and remember experiences shared and enjoyed together long after the event. In music, there is always the interplay between composer, listener, symbolic language-like rules, and the ambiguous, metaphorical, inexpressible, and spiritual aspects of subjective imagination and active listening.

2 Differentiating Between Music Therapy and Therapeutic Music

The distinction between music therapy and therapeutic or healing music is relevant here. Music therapists have expertise and qualifications in "music therapy." They use goal-oriented therapeutic approaches to music in a variety of settings including aged care, rehabilitation and restorative care, and many related fields. In practice, "*music therapy* is the use of music as a tool in interactive therapy, while *therapeutic music* uses music and music only as the therapy itself" (Riley 2010, p. 108). Professional music therapists often combine music and other disciplines, such as exercise, art, and so on.

In the USA, the National Standards Board for Therapeutic Music (NSBTM) and the American Music Therapy Association (AMTA) distinguish between *music therapy* and *therapeutic music* (which includes the work of Certified Clinical Musicians, Certified Harp Therapists, Certified Healing Musicians, and Certified Bedside Harpists). In Australia and the UK, music therapy requires different training and qualifications from either music performance or therapeutic musicianship.

While music at the bedside of a patient is "prescriptive," it is a *service* (not a performance) – a "compassionate action without agenda" (Riley 2010, p. 109). The appropriate music cannot be anticipated, and the musician usually cannot ask the patient directly about their medical condition and treatment. Instead, the therapeutic musician responds to observed cues, body language, vital signs, monitors, and breathing. The patient is the sole attention of focus, in the moment.

This chapter focuses on therapeutic music in palliative care settings, in which music responds to the patient rather than aims to cure or rehabilitate. The "healing" that occurs concerns wholeness and well-being of mind and soul, as much as of body. If live instrumental playing is utilized, the musician intuitively and spontaneously responds to the patient's status. If recorded music is utilized, it is selected specifically for a patient (e.g., by a friend, relative, or the patient themselves). Music may be used therapeutically by a non-musician to enhance the quality of care, which is undertaken by any member of a multidisciplinary team or combined with pastoral care or relaxation approaches.

Musicians and volunteers (who are not formally trained in music therapy or who are not Certified Clinical Musicians) often adopt a responsive, therapeutic approach, too. Yet others

may volunteer to perform music as entertainment: community groups and children's choirs may visit and sing or perform music in nursing homes, hospices, hospitals, etc. The latter is valuable for its distraction and levity; however it is geared toward entertainment rather than intentional healing intervention and tends to occur in group settings and social spaces.

3 The Link Between Music and Well-Being from Antiquity

Historically, efforts to relate structures in music and the universe and the human body hark back to theories of vibrations, and parallel forms found in the micro- and macrocosmos were already well-established in the antiquarian world of Pythagoras (c. 500 BC). The corresponding connections in periodicity have been associated with revolutions of celestial bodies and planets, the bodily fluids or "humors," somatic disturbances, and consciousness. Before instruments were developed for accurately measuring frequency, theories of relationship could still be calculated by using the ratios of vibration that produce the natural overtone series that echo forms in nature such as resonating cylinders, reeds, strings, etc. (Wigram et al. 2002, pp. 22–23).

From these ideas we retain the concepts of "attunement," "resonance," "sympathy," and "harmonizing" that have both metaphysical and physiological applications. "Attunement" is used not only in contemporary developmental psychology (Stern) but also in Løgstrup's theory of music education.

Therapeutic and healing qualities of music are present in many traditional and ancient indigenous cultures. This includes medicine men, shamans, chanting and meditation traditions, vibrational healing, spiritual and existential music, and pre-Renaissance healing visionaries such as Hildegard von Bingen (musician, visionary, nun, and physician). At the height of Western scientism developed in the Age of Reason, which really harks back to the influence of Classical Epicureanism, we frequently observe a false dichotomy depicted between arts and sciences. It is not surprising that in our reductionist and positivist society of the West, healing with music and the power of "an art" to affect physiological and mental changes is met with skepticism in some circles. Nonetheless, in African, Australian Aboriginal, and various Asian cultures, to name a few, there are millennia of appreciation for the subtle links between inner and outer well-being and arguably a greater appreciation of whole-person wellness that does not depend on a modern clinical model.

Modern psychologists, however, acknowledge the interaction between mind and medicine, seen and unseen, physical and psychological, experiential and conceptual: the phenomenological experience of humanness. Philosophy, too, has largely rejected the Cartesian divide between cognitive and somatic experience. Grand connections, such as music of the spheres, harmony in the universe, and relationships between aesthetics, beauty, nature and art, perfection, and mathematics, date back to the Classical writings of Plato and Aristotle, persisting through the golden ages of fine art in work by multidisciplinarians such as Leonardo da Vinci, Michelangelo, Albrecht Dürer, Johann Sebastian Bach, Palladio, etc. A contemporary medical model clearly emphasizes pharmacology and physiological symptom management over the importance of spiritual and emotional wellness in a patient's overall diagnosis, thus needing adequately integrating whole-person healing in the treatment approach.

Medieval theorists, such as Robert Fludd in his 1617 'Divine Monochord' (James 1995, p.130) and Agrippa von Nettesheim's theory of 1510 (Wigram et al. 2002, p. 25), correlated mind-body-spirit in terms of the physical world, human body, and vibrations in music; language, human mind, and notes and intervals or "grammar" in music; and the cosmos, human spirit, and divine proportions.

Western philosophers ranging from Plato, Aristotle, Augustine, Schopenhauer to Nietzsche consider the theoretical and practical role of music for the individual and health. Arabic (Muslim) physicians were among the first in the world to have used music medicinally as an integrated element of whole-person health as early as the

eleventh and twelfth centuries. Paradoxically, these seemingly antiquated ideas have been revived through quantum physics, in terms of particle energy, rather than merely vibrational waves and the paradoxical relationship of concurrent wave and particle characteristics.

3.1 The Healing Harp in Antiquity

The harp, lyre, and psaltery were interchangeable terms in ancient times – i.e., a plucked chordophone. A 15,000 BC cave painting of a hunting bow shows the possible origin of plucked strings. Early Chinese healers attributed health to the C'hin zither-like instrument. In ancient Egypt, harps were part of the court consort and used in storytelling, songs, and tributes to deities. Harp and lyre were believed to mobilize fertility and usher in births. Sarasvati, the Hindu goddess (wife of Brahma), used "harp" to guide people and gave humans the arts. She is often depicted playing the "vina" arched harp. Ancient Greeks believed the gods communicated with people through harp or lyre music. In the Middle East, lyres had seven strings associated with Pleiades, the constellation, and represented a microcosm of universal order and harmony.

In Scandinavia and Europe, harps were also associated with magic and enchantment in mythology. Symbolic of peace and connection to the "other" world, harps were linked to sleep, to release of tears, and in Ireland 2000 BC, to the Danen people or faeryfolk. Again harp was linked with fertility, agriculture, nature, faery folklore, and the heart of the Gaelic culture. Celtic nobles and Druids held the harp in high esteem – teachers, judges, shaman priests, and holistic healers who used subtle energies, herbs, and bards and musicians/poets were the keepers of knowledge of ancient lore.

The biblical King David soothed King Saul (who was speculated to be depressed) in approximately 1100 BC with music of the *kinore*, an early lyre. Pythagoras of Samos developed the harmonic series overtone scales and Western modes and associated different emotions with different tunings. In 324 BC Alexander the Great's sanity was restored by music of the lyre – recognized for healing and calming. Harp was considered to be a link between worlds and used as a guide through death process. In Mesopotamia in Ur, early lyre instruments have been found. Harpies were harbingers of death, who sometimes heralded fearful times, and the harp ushered the soul to heaven in the Judeo-Christian tradition.

4 A Brief Overview of Music for End-of-Life Care and Dying Well

Thanatology is the scientific study of dying. Music thanatology is live music (often harp or vocal music) at the bedside of dying patients to relieve suffering from physical, emotional, and spiritual pain. It is generally responsive (sometimes called "prescriptive"), the musician interacting with the patient's biomarkers, such as heart rate, breathing rate, mood, anxiety, etc.

Music has had a fundamental place in song and dance in every tribal culture, often quite rhythmically complex. In the Western tradition of healing music, musicians such as Stella Benson have identified harmonic modes with particular healing qualities and theories of specific sounds, modes, and instruments that have universal healing powers:

> The word *Thanatos* comes from the Greek, and refers to the mythological figure who is the twin brother of Sleep (*Hypnos*) and the son of *Nyx* or Night. There are many kinds of thanatologists today – medical, academic, theological, psychological . . . In its sole focus on the physical and spiritual care of the dying with prescriptive music, it is also a pastoral art which takes the words of the [Christian] Gospel seriously, and turns toward the face of suffering without reserve. (The Chalice of Repose 2016)

Since the 1950s, music therapy was recognized as a vocation. The (USA) National Association for Music Therapy and American Association for Music Therapy converged in 1998 to form the current American Music Therapy Association (AMTA). Music therapy according to their definition uses "clinical and evidence-based music interventions to achieve individualised goals"

(Riley 2014, p. 8). The goal of music therapy is to "address a range of physical, emotional, cognitive and social needs of individuals" across a range of settings and needs including hospitals, psychiatric care, community mental health, rehabilitation and day care centers, residential nursing homes, in schools and in private clinics. Music therapy has been effectively utilized in assisting people with physical and cognitive impairments and learning disabilities.

Key figures in the development of therapeutic music include Dr. Ron Price (founder of Healing Harps – who found neurological benefits of playing harp with palsies and dystrophies and other neurological challenges), Therese Schroeder-Sheker (who established The Chalice of Repose music thanatology project to pastorally support peaceful and dignified death), and Sarajane Williams (who established therapeutic harp to help people with psychological conditions including chronic pain, stress, and depression and vibroacoustic harp therapy using the resonance and vibrations of an acoustic instrument to palpably affect the client) (Riley 2014, p. 8). A number of educational programs emerged offering this bedside approach to healing music: the International Harp Therapy Program, International Healing Musician Program, Clinical Musician Certification Program, and the Music for Healing and Transition Program. Thanatology and music vigil are terms specifically used for individually attentive end-of-life settings. "Healing" has the broader meaning of restoration, making peace, improving overall well-being including satiation of emotions and soul, rather than the more specific implication of "cure" that generally pertains to eradicating symptoms of disease.

The use of clear melody or more atmospheric textural sound depends on the situation and the patient. Music composed mostly of chord progressions and non-melodic structures suits those needing deep relaxation and sleep, as well as people in the final moments of life, because melodic lines and metered rhythm in a gentle tempo can help engage the body and "encourage stability of vital signs" (Riley 2014, pp. 22–23). Riley posits that major keys are suited to hospital environments and minor keys may be suited to hospice or palliative care setting, though modal improvisation allows the musician to oscillate from one to the other with ease. As a generalization, a faster tempo should be reserved for situations when the alert patient requests it, and for most situations a slow or moderate tempo is more conducive to calm and relaxation. Other research in the area of dementia care suggests that moderate to slow music evokes a calmer dopamine-induced response, and very fast energetic music is associated with the cortisol (stress hormone) "fight or flight" reaction. The effect on the body should be observed.

4.1 Instruments for Therapeutic Music

The guiding principle is to use instruments that are not loud and intrusive or disruptive; therefore, many acoustic instruments and well-selected keyboard sounds work well. Patient preference should be taken into account. Plucked strings, such as guitar or harp (with nylon or gut strings), are more appropriate than metal-stringed instruments. Bowed instruments can be muted, and wind instruments played gently. Amplified instruments are usually too loud to be relaxing and may affect other patients and staff. While drums are sometimes used in music therapy participatory groups, they are seldom used in therapeutic music at the bedside.

Instrumental register also impacts the effect. "Pleasing" tones of lower and mellow instruments often sound more appropriate than high-pitched potentially annoying sounds or shrill tone. Children can tolerate higher pitch ranges.

4.2 Tailoring Musical Elements to the Patient

Improvisation gives the therapeutic musician the elasticity to adapt to the situation more easily than prepared learned music. Learned music may also be adjusted in register and tempo to suit a certain context.

Rhythmic music, even slowly lilting music, invites involvement and entrainment (synchronizing listening, breathing, and movement to match the beat). This can help a person to breathe at a steady slow rate, for instance, which is linked to relaxation, as understood in meditation. Regular slow rhythm is antithetic to panic and stress.

Nonrhythmic music, more atmospheric and nebulous in character, can be appropriate to the atmosphere of impending death as vital signs are fading, conducive to a peaceful death. Peaceful, nonrhythmic music promotes tranquility and relaxation. Sometimes the musician plays on after the death to hold the meaningful atmosphere with family and friends. Nonrhythmic music can also be fitting for "relieving pain and stress" (Riley 2014, p. 27). Riley suggests that familiarity from early in a person's life is valuable for elderly patients and people with dementia. This requires familiarity with music of, say, the 1920s–1950s, as well as culturally specific knowledge.

4.3 The Chalice of Repose Project

The Chalice of Repose Project is one of the founding therapeutic music organizations (established in 1973 now spanning the USA), calling itself the "voice of music-thanatology" – providing "beauty, intimacy, reverence in end of life palliative and pastoral care" (The Chalice of Repose 2016). Music thanatology derives profound spiritual inspiration and meaning from the Benedictine Cluniac tradition of monastic medicine. The Chalice of Repose Project contemplative curriculum "re-unites medicine, spirituality and music," working "towards the relief of physiological pain and spiritual suffering that may be eclipsing the quality of life at the end of life" (The Chalice of Repose 2016).

Deathbed vigils aim to bring peace, tranquility of silence, and a shift to acceptance. Music thanatology involves intimate concentrated person-to-person connection, entrainment of sound, and breathing. The musician's goal is to support peace-filled, blessed, or conscious dying.

Silence moves (usually) toward synchronization and entrainment, often leading to pain relief, decreased heart rate and pulse, stabilized breathing patterns, change in body temperature, deep restorative sleep; emotional, mental, or spiritual release; and profound relaxation. Sometimes, patients decrease requests for pharmaceuticals.

5 The Relational Facilitation of Music in Care

If progress of disease leads to increasing isolation, the music-therapeutic relationship may provide important interpersonal contact (Aldridge 1999, p. 22). Tenderness is an important quality in loving relationships. Listening to music together, playing music together, or even the instrumentalist and patient bond can legitimize simple holding of hands. That two people are listening to music and exposing their emotions and vulnerability together creates a kind of unspoken intimacy and sensitivity within an acceptable manner of feeling closeness.

The choice of musical engagement, e.g., active creativity such as art therapy or making music in a group, a metaphor for new growth, creativity, and materiality may not suit someone aware of their deteriorating corporeal condition, for whom it may highlight weakness or incapacity, whereas listening in or singing along more calmly might be entirely appropriate. Providing "enabling" experiences or "empowering" experiences that someone can execute gives them freedom and accomplishment. This independence is especially important for a person with high care needs, to maintain their dignity and agency. Usually providing this opportunity through music-making or participation has no clinical disadvantage yet restores some control, decision-making, and expression.

Aldridge says that what patients and friends and families want "is to be fully alive even in the face of impending death" (Aldridge 1999, p. 24) in the presence of relationships, including opportunities for expression and sharing experiences, which may be valuable to ameliorating suffering. Music emphasizes the lived body as sensed, not only as spoken words, i.e., a felt and emotive

response to a palpable and somatic sensory experience that may be difficult to articulate in words.

Music is human contact, even when someone is in a coma. Singing "goodbye" (Aldridge 1999, p. 102) is important so that someone is not alone when dying and dies at peace.

Indications for therapeutic music may include:

- Coping difficulties
- Depression, withdrawal
- Isolation
- Difficulty expressing thoughts, feelings, needs, and desires
- Difficulty exploring spiritual and existential issues
- Distressing physical symptoms (complex pain problems, persistent nausea, anxiety and fear, restlessness, insomnia, dyspnea, disorientation and confusion, and dysphasia
- Cultural language barriers (Aldridge 1999, p. 69)

6 The Neuroscience of Listening to Music

We respond to music physiologically or "viscerally," to the material properties of sound. Medicine refers to this effect as musical "stimulus." The syntactical or organizational level of music imbues it with therapeutic aspects of imprecise description and interpretation. The "semantic" or "message" level of music conveys emotional expression and metaphorical meaning. The "pragmatic" level of music as a social, interactive phenomenon also has a therapeutic purpose in facilitating interaction, connection, communication, and social experience (Wigram et al. 2002, p. 40). Therapeutic musicians work alongside neuropsychologists and psychologists to understand the brain's nonverbal functioning, in areas such as history, identity, and the effects of auditory perception and musical memory; auditory imagery (equivalent to visual imagination), brain processing of musical input, effects of musical abilities, idea formation, and the implications of performance; and participation or active creativity (composition).

Psychoacoustics describes the effect of hearing, such as the physiological characteristics of the ear, on sound perception. Attributes such as the shape of the pinna (external shell-like ear structure), interaural distance (distance between the ears that contributes to spatial understanding of sound in three dimensions around the body, source location, and proximity), loudness, and frequency acuity filter our experience of sound. The phasing and delay of binaural sounds can have interesting psychoacoustic effects on the body that manifest as physical sensations.

Many parts of the brain are involved in the appreciation (and performance) of music. While this means that certain aspects of musical experience will be affected by localized lesions or brain damage, the generalized neurological stimulation that occurs listening music also works to the patient's advantage in that musical appreciation usually outlasts dementia, traumatic brain injury, other cognitive impairment or partial deterioration of senses including hearing. For example, people who have experienced stroke affecting one hemisphere of the brain can often sing better than they can speak with a therapist. More complex musical tasks such as the creative activities of composition or performance involve the cerebral cortex, subcortical motor and sensory nuclei, and the limbic system, combining left-brain dominant structuring and mathematical and organizing functions with right-brain dominated creative, emotional, and "spiritual" elements in a singular activity. Recent brain plasticity research, however, suggests that the hemispheric localization can also change adaptively, and there is currently some controversy about hemispheric localization in music. Despite an abnormally high incidence of blind musicians or blind people pursuing music ably, generally "the auditory system, visual system, somatic motor and sensory systems and memory all play an important role in the appreciation and performance of music" (Wigram et al. 2002). In addition, culture, conditioning, and training affect musical memory.

"Why do songs from your past evoke such vivid memories? Listening to music engages large scale neural networks across the entire brain" (Bergland 2013), ranging from timbral

activations in cognitive areas of the cerebellum, sensory area, and gray matter of cerebral hemispheres to musical pulse and tonality that recruit the cortical and subcortical cognitive, motor, and emotion-related circuits, supporting the idea that music and movement are intertwined. Limbic areas of the brain, associated with emotions, are also involved with rhythm and tonality processing, while the default mode network engaged in timbral interpretation is assumed to be also associated with creativity and imagination. Aimee Baird and Séverine Samson found that: "Music was more efficient at evoking autobiographical memories than verbal prompts of the Autobiographical Memory Interview (AMI) across each life period" (Bergland 2013).

Music can play a helpful role in anesthesia. Spintge's studies especially have found that music (anxioalgolytic music as distinct from merely relaxing music) significantly reduces distress, anxiety, and pain suffered particularly in operations where the patient is conscious and under spinal anesthesia and improved presurgical compliance, thereby reducing the amount of subsequent medication needed for procedures using other than general anesthetic (Spintge 1982). This reduction in anxiety could be translated to intravenous cannulation and other potentially uncomfortable processes in palliative care.

7 Effects of Music on the Mind and Emotions

It would be fair to say that we don't fully understand the emotional effect of music; however, generally music that is more meaningful (and therefore familiar) for a person has greater emotional impact than music that is not meaningful. This is the motivation for attempting to understand the music of relevance and importance to patients in the palliative care setting – i.e., music with associations, memories, and past experiences (good or bad). The human relation to music is a lifelong development, not only linked to the psychology of early development in childhood, for instance. Humanistic psychology related to existential and transactional therapeutic theories have been especially influential in the development of music therapy. While traditional music therapy may look to the supportive, explorative, or regenerative characteristics of a piece of music, the more open approach of therapeutic music in death and dying looks beyond psychotherapeutic potential to experiential, existential, and aesthetic qualities that resonate for the individual. Nonetheless, the steady somewhat predictable, rhythmic, recognizable gestures that lend reassurance reinforce psychotherapeutic principles, such as Pachelbel's *Canon* – a series of melodic variations over a cycling ground bass.

According to Riley, "Studies in mind-body sciences have indicated that memories, experiences and emotions are stored not only in the brain but in the cells of the body as well. There is no boundary between mind and body . . . Emotions that arise may be perceived as positive or negative, but *catharsis is almost always healing*" (Riley 2010, pp. 34–35). Music can draw out unexpressed emotions and help us feel, explore, and express them, including anger, sorrow, and grief. Bill Moyers in *Healing and the Mind*, and Candace Pert in *The Molecules of Emotion*, supports this view that repressed negative emotions are toxic and that appropriate expression has a positive effect on the body (Riley 2010; Pert 1999).

The Guided Imagery and Music method – The Bonny Model – is practiced on North and South America, Oceania, and approximately ten European countries. Its pretext is music-centered investigation of consciousness, where imagery is evoked during music listening – leading to an unfolding of inner experiences "holistic, humanistic, transpersonal and allowing for the emergence of all aspects of human experience: psychological, emotional, physical, social, spiritual and the collective conscience" (Wigram et al. 2002; Bonny 1990).

Various other established music therapy methods, such as the Nordoff-Robins method, or even free improvization therapy, are relatively formulaic and therapist-led in contrast with the paradigm advocated in therapeutic musician certification which focuses on the musician *responding* to the patient, rather than leading or facilitating the interaction. The latter is often well

suited to the context of palliative care when patients may be quite frail, inert, or somewhat cognitively "hazy" due to medication. The horizon for therapeutic music in palliative care is more focused on comfort, relaxation, pain relief, distraction from the medical environment, spiritual and existential reassurance, companionship, and expression of emotions.

Characteristics of potentially **stimulating** (animating, energizing) music:

- Unpredictable changes in tempo
- Unpredictable or sudden changes in:
  - Loudness
  - Rhythm
  - Timbre (tone color)
  - Pitch (register)
  - Harmony (e.g., unexpected dissonance or change of key/modality)
- Wide variety in texture
- Unexpected accents
- Lack of perceptible structure

Overall, these characteristics are united by surprise, unpredictability, dramatic changes, dramatic variety, and inconsistency (Wigram et al. 2002, p. 138).

In contrast, these are characteristics of potentially relaxing music:

- Stable tempo (speed)
- Stable or only gradual changes in:
  - Loudness
  - Rhythm
  - Timbre (tone color)
  - Pitch
  - Harmony
- Consistent texture
- Conventional harmonic modulation
- Cadences, or phrase-endings
- Predictable melodic lines
- Identifiable or inherent structure and form
- Gentle timbre (sonorities)
- Few accents, especially of an irregular nature

Thus, overall, these characteristics involve consistency; reliability; predictability (related to familiarity of music or stylistic tendencies); stability; minimal variation, without surprising/jarring shocking or dramatic changes; and change only through incremental steps (Wigram et al. 2002, pp. 138–139).

These generalizations can be used to transcend genres or styles. It is obvious why it has led to some people generalizing that Baroque music fits well; however that does not take into account the stylistic tastes of the individual that can usually also be met by choosing appropriate music within the kinds of music that is favored, e.g., smooth jazz or lyrical calm popular music, slow sonorous movements of Romantic music, etc. Genres of music whose characteristics tend outside of these guidelines will be the most difficult to satisfy, e.g., finding relaxing rap music, because it is almost always fast tempo with a reliance on syncopation. These characteristics can also guide improvisation by the therapeutic musician, e.g., Stella Benson advocates gently lilting consistent rhythmic music within particular modes for playing harp at the bedside for a person in palliative care or choices of recorded music for the patient. Predictable music offers safety and stability that can meet needs of certain patients.

Auditory pattern recognition is called "active listening." Long periods of overstimulation create fatigue, dizziness, and nausea. "Television addiction" in humans watching fast-cut video is a genuine phenomenon that numbs this response. Auditory overload leads to confusion and fatigue which may, in turn, manifest in frustration, agitation or emotional upset, and problematic behaviors – for animals or humans and especially for people who cannot express themselves verbally (aphasia) – and eventually auditory cognitive overload leads to anxiety. This effect is exaggerated in people with dementia who may have difficulty locating sounds in space and associating a sound source with its purpose or meaning. Attention consumed in active listening is not available for other tasks. Chronic overstimulation invokes the mind-body syndrome of perpetual fight or flight *sympathetic overdrive*. For this reason, careful attention should be given to the intensity and duration of music used therapeutically, especially anyone with dementia or other cognitive impairment that affects sensory overload.

8 Effects of Music on the Body

Vibroacoustic music is a receptive form of therapy in which the patient directly experiences the vibrations of the music through contact with a resonating surface. This can range from a large resonant instrument such as the harp to a developing range of vibrotactile instruments invented in Japan and the USA using extremely low frequencies, for example, pulsed and sinusoidal (sine wave) tones of very low frequency (between 30 and 70 Hz). Vibroacoustic therapy is reportedly effective for pain disorders such as bowel problems, fibromyalgia, migraine, menstrual pain, neck and back pain, and rheumatism. Therapists will adjust the frequencies used according to the pathology (Chesky and Michel 1991).

Riley states that "states of mind do not dictate the body's status, but they do *affect* the body, sometimes profoundly" (Riley 2010, p. 89). Correlates include heart rate, nausea, perspiration and stress, "fear" responses, and physiological responses to the stress hormones, cortisol, and adrenaline. Negative states of mind can also inhibit endorphin production, and reduced serotonin levels may be associated with depression and suppress immune responses. Stressors can be worry, grief, or too much responsibility, for example. Thus, a holistic approach to treatment includes body, mind, and spirit and awareness of this mind and body interaction (Riley 2010, p. 88).

A relaxed state in which pain relief is induced by listening to music is called "audioanalgesia." A related phenomenon is "psychoneuroimmunology" that examines immunologic neuropeptide activity and the body's own capacity to heal when in a relaxed state (Drohan 1999). One of the earliest documentations of the effects of music on humans is Helmholtz's text, *On the Sensation of Tone*, written in 1862 (Helmholtz 2003; Benson 2003).

Anecdotal reports from palliative care are substantiated by empirical evidence including studies by Bailey (1983), Curtis (1986), and Whittall (1989). Bailey found that cancer patients were less tense and anxious and experienced a more positivity and vigor listening to live music than the corresponding recorded music. In her review of 465 cancer patients receiving music therapy, Bailey reported a reduction in pain, mood improvement, and improved communication. Curtis and Whittall's studies corroborate the promotion of pain relief and relaxation, as well as contentment. A decrease in heart rate and respiration rates was measured among a small number of people during intervention of music with guided imagery, deep breathing, and progressive relaxation exercises that suggested a reduction in anxiety (Whittall 1989).

9 Different Formats of Therapeutic Music

There is great diversity to the range of techniques that music therapists and therapeutic musicians use in palliative care to "enhance quality of life . . . and ease suffering: musically supported individual counselling (Munro 1984); improvisation (Delmonte 1993; Salmon 1993); music to facilitate communication between the patients and their significant others (Munro 1984; Salmon 1993); life-review including music (Beggs 1991); music-facilitated pain control and relaxation (Munro 1984); guided imagery and music (Bruscia 1991; Salmon 1993); and group work" (Aldridge 1999, p. 44).

Common themes that emerge in creative musical reflections include self-reflections; compliments; memories; reflections on significant others (including pets); expression of adversity; imagery; prayers; care experiences and experiences of love; gratitude to family members, staff, and God; continuing to remember close people who are deceased; nature imagery and scenes; and the fight with cancer or degenerative disease (Aldridge 1999, p. 55). Staff can assist people by facilitating them choosing their own music for passage and transitioning out of life.

9.1 Different Methods in Music Therapy

Some well-known techniques from music therapy that may be used for therapeutic music in palliative care include:

- Guided imagery and music – the Bonny model
- Analytically oriented music therapy – the Priestly model
- Creative music therapy – the Nordoff-Robins model
- Free improvization therapy – the Alvin model
- Behavioral music therapy

The extent to which patients elect participatory, active, or passive music approaches will depend on how well they are. People in the early course of palliative care may find participatory methods useful for diversion from pain and procedures, whereas weakness and medication may diminish the ability to be creative as the palliative care trajectory advances.

To sound healing may be added techniques including toning, healing with gongs/overtones, body and voice work, drumming, and sound environments or vibrotactile apparatus. Crowe and Scovel (1996) suggest that music therapy and sound healing are different poles on a spectrum. Pragmatism and an open mind are probably useful in the context of palliative care where the objective is maximizing quality of life rather than pursuing a cure.

Hanne Mette Ochsner Ridder (2013) highlights the diversity and non-homogeneity of older adults. Older adults constitute the majority of people in palliative care settings even though it is important to be able to address the needs of people of all ages and experiences (e.g., in 2016, around 90% of HammondCare Greenwich Hospital's palliative care inpatients (in Australia) were senior or elderly, and approximately 91% had cancer). Elderly people may be especially affected by changing relationships to new people, new surroundings, new routines, the disturbing behaviors of other patients, staff who invade their personal space in care situations, and time-poor staff (Wigram et al. 2002, p. 188). Continuity and familiarity of relevant music can be beneficial in this situation to distract from change and disruption, as well as to provide some stability and reassurance. Music in the room or via headphones and a personalized music device can be used as an interactional tool and to ease the institutional setting of a hospital.

9.2 Biomagnetic Fields and Frequency Intervention

Therapeutic musicians can make use of beneficial resonant frequencies and repetition of specific notes that patients can physically feel reverberating through their bodies. Different organs and body structures are associated with different frequencies, though a frequency-related approach should not be formulaic. Riley uses the expression frequency not only to refer to pitch/frequency, measured in Hertz, but also to refer to periodicity of a repeating event. For example, a practitioner may play in a tempo mimicking the heartbeat, to encourage entrainment to that beat.

Example of cyclical body rhythms:

- Adult heart rate averages around 60–80 beats per min.
- Healthy adult respiration averages 12–16 breaths per min.
- The gastric cycle that controls the stomach contracts on average once per 3 min.
- The intestinal cycle contracts in waves approximately once per min.

Brain wave frequencies are described as alpha, beta, delta, and theta frequencies. Normal frequencies are generally:

- Delta (deepest sleep) = 1–3 cps (cycles per second)
- Theta (sleep) = 4–8 cps
- Alpha (light slumber) = 9–16 cps
- Beta (awake) = 17–22 cps (Riley 2010)

Mathematician Barbara Hero and sound healers – Jonathon Goldman and Kay Gardner – have written about the resonant frequencies for each organ and function in the body, with the caveat that bodies are individual and this is not an exact science. Furthermore, some frequencies are multiplied by octave factors in order to be musically presented in the audible range. Some vibrational therapists, such as Bruce Tainio and Gary Young, believe that changes from normal frequency range produce illness.

"Cymatics" is the term given to visible effects of frequency on matter drawing from the work of Ernst Chladni (1756–1827) and, subsequently, Hans Jenny (1904–1972), e.g., the waves, ripples, and formations in different densities of liquids in response to particular frequencies and intervals: visible waveforms, dissonance, and geometric patterns (Jenny 2016). Cymatics uses audible sound frequencies for specific healing stimulation. This approach can be traced back to ancient wisdom traditions (Cymatics Source 2016).

9.3 Toning and Chant

Chant such as repetitive use of words, phrases, or sounds that cause overtones to resonate in the body has long been part of meditation, faith traditions, and ancient wisdom, for example, Medieval Christian chant, Indian Sanskrit mantra, Vedic or Upanishad scripture (Riley 2010, pp. 92–93), Tibetan Buddhist Tantric overtone singing, and in Africa. Such chanting often combines both a rhythmic effect and certain modes or intervals that elicit harmonic overtones. For instance, a close interval will create "difference tones" or a beating sensation relating to the size of the interval, or high overtone harmonics may be heard above extremely low register tones. Certain vocal and throat techniques bring harmonic overtones into audible range. Due to the phenomenological experience of integrated mind state and physiological vibration, chant can be understood as holistic in both the medical and philosophical sense. Generally, this type of chant is more related to meditation than "music" per se. Its psychological effect is of greater importance than melodic features. When a person is actively involved in chanting, not only the palpable sensation of the vibrations and voice but also the long rhythmic periodicity of breath cycles and slowed respiration affects the body. Toning (i.e., chant without the use of words or syllables) has been linked to melatonin production according to Dr. Ranjie Singh and Marc Micozzi, musician Fabien Maman, and several ancient belief systems including Qigong, Taoism, Egyptians, and Zoroastrian rituals and yogic traditions (Riley 2010, p. 91).

9.4 Allopathic (Complementary) Modalities

Many alternate or complementary modalities of therapeutic music and sound have grown up alongside conventional medicine since the 1970s.

Some examples include:

- Drumming
- Harp therapy
- Music thanatology
- Music therapy (interactive/participatory)
- Sound tables
- Chanting and toning
- Vibroacoustic harp therapy

Therapeutic music may be characterized by:

- Intention – always for the good of the patient, whatever that may be, putting aside personal satisfaction
- Taking neither credit nor blame for the effect of genuinely delivered music
- Playing simple rather than complex music for healing, not performance; relief and blessing, not entertainment
- Healing not curing – restitution to wholeness of mind and spirit, not eradication of physical illness or injury – e.g., reducing perception of pain, promoting better sleep, and facilitating relaxation

9.5 Harp Thanatology

Why the propensity to use harp in bedside vigils of people nearing death?

The rationale is not related to heavenly imagery. While monadic or melodic instruments play one note at a time, the harp is able to capture chords, harmony, and resonance – i.e., multiple notes simultaneously. A "travel" or Celtic harp is also relatively portable, allowing the instrument to come to the bedside in a range of settings. The volume of harp allows it to be played softly and calmly in a confined space. The pitch range of the instrument also permits the musician to harness mellow resonant low-frequency notes in

prescriptive music empathetic with relief of pain and suffering. Finally, the *timbre* (tone color) of a well-plucked harp is widely considered to be pleasing and soothing. The anatomy of the harp with its large soundboard and open holes in the back emits the tone with vibroacoustic properties that some believe are healing and certainly viscerally palpable. Some people will sit so that they can rest their back on the harp and literally feel the vibrations permeating their physical body. The polyphonic nature of the harp makes it suitable for encapsulating relevant harmonic modes. Stella Benson's book on *Healing Modes* ascribes different elevating and calming moods and healing purposes to different harmonic modes.

What is so especially healing about the harp?

Sympathetic vibrations are resonances perceived in the body vibrating with string and overtones (harmonics), crossing between the spiritual and physical realm. Others have suggested that the beautiful aesthetics of sound and shape of the harp echo the golden sequence (or Fibonacci series of ratios with "universal" appeal). The ADSR (attack, decay, sustain, and release) of a soundwave determines its timbre (or tone color). The harp has an especially long decay envelope or resonance and energy exchange. Dr. Abraham Kocheril has written about the organizing and calming effects of harp music on chaotic electrophysiology (cardiac arrhythmia), believing that the characteristics of the instrument influence physical symptoms.

10 Music and Pain

"Pain occurs in the physical, emotional, and spiritual realm" (Benson 2003, p. 19). Perception of pain is shaped by many aspects, such as gender, culture, how pain affects the patient's life, stress or anxiety, previous experience with pain, outlook, and other psychological factors. Hence, different individuals will have a different "pain threshold." "Music is known to reduce the sensation of pain, fear, anxiety, need for excess anaesthetic agents . . . recovery rates, mortality rates, hospital stays . . ." and requests for medication. People who are experiencing post-traumatic stress disorder (PTSD), financial or other life instability and stress, or depression, for example, may perceive a greater impact of pain from injury or disease.

Physical pain affects several measurable characteristics, e.g., blood pressure, immunoglobulin levels, and skin temperature (Benson 2003). Other indicators of pain can include moaning, quick or intermittent inhalation/exhalation, holding breath, muscle tension, tight jaw, facial grimaces, fisted hands, knees to chest, moodiness and restlessness, and sensitivity to light.

Music can be used as a noninvasive analgesic. For musicians playing live, Benson suggests slowing down tempo and simplifying melody and harmony, shifting from moving harmony toward a drone, correlating with increased pain. In other words, more spacious, calm music is advocated for people with a high level of pain and more rhythmical, elaborate music for people with a lower level of pain.

Linda Bloom (2016) suggests that pain should be considered as the "fifth vital sign." Bloom criticizes overprescription, especially of addictive narcotics and patient-managed expectations of pain relief in the USA. She believes that "patients are led to expect that they will have 'little or no pain'" and that powerful and addictive pain medicines are automatically provided in response to patient-assessed pain scales, whereas according to Bloom, 73 RCTs on the role of music conducted by Dr. Catherine Meads at Brunel University found that music reduces pain before, during, and after surgery. Meads states that: "This level of relief is comparable to that achieved by a dose of pain-relieving drugs."

According to the International Association for the Study of Pain, pain is an "unpleasant sensory and emotional experience associated with actual or potential tissue damage . . . Pain is both a sensory process felt in the body, and a subjective phenomenon, influenced by the psychological and emotional processes of each given brain" (Bicknell 2011). The brain and nervous system sense and process vibrations. "The spinal cord is composed of nerve bundles carrying different

kinds of sensation; heat and cold; pain, pressure, and vibration" (Thompson 2010). The processing of pain involves both the peripheral and the central nervous system. During musical vibrations, the nerve tracts for vibrational sensing are "preoccupied or "overloaded," effectively disrupting pain sensation. As a pain control feature, musical sound is good and vibratory sound may be even better. Furthermore, the emotional and spiritual effects of music impinge on physiological and psychological responses. The brain has endogenous opioids, and other neuropeptides, such as oxytocin, that may be stimulated and released by hearing music.

With regard to relaxation, the effect of music has been measured on the autonomic nervous system, manifests in a reduction in sympathetic arousal, and increases in parasympathetic activity (Warth et al. 2016).

11 Music and Agitation

Agitation is common among people with dementia, people in the terminal stage of end of life, and as a result of some medications. The so-called agitation is often the expression of an unmet need, especially when someone is unable to communicate verbally. "High levels of agitation are . . . associated with low levels of quality of life" (Samus et al. 2005), and the "use of psychotropic medication is associated with reduced quality of life" (Ballard et al. 2000). Agitation can be linked to stressful triggers or activities such as visitors, grooming, bathing, or mealtimes (Beilharz 2017) and medication "breakthroughs." Music can be a helpful diversion from social triggers, especially if introduced *before* the trigger activity. Music can be helpful getting to sleep or distracting from tense procedures and situations.

"Cognitive impairment lowers the stress threshold so that external stimuli are more likely to cause agitation" (Gerdner 2012). Individualized music intervention "overrides the stressful environmental stimuli that the cognitively impaired person cannot synthesise, and instead evokes remote memory with pleasant associations, decreasing agitation" (Gill and Englert 2013). It has been shown that brain activation in response to a painful heat stimulus is significantly reduced when a person focuses attention on a musical or auditory stimulus instead of focusing on the heat stimulus. Thus distraction is a genuinely effective counter-pain measure (Bushnell et al. 2000).

12 Spiritual Support

What makes a person feel whole? Anthony Storr (1992) refers to the phenomenon of music as "mental furniture," i.e., the music that plays in our head un-summoned. It could be argued that if someone is accustomed to having one's "mental furniture" present and stoked from time to time, then to remove its stimulus is also to lose something stable, familiar, and comforting. For many philosophers, including Schopenhauer, Kant, Hegel, Nietzsche, Freud, and Jung, among others, the metaphysical quality of music permeating inner life (inhabiting spiritual vitality, as it were) also imbues it with power to create *meaning* and passion. Nietzsche went so far as to say that music made life worth living.

12.1 What Is Spirituality?

There are many different definitions of spirituality; however there is consensus that aging, dying, and enduring disease involves a spiritual dimension. It is often a time of life when various changes occur including physical, relationships, dependency and support needs, looking backward and forward through life, assimilating experiences and information differently, emotional needs and feelings, wondering about end of life and legacy, diminishing importance of material riches, and growing emphasis on experiences and relationships.

"The spiritual dimension focuses on meaning of life, hope and purpose, explored through relationships with others, with the natural worlds and with the transcendent" (Mowat and O'Neill 2013). Evidence suggests "genuine and intentional

accompaniment of people on their ageing journey; giving time, presence and listening are the core of good spiritual practice."

Tools in the practice of listening and presence include reminiscence, life-story keeping, creative activities, and meaningful rituals (signifying practices) that help with processing change. Many people receiving palliative care have complex conditions, including pain management and cognitive or psychological issues, which also require spiritual support.

Spirituality often involves the search for meaning in a spectrum from centrality of divine presence at one end and the secular concept of inner life, personal belief, and focus on self at the other end.

To think about the supporting role of music in spirituality, it is helpful to consider various manifestations of spirituality. In secular society, there is a distinction between the terms "spirituality" and "religion," which has become particularly enunciated because many contemporary forms of spirituality do not involve a faith or religion. This clarification has emerged as participation in organized religion has declined and interest in spirituality has ascended, a move from creaturely worship to autonomous subjectivity, a movement from faith in God to faith in self, especially the postmodern sense of self-sufficiency (Swinton and Pattison 2010).

12.2 Music as an Alternative to "Hyper-cognition"

Hyper-cognition refers to the overemphasis on cognitive ability to the detriment of other capacities. Due to its deep emotional connection, arguably transcendent qualities, and relative portability, music provides a way to bring ritual and liturgies (and reminder of community involvement) into the home, hospital, or hospice palliative care.

Music can carry associated feelings of belonging; reassurance; acceptance; hope; forgiveness; acquiescence; compassion; peace; resolution in relationships; purpose, meaning, and context in the vast cosmos; and plane of time.

There is a close link between anxiety or stress and pain. People with post-traumatic stress or depression, for example, may be more sensitized to pain, meaning it is worse for them than it would be otherwise. Conventional chronic and severe pain management, unfortunately, often serves people living with cognitive impairment very poorly. It is estimated that a large group of palliative care patients have cognitive impairment due to confusing medication, metastases in the brain, primary tumors, other disease conditions, or aging and dementia.

A number of alternative methods used for pain management are principally cognitive, such as relaxation and meditation techniques and cognitive behavior therapy (a process of analyzing, abstracting, and objectifying feelings that accentuate anxiety and pain). It is helpful to offer less cognitive and more intuitive ways to relax, appease anxiety, and access meditative or reflective calm for spiritual reasons, because conventional meditation techniques, even breathing exercises or concentration meditation, are not suited to a person with cognitive impairment or pharmacologically impaired concentration.

Music has an important place in spirituality, especially in palliative care. People with cognitive impairment need to be released from the responsibility or expectation of reciting liturgy or prayers, naming requests for forgiveness or meditation. They should be given alternative methods of belonging to their community and finding communion, reconciliation, hope, peace, comfort, and reassurance.

Many older people in palliative care also have dementia. Oliver Sacks in *Musicophilia* (2008), and Cohen and Eisdorfer in *The Loss of Self* (2002), writes about the benefits of music in the context of identity because dementia is most tragically often associated with a disintegration of identity. Music can foster a sense of self and identity that is not contingent on memory but rather on character expressed through musical taste, an embodied response and feelings, stimulation of memories of significant events and associations, and a sense of familiarity and "homeliness."

12.3 Using Music to Support Spiritual Well-Being in the Hospice

Supporting the spiritual well-being of people involves appreciation of these intricacies and looking for opportunities when alternative approaches to spirituality, such as music engagement, can be of value without compromising cultural identity. Ideas should be adapted to the individual's experience and background.

David Vance writes: "Many spiritual and religious activities rely on more *resilient* cognitive features such as procedural memory and limbic system aspects of attachment and motivation" (Vance 2004). By "resilient" Vance means enduring through all stages of cognitive impairment, medication, or dementia. Russell Hilliard reviewed the empirical evidence for music therapy in hospice and palliative care. While he focuses on visits by expert music therapists (as distinct from music engagement more broadly as part of everyday care), the results corroborate the impact of music in supporting comfort and reduced stress toward the end of life. "The primary goal of palliative care is to promote patients' quality of life by alleviating physiological, psychological, social and spiritual distress, and improving comfort … There are several forms of complementary therapy (e.g., massage, art therapy, aromatherapy, reflexology, therapeutic touch) … [and] the emergence of an evidenced-based approach to music therapy in end-of-life care" (Hilliard 2005). There is a rich array of qualitative studies that report music's ability to support end-of-life care and address patient and family needs.

Needs often treated by music therapists in end-of-life care include:

- The social (e.g., isolation, loneliness, boredom)
- Emotional (e.g., depression, anxiety, anger, fear, frustration)
- Cognitive (e.g., neurological impairments, disorientation, confusion)
- Physical (e.g., pain, shortness of breath)
- Spiritual (e.g., lack of spiritual connection, need for spiritually based rituals) (Clements-Cortes 2004; Cunliffe 2003; O'Callaghan 1993)

A considerable concurrence of depression, anxiety, and loneliness may be experienced by people in palliative care due to their social isolation, uncertainty, and feelings of helplessness. In hospice and palliative care, therapeutic musicians treat the many needs of patients *and families* receiving care.

Wlodarczyk investigated the effect of music therapy on the spirituality of people in an inpatient hospice unit. Statistical analyses indicated a significant increase in well-being (using a spiritual well-being scale). His study supports the use of music therapy to increase spiritual well-being for the terminally ill (Wlodarczyk 2003). "The expression and discussion of feelings of loss and grief can be very difficult for terminally ill patients. Expressing their emotions can help… experience a more relaxed and comfortable state" (Clements-Cortes 2004). For people who have very little or no speech, the *only* realistic way for them to express their responses is through emotional expression, and music is one way to feel together, to sing or make music, to harness music that encapsulates a poignant sentiment, or to stimulate volubility so that people can utter and release strong emotions.

12.4 Cultural Sensitivity

Spirituality is an aspect of *cultural competency.* "Cultural competence" refers to: "The process by which individuals and systems respond respectfully and effectively to people of all cultures, languages, classes, races, ethnic backgrounds, religions, and other diverse factors in a manner that recognises, affirms, and values the worth of individuals, families, and communities and protects and preserves the dignity of each" (Jutlla 2016). At least a minimal understanding and of varying attitudes to acceptable music in different faiths (e.g., karma and reincarnation, afterlife, necessary rituals, stigmas, and taboos) is necessary to support the end of life and illness with sensitivity, dignity, and respect using music tailored to the cultural situation.

Christians believe in eternal life after death. Music can be used to reinforce "hope," restoration

of the perfect relationship with God, satiety that does not depend on earthly or material possessions, health, or physical wellness. Music, especially familiar church music, can reinforce a person's sense of belonging and community, fellowship, and sense of being part of a larger entity, the Church. Christians believe that human creatures have intrinsic worth as God's creations, made in His image. This value is not undermined by frailty, illness, or disability. Songs that evoke God's limitless love and grace may provide reassurance and comfort to the believer. Music can be used to mark seasons of life and for faithful contemplation. Apostle Paul suggests that singing and music-making is a collective worship experience: a harmonizing act of inclusion, oneness, community, and communion in the Holy Spirit, embodying the unity of the Church, a corporate act of thanksgiving and praise, and an edifying, unifying imperative (Ephesians 5:18–21).

Hindu religious observance can include prayer, meditation, bathing and cleanliness, dietary needs, and astrological beliefs. The needs of the individual are contextualized in the greater unit of the family, culture, and environment (Coward et al. 2000). Hinduism encourages family members to take a role in care of family members, and selecting and listening to music together can provide a tangible way to be involved in caring. Hindus believe that all living beings possess a soul that passes through successive cycles of birth and rebirth (reincarnation). The great sitar performer, Ravi Shankar, said: "We view music as a kind of spiritual discipline that raises one's inner being to divine peacefulness and bliss … Thus, through music, one can reach God" (Hindu Music 2016). The Indian poet and Nobel Prize winner, Rabindranath Tagore, wrote: "For us Hindus, music always has *a transcendent meaning,* even when its intentions are by no means mystical or religious, but epic and amorous. Above all, music tries to touch the great hidden reasons for happiness in this world" (Hindu Music 2016).

Like Hinduism, Buddhism has the concept of karma (consequences of past actions – in this life or previous incarnations) and reincarnation. The latter means that the way of dying, dying well, and peace and non-agitation at end of life are important for a good reincarnation. Buddhism often uses music as part of spiritual practice, especially in temple practice and many forms of Buddhism practice meditation (by laity as well as monks and nuns). Buddhism takes on local cultural hues wherever it is, such that different manifestations have quite distinctive practices and cultural inflections. Aspects of food, dress, music, humility, and so on adapt within the local environment, from Nepal, India, and Tibet to China, Korea, Japan, India, Thailand, Sri Lana, Cambodia, and Myanmar. Despite this immense variety, most forms of Buddhism have meditation as part of their practice, and in various cultures this is assisted by "music," where music is not "entertainment" but chant, drones, liturgical recitation, and sound vibration as part of the spiritual experience. Music that we might otherwise call soothing or calming is an aid to concentration, immersion, mindfulness, or even working to achieve a "no mind" state of detachment from active thoughts running around in the head. Pain and anxiety can bear all the traits of repetitive, persistent, or obsessive thoughts that detract from quality of life.

Islam provides Muslims with a code of behavior, ethics, and social values, which helps them in tolerating and developing adaptive coping strategies to deal with stressful life events (Sabry and Vohra 2013). There is considerable variety in the attitudes toward music, and so consideration is needed as to when and whether music engagement is an appropriate intervention in care for people of Islamic faith. Drawing from his thorough understanding of Shari'ah, rather than simply quoting the Qur'an or a Hadith, Imam Afroz Ali suggests that it is "important to note that music and singing are essentially two different things … The kinds of singing, which are unequivocally prohibited, are those which contain the celebration of the material world and includes sexual connotation and… inappropriate speaking … [that] remove a person away from the worship and appropriate presence with Allah" (Ali Imam 2016). The kinds of singing that *are* permitted are musical matters that glorify Allah and praise the Prophet. It is also permissible to sing in general

terms about happiness (rather than about Allah specifically). Frivolous instrumental music, without singing, music purely for dance and sensual enjoyment (called *malahi*), is prohibited and abhorred. In a therapeutic or spiritually supportive capacity, great care should be taken to exclude lyrics and instruments that do not fit these criteria. Regarding the concept of whether music is allowed (halal) or forbidden (haram) in Islam, we can find different views from Islamic scholars; however, generally music is not considered forbidden in Islam as long as it is a therapeutic need. A millennium ago, Muslim physicians were considered leaders in medicine and innovative alternative therapies, now considered modern, including music therapy. In the past, Islamic researchers found that music has a great effect as a treatment of depression, insomnia, stress, schizophrenia, dementia, and childhood-related disorders like autism (Hanser and Thompson 1994).

Receptivity toward music in Judaism is similar to Christianity, and there is a rich use of music in Jewish culture, whether celebratory or serious.

13 Implementing Music in Palliative Care

Following are some approaches to implementation, ranging from bringing in expert performers, volunteer musicians, and trained therapists or providing recorded music on portable devices for listening with headphones that can be organized by staff or family and friends.

13.1 Engaging a Musician in Palliative Care

For the musician, a reexamination of values is important preparation for creating music for healing. This includes discarding investment in being right, exclusivity, attachment to past experiences, or expectation. Music for well-being is about an attitude of *sharing* and *encouraging*, and self-acceptance, rather than *showing* or *performing*. Therapeutic settings are frequently challenging. Concurrently, musicians need to deliver nothing less than their best, unselfishly, and with passionate commitment. The therapeutic musician must develop focus and relaxation, and relaxed posture and breathing that coheres with the musical expression, especially in a context when the musician is trying to help a patient relax, rest, or calm anxiety.

13.2 Considerations for Different Settings

The purpose of palliative care is patient comfort, especially pain control for people with medically incurable conditions, and enabling a peaceful and dignified death when appropriate. Not all patients in a palliative care ward or hospice are near to dying but may be there for symptom management. Music can extend to supporting the grieving process.

Acute hospitals typically have more monitoring equipment (O_2 SATS, temp, BP, HR) that often displays vital signs obviously for the therapeutic musician.

It is important to understand the *milieu* and environment (Aasgaard 1999), e.g., tailoring therapeutic music to suit the different settings and expectations of the palliative care ward, general hospital, hospice, or residential care home in which someone receives palliative care or, increasingly, the individual's home and community palliative care. Music ties in with meals, visitors, notions of privacy, and many situational and environmental factors and needs to be sympathetic with creating as relaxed and homelike environment as possible.

Sound in the environment of the home or ward for the person receiving palliative care influences tranquility, privacy, and ability to reflect. Reducing the noise from hospital equipment, alerts and announcements, clattering trolleys and foot traffic, visitors for other people, etc. will improve the experience for the patient and allow them to hear their own therapeutic music more clearly and immersively. Portable music devices and headphones are ideal in this setting rather than loudspeakers to help with occlusion and sound isolation.

13.3 Infection Control

A visiting or volunteering musician may be unfamiliar with requirements of infection control, both to protect the patient and themselves. The health professional may need to provide guidance. This includes sterile equipment, hand-washing protocols, quarantining, avoiding cross-contamination, and precautionary protection of patients and staff. Contagion is a higher risk for immune-compromised individuals who are unwell. Hospitals carry an inflated infection risk (nosocomial infection). Hand-washing and avoiding surface contact are the best strategies for reducing this risk.

13.4 Recorded Music for Individual Listening

Recorded music on portable devices has the several advantages. Firstly, the headphones allow a patient to use music to mask the operational noise of other people and equipment, an immersive environment that occludes or masks noise, chaos, and stress triggers. Secondly, it is not intrusive for others, as compared with small loudspeakers. Thirdly, a simple device, such as an Apple iPod or comparable MP3 player, for example, allows most patients to control the music themselves, thereby being proactively involved in their own music intervention and with the flexibility of being able to listen anywhere and at any time. The latter is very beneficial when music is deliberately used to aid going to sleep or to overcome pain and restlessness, i.e., at any time of the day. Individualized music can also be tailored with a list of music that is both calm and fits into the patient's tastes and interests for the greatest emotional and spiritual impact.

Music can be organized by staff forming part of the whole-person service, or music may be provided by the family and friends as a way to be meaningfully involved in care. If a patient is not able to explain their own interests in music, friends and family are often able to provide this information.

14 Conclusion and Summary

This chapter has looked at the potential impact of therapeutic music in palliative care with special attention to its impact on diversion and minimization of pain perception and calming physiological and emotional effects that can assist in reduction of restlessness, agitation, and anxiety. Further areas of physiological and emotional impacted by music intervention include stimulation of appetite, aiding getting to sleep, reducing agitation, and behaviors triggered by specific events or activities, such as bathing, visitors, and medical procedures. This chapter has outlined the key distinctions between therapeutic music and music therapy: their respective applications and practitioners. The way in which music affects physiology, the brain and mind have been discussed along with a number of approaches in mainstream therapeutic music and some concepts of vibrational therapy from alternative medicine practices. A brief outline of music in relation to health from antiquity to the present, from historical and philosophical perspectives, has been provided for those who are interested in the origins and long cultural background of the healing role of music. A very brief introduction to cultural and faith-related sensitivities points to the importance of cultural competency and sensitivity in multicultural and diverse care delivery.

Most significantly, engagement with music can facilitate relational interaction with family, friends, and care staff and provide companionship, reminiscence, and reinforcement of identity in times of change or isolation. Music has been used therapeutically to help people express emotions and anxieties that are difficult to verbally articulate, and to vent repressed and abstract emotions, especially those associated with dying, resolution of relations, existential issues, and fears. Music engagement provides a complementary modality for supporting emotional, psychosocial, and spiritual needs to balance the physical and medical care that form part of whole-person understanding in palliative care.

Music has a valuable contribution at various stages of palliative care, dying and death, both for the individual in care and for their family and

friends, in coming to terms with emotions and assisting with a calm, dignified environment. Throughout the palliative care trajectory, individualized music provides a flexible and proactive, potentially self-managed intervention that gives the patient some control over their environment, feelings, and pain management as appropriate in a situation where many aspects of their care are not in the patient's own control. Music can be a gentle and subtle way to support spiritual, existential, and deep nonverbalized needs, especially for those who do not identify with a faith community but who, nonetheless, have spiritual and emotional needs that are not addressed by medical care. As a modality, music can often be used in partnership with other therapies to facilitate movement, creativity, creating a legacy, for meditation and reflection, and with pastoral care.

Given its inexpensive nature and lack of side effects, music can provide a very effective, meaningful therapeutic intervention and enhancement to life quality without risk. Music can manifest in a range of presentations ranging from live music at the bedside and vigils by specialist therapeutic musicians to the provision of recorded music on a portable device tailored to individual tastes and needs, supported by any member of the care staff or family and friends, without the need for musical or technological expertise.

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Sexuality and Intimacy

45

Agnes Higgins and Geralyn Hynes

Contents

Abstract

A primary goal of palliative care is to provide "active total care" and improve quality of life of the person and their family. As sexuality is an integral part of the uniqueness and personality of every human being, failure to acknowledge this aspect of an individual in the palliative care context implies failure to acknowledge personhood. Navigating changes in sexual function and relationships is challenging for all people; however, for people who have a diagnosis of life-limiting illness, there are extra challenges and losses. Despite living in the "shadows of impending death," evidence suggests that the expression of sexuality and the need to connect in an intimate way continues to be an important part of people's

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_40

lives, even in the last weeks and days of life. This chapter explores the impact of life-limiting illness on sexual expression and provides some guidance to practitioners in responding to people's needs. The chapter moves beyond the binary division of gender and heterosexual relationships to discuss the needs of people who identify as LGBT and those who experience disenfranchised grief. While sexuality and sexual expression is a positive force in many people's lives, for others, it is a source of trauma and distress, and palliative care practitioners need to be aware of issues, such as sexual trauma and sexual disinhibition, and be in a position to create a safe accepting space, where people feel safe, validated, and supported.

1 Introduction

A primary goal of palliative care is to provide "active total care" and improve quality of life of the person and their family. As sexuality is an integral part of the uniqueness of every person, it follows that practitioners should proactively address this aspect of the person's humanity and human experience. At present, palliative care practitioners are not immune to the wider societal discourse around sexuality that positions sexuality as a taboo and embarrassing subject or frames discussions on sexuality and intimacy within a youth and health orientation. Consequently, the burden of responsibility seems to be on the ill person to initiate discussion. Thus, the challenge for practitioners is to break the cycle of silence and taboo that persists around sexuality and provide person- and family-centered care in a way that reflects and truly acknowledges the person's sense of self.

Navigating changes in sexual function and relationships is challenging for all people; however, for people who have a diagnosis of a life-limiting illness, there may be extra challenges. This chapter explores the impact of life-limiting illnesses, such as cancer, and their treatment on sexuality and sexual expression and provides some guidance to practitioners in responding to people's needs. This chapter moves beyond the binary division of gender and a heterosexual focus to incorporate the needs of people who identify as LGBT. It also discusses issues which receive little attention within the palliative care literature, namely, sexual trauma and sexual disinhibition. These gaps in palliative care literature and the broader dearth of research on sexuality in palliative and end-of-life care are noteworthy, not least because they are in direct conflict with the notion of total care, total pain, and personhood, concepts that are integral to the philosophy of contemporary palliative care.

2 The Complexity of Sexuality

The literature abounds with definitions of sexuality from many different perspectives with no single understanding or clinical definition of sexuality emerging. Taylor (1983 : 54) suggests it is "the constellation of physical and psychological traits that make us male or female," with Wilmoth (2006) being of the view that sexuality, like pain or fatigue, is what the person says it is. While recognizing that sexuality is a very individualized and personal concept, and is best defined by the person, the World Health Organization's (WHO) definition, which is the most common one cited in the literature, is used here to elucidate the various dimensions of sexuality.

The Pan American Health Organisation/World Health Organisation (2000:6) defines sexuality as "...a central aspect of being human throughout life encompasses sex, gender identities and roles, sexual orientation, eroticism, pleasure, intimacy and reproduction. Sexuality is experienced and expressed in thoughts, fantasies, desires, beliefs, attitudes, values, behaviours, practices, roles and relationships. While sexuality can include all of these dimensions, not all of them are always experienced or expressed. Sexuality is influenced by the interaction of biological, psychological, social, economic, political, cultural, legal, historical, religious and spiritual factors."

This broad definition emphasizes the all-encompassing nature of sexuality, which is an integral part of the personality of every human being. Sexuality is a relational experience with oneself, as well as an attraction and connection

with others. While sex is an aspect of sexuality, sexuality is more than sexual activity. Sexuality is also about intimacy and closeness and is as much about fantasies and dreams as it is about desire and erotic sexual pleasure. The PAHO/WHO definition also draws attention to the fact that sexuality encompasses feelings, values, and ideas as they relate to gender identity, sexual orientation, and gender roles and are intimately bound up with one's self-concept, self-esteem, and body image.

The term "sex" is usually used to describe the physical "sexual act," but it is also used to identify a person's designation at birth as male or female based on their anatomy (genitalia/reproductive organs) or biology (sex chromosomes and /or hormones). Although the term "gender" has traditionally been tied to reproductive anatomy (the person's genitals) and framed as a male-female/boy-girl binary, gender goes beyond the binary division of male and female and includes people who identify as transgender, gender fluid, and gender nonbinary. The term "sexual orientation" refers to a person's physical, emotional, or romantic attraction to another person. Although people's sexual orientation does not always appear in definable or fixed categories, traditional constructions of sexual orientation include attraction to the opposite sex (heterosexual), attraction to the same sex (lesbian (L) or gay (G)), attraction to both sexes (bisexual (B)), and attraction to neither.

Finally, the definition highlights that the expression of sexuality involves complex brain or biological processes that are influenced and mediated by wider social, historical, cultural, religious, and political structures. It is also part of our being whether we are partnered, single, sexually active, or celibate; is not limited by age, health status, or functional abilities; and is an aspect of one's being, which exists and changes across the life span.

3 Barriers to Discussing and Expressing Sexuality Within a Palliative Care Context

In a recent systematic review of the literature on patient-provider communication about sexual concerns with cancer patients, Reese et al. (2017) concluded that sexuality needs are unacknowledged and unaddressed for many people, particularly women. Similarly, in the few studies involving palliative care patients, a particular concern was the failure of practitioners to provide a context or space to discuss sexuality or acknowledge the loss and grief they were experiencing as a result of changes to their sexual selves and their intimate relationships (Taylor 2014a). Loss and grief has the potential to contribute to "total pain" and total distress.

Some research about why the topic of sexuality and intimacy remains a taboo in clinical practice settings has been published. Several studies indicate that lack of knowledge, confidence, and skill prevents practitioners from opening a discussion on what they perceive as a deeply personal aspect of life (Reese et al. 2017). Practitioners report feelings of personal discomfort, including fearing that they will offend the person, open up a "Pandora's box" or "can of worms," or transgress some medicolegal or cultural boundary, should they initiate a discussion on sexuality (Hordern and Street 2007; Dyer and das Nair 2013). Health practitioners also report a reluctance to discuss issues as they perceive it inappropriate due to the age, gender, culture, or religion of the person and wonder whether the person would consider sexuality as a legitimate topic for discussion (Dyer and das Nair 2013). The biomedical and pathophysiological approach to care that underpins the practice of some practitioners may result in the ill person being viewed in terms of "diagnosis" and symptom management, resulting in the conversation being "steered" away, albeit unconsciously, from issues of intimacy and relationships (Hordern and Street 2007). In keeping with this approach, practitioners may view the person as asexual or believe that they agree with the emphasis on the disease, are not concerned about sexual issues, have lost interest in that aspect of their life, or are too unwell to discuss sexual intimacy and relationship needs (Hordern and Street 2007; Dyer and das Nair 2013). This may be particularly true in the context of older age and palliative care.

Other factors that maintain the silence around sexuality include structural barriers,

such as: lack of time, lack of privacy within care settings, lack of clear care pathways, and perceiving sexuality issues to be beyond the person's scope of practice, requiring input from some other specialist or discipline (Hordern and Street 2007; Kotronoulas et al. 2009). These fears and concerns may be compounded if the person identifies as LGBT. Although studies that explore palliative care practitioners' responsiveness to the needs of LGBT people are sparse, what is available suggests that practitioners lack knowledge on LGBT issues, presume heterosexuality, and hold ambivalent attitudes toward LGBT people (Harding et al. 2012; Marie Curie 2016).

In many studies practitioners report waiting for the person to seek help. This passive stance, which assumes that patients will seek support and spontaneously open a discussion on their intimate relationships and sexuality, contrasts sharply with the proactive person-centered approach that underpins the philosophy of palliative care and has received attention in the literature with particular reference to suffering and total pain. Total pain as suffering is understood as encompassing physical, psychosocial, and existential distress or struggles, and addressing it remains the most important defining characteristic that distinguishes palliative care from other care provided to patients in hospital. The passive waiting stance of practitioners also ignores the possibility that many people may perceive sexuality as something that they should not openly discuss or indeed they may lack the confidence or skills to open a discussion. If the expression of sexuality is an intrinsic part of our humanity, then its inclusion within a person-centered approach to palliative care is needed.

4 Sexuality and Person-Centeredness

Understanding person-centeredness and holism invites a question on what it means to be human. In her early development of the modern hospice and palliative care movement as we know it, Cicely Saunders was introduced to the writings of Viktor Frankl's *Man's Search for Meaning* and subsequently referred to her copy as "dog-eared and marked almost to extinction" (Saunders 2006: 161). Though few of Frankl's works were translated into English at the time, in *Man's Search for Meaning*, he summarized his understanding of the person and being human (Frankl 1963). This was to have a strong influence on Saunders' theory underpinning palliative care and continues to the present. For Frankl, there are three dimensions to the human being: body (*soma*), mind (*psyche*), and a core, which is spirit (*noös*). These dimensions penetrate one another. The *soma*tic plane includes all things physical; the *psyche* plane is where cognition and emotions reside and so includes emotional states, moods, sensation of drives, instincts, desires, and passions. Also, the *psyche* plane includes intellectual talents, acquired behavior patterns, and social impressions.

The noetic dimension includes that which is uniquely human, the freedom to take a stance, such as against biopsychosocial determinants. This is where values and love reside. A person has a psychophysical overlay but is also spiritual so that "(b)y being centred around the existential personal core, being human is not only individualised but also integrated" (Frankl 2011:34). Wholeness implies the integration of the *soma*, *psyche*, and *noös*. Without spirit, wholeness does not exist. In this, Frankl makes a clear assertion to the proponents of holism (and therefore, palliative care) in healthcare. It is worth noting that Frankl did not agree with the English translation of *noös* to spirit because of the religious connotations. There is much that can and has been said about Frankl's contribution to the philosophy and principles of palliative care. Crucially and for our purposes here, as an integral part of the personality of every human being, sexuality finds expression through all three dimensions: *soma*, *psyche*, and *noös*. Failure to acknowledge this in an individual in the palliative care context implies failure to acknowledge the person and thus, deny their personhood. Understanding the impact of life-limiting illness and its treatment on sexuality is therefore a core aspect of palliative care.

5 Impact of Life-Limiting Illness and Its Treatment on Sexuality

The impact of life-limiting illness on sexuality is well documented within the literature. Numerous studies have been published, including systematic reviews of the research evidence and reviews of the impact of gynecological cancer (Abbott-Anderson and Kwekkeboom 2012; Gilbert et al. 2011), colorectal cancer (Traa et al. 2012), testicular cancer (Nazareth et al. 2001; Carpentier and Fortenberry 2010), penile cancer (Maddineni et al. 2009), vulvar malignancy (Aerts et al. 2012), breast cancer (Gilbert et al. 2010), and prostate cancer (Tucker et al. 2016; Paterson et al. 2015). All of these highlight the impact of cancer on the physical, psychological, and social/relational aspects of sexuality across a range of ages and cultural groups. Although, for ease of presentation, the next section discusses the impact of cancer under three headings, the interrelationships between the physical, psychological, and relational aspects of sexuality as they relate to the wholeness of the person should not be overlooked (see Tables 1 and 2 for overviews of the effects reported within these reviews).

Table 1 Overview of findings from systematic reviews on impact of cancer on men

Men	Physical (Sexual response cycle)	Psychological (Emotional and cognitive responses that influence sexual response)	Relational aspect (Relationship with self and desire for intimacy with others)
Penile cancer Maddineni et al. (2009)	Reduced sexual desire Loss of orgasm Mild-moderate erectile dysfunction Reduced sexual satisfaction	Psychological distress and posttraumatic stress disorder	Not addressed in the review
Prostate cancer Tucker et al. (2016) and Pateerson et al. (2015)	Erectile dysfunction Diminished libido Decreased ability to ejaculate Change to penis shape and size	Feelings of loss and grief at diminishment as a man Guilt at not being able to function as a man Shame, embarrassment, anger	Difficulties relating to partner Doubting ability to sexually satisfy partner Distancing, withdrawal, and avoidance of sexual intimacy Reluctance to have sex in case PSA level would increase
Testicular cancer Nazareth et al. (2001) and Carpentier and Fortenberry (2010)	Ejaculatory dysfunction Erectile dysfunction Reduced or loos of orgasm Decreased sexual drive/ desire	Decrease sense of attractiveness Feel less masculine Desire to look “normal”	Decreased sexual intercourse Self-conscious about missing testicle
Colorectal cancer Traa et al. (2012)	Ejaculatory dysfunction Erectile dysfunction Orgasmic dysfunction Reduced sexual desire	Body image change due to stoma	Having radiotherapy and/or having a stoma predicted less sexual activity

Table 2 Overview of findings from systematic reviews on impact of cancer on women

Women	Physical	Psychological	Relational
Gynecological cancer Abbott-Anderson and Kwekkeboom (2012) and Gilbert et al. (2011)	Dyspareunia Vaginal dryness Vaginal atrophy Reduced vaginal size Difficulty becoming sexually aroused Decreased genital sensation, decreased genital swelling Difficulty or inability to achieve orgasm Decreased sexual satisfaction Postcoital bleeding Fatigue Menopausal symptoms	Altered body image Loss of femininity/ not feeling like a woman Feeling less attractive sexually Lack of feeling or emotion Psychological distress associated with infertility Decreased interest in sexual activity Decreased enjoyment Fear of transmitting cancer to partner Fear of pain with intercourse and fear of reoccurrence of cancer	Reduction in frequency of sexual activity Communication problems with partner and inability to discuss sexual concerns with partner Blaming the sexual relationship or partner for cancer Change in partners interest or loss of interest in sexuality activity Partners becoming emotionally distant Adverse impact on future intimate partner relationships
Vulvar Aerts et al. (2012)	Difficulty with arousal and orgasm Dyspareunia Fatigue	Moderate reduction in sexual desire Dissatisfied with sexual relations Reduced self-confidence Less acceptance of body Loss of self-confidence	Worsening of emotional relationship with their partner Improvement in relationships and an increase in emotional closeness with partner Fear that sexual activity would result in reoccurrence Fear of transmitting cancer to their partner
Breast cancer Gilbert et al. (2010)	Decrease in sexual interest/desire Decrease in sexual arousal Dyspareunia or coital pain Vaginal dryness Numbness if previously sensitive breast Difficulty achieving orgasm Fatigue	Negative body image Feeling sexually unattractive Loss of femininity/ feeling “half a woman” Depression/anxiety Grief at loss of breast Feeling “old”	Withdraw from their partner as feel unattractive Dislike being naked
Colorectal Cancer Traa et al. (2012)	Dyspareunia Vaginal dryness	Feelings of disgust at stoma	Worry about reaction of partner to the stoma Radiotherapy and having a stoma predicted less sexual activity

5.1 Physical Aspect of Sexuality

In relation to the physical aspect of sexuality, numerous studies highlight the impact of surgery, radiotherapy, and chemotherapy on the sexual response cycle. In all the reviews involving people diagnosed with cancer, experiences of decreased sexual desire, sexual arousal, sexual function, orgasm, as well as a decline in sexual activity and sexual satisfaction were reported. While the impact of the treatment is unique to each person, most of the sexual problems experienced resulted from damage to the anatomical or physical structure associated directly or indirectly

with sexual activity, including the autonomic nervous system, endocrine system, and vascular compromise of the genitals. For example, surgery may shorten the upper vagina in women or damage nerves or blood supply to the penis in men. Radiation therapy, particularly to the genital area in women, is associated with decreased vaginal elasticity, difficulty with genital sensations, vaginal atrophy, and vaginal stenosis (Gilbert et al. 2011), and studies involving men report temporary or permanent erectile dysfunction, irritation to the urethra causing pain during ejaculation and maturation, and infertility (Nazareth et al. 2001). In addition to loss of fertility in young women, chemically or surgically induced menopause is associated with difficulty with sexual desire and arousal, loss of pleasurable sexual sensations, vaginal dryness, and decreased intensity of orgasm. Men treated with androgen deprivation therapy report variable degrees of erectile dysfunction, loss of sexual dreams, and feminizing effects, such as hot flashes and an increase in breast tissue (Sountoulides and Rountos 2013). Many of the prescribed medications also impact on sexual function, which may be exacerbated within a palliative care context due to a combination of polypharmacy, multi-morbidity, and decline in health status.

Sex function and sexual behavior also depend on physical energy, mobility, and vitality. As diseases advance, symptoms such as dyspnea, pain, fatigue, and restricted mobility can make the physical expression of sexuality problematic. Studies involving people with a diagnosis of motor neuron disease (amyotrophic lateral sclerosis) highlight the impact of physical weakness, fatigue, and restricted mobility on sexuality (Taylor 2014a, b), with studies involving people with lung disease revealing how dyspnea and the fear of causing dyspnea can impact on sexual function (Lindau et al. 2011). In addition, neutropenia, which predisposes the person to infection, can make sexual contact inadvisable if the partner has an infection. Likewise, thrombocytopenia and the associated risk of bleeding make vigorous genital intercourse or anal intercourse inadvisable (Matzo et al. 2013).

5.2 Psychological Aspects of Sexuality

While the physical changes, such as decline in sexual desire, the frequency of sexual activity, orgasm, and sexual satisfaction, have received greater attention in the literature, several of the reviews highlighted how these effects extend beyond the mechanics of sexual function to impact on the emotional or psychological landscape of the person. The sociocultural discourse that surrounds the body can also have a profound impact on the way the person interprets and gives meaning to the changes experienced. Consequently, disease and treatment can also inflict "invisible assaults" (Gilbert et al. 2011:54) that impact on intimacy and sexual expression.

Altered body image appears to be one of the most challenging issues facing patients. Body image is a product of perceptions, thoughts, and feelings about body size, appearance, attractiveness, competence, and function. Although highly subjective, negative perceptions of body image have been reported in many studies involving men and women. Following surgery, people are often left with mutilating scars or the absence of a body part that was not only an expression of gender, sexuality, and sensuality but an important part of the ideal self and sexual self-concept and expression. The problems reported included dissatisfaction with appearance, perceived loss of body integrity, reluctance to look at oneself naked, feeling less sexually attractive, self-consciousness, and embarrassment about appearance (Abbott-Anderson and Kwekkeboom 2012; Gilbert et al. 2011; Traa et al. 2012; Maddineni et al. 2009; Aerts et al. 2012; Gilbert et al. 2010). The construction and linking of certain body parts with ideals of femininity and masculinity can also have a significant impact. Cancer in organs, such as breast, uterine, or vulva, that have traditionally been constructed as symbols of motherhood and femininity can seriously impact women's sense of identity and well-being. While some women do not report negative changes, the majority of evidence indicates that women who have breast or gynecological cancers experience a range of feelings including decreased feelings of sexual

attractiveness, fear, and insecurity about ability to perform sexually as well as feeling a loss of femininity and "womanliness." In Gilbert et al.'s (2010) review, women who had a mastectomy reported greater body image and sexual attractiveness issues than those who received breast conserving surgery or reconstruction. Similarly, for men psychological distress can occur through a reduced sense of masculinity as a result of cancers that effect testis and penis, all aspects of the body that are imbued with symbolism and social meaning that is highly gendered (Maddineni et al. 2009). A pervasive theme within Tucker et al.'s (2016) meta-synthesis of studies of men following prostate cancer was one of loss and grief, with men reporting a deep sense of being diminished as a man and as a lover because of the treatment.

Cancer does not have to involve organs associated with sexual function to impact on sexual self-esteem and sexual self-concept. Although head and neck cancer does not impact on sexual function, studies indicate that the facial and neck disfigurement associated with these cancers can have a particular negative impact on body image and intimacy (Low et al. 2009). In Traa et al.'s (2012:23) review on colorectal cancer and sexuality, having a stoma was a strong predictor of sexual and intimacy problems, with those who "could not reconcile their own experience of disgust or the potential reaction of the partner to their ostomy" choosing to avoid sexual activity altogether.

5.3 Relational Aspect of Sexuality

Even though there is a distinct lack of research from a relational perspective, what is available suggests mixed outcomes. In some studies participants reported that the burden of disease and treatment negatively impacted on their intimate relationship. Some men and women reported being overwhelmed with worry about their partner's reactions to their body changes, with others reporting a decrease in their partner's sexual interest and emotional intimacy, which they perceived as a negative reaction to their body changes (Abbott-Anderson and Kwekkeboom 2012). Research also suggested that some men and women were so fearful of disappointing their partner sexually that they withdrew and distanced themselves as a protective mechanism (Abbott-Anderson and Kwekkeboom 2012; Tucker et al. 2016). Others avoided intimacy in response to fear of pain and fear that the cancer would return (Abbott-Anderson and Kwekkeboom 2012). Some patients who had radiotherapy particularly to the sexual organs or had cancer in organs associated with sexual function reported fearing that they would damage their partner through intimate sexual contact or feared transmitting the cancer to their partner (Cort et al. 2004). However, others reported engaging in coital sex primarily to satisfy their partners, in case the patner sought sexual pleasure elsewhere (Gilbert et al. 2011; Abbott-Anderson and Kwekkeboom 2012).

Studies that have explored partners and spouses of the ill person suggest that intimacy and sexual contact may diminish for reasons other than the physical and psychological changes that the disease or treatment has on the ill person's body image, sexual desire, and function. For some partners, the shadow of impending death, their partner's failing body, and their partner's inability to respond to their touch were significant barriers to maintain a sexual relationships (Taylor 2014a, b). Similar to the ill person, partners may also have a number of fears and anxieties about initiating a sexual or intimate relationship. Partners may fear dislodging drains and tubes, fear hurting the person, fear that love making would sap the person's energy, and fear that the person might die during love making, while some may experience guilt about feeling desire when their partner was facing a life-limiting illness (Higgins 2012). As the disease progresses and the person becomes more dependent on the partner for care, traditional marital roles change for both individuals; consequently, the intimate and sexual aspect of the relationship may become marginalized as a result of exhaustion, or due to changes in role from intimate partner to career. A balance of cognitive abilities is also a critical element in the maintenance of healthy relationships, and loss of cognitive ability can result in profound changes to a couple's relationship (Wadham et al. 2016).

Partners of people with dementia also have another dilemma in wondering if they are taking advantage of their partner when initiating sex, particularly when it is difficult to determine if it is a consensual act (Wornell 2014).

A key factor associated with many of the relationships where intimacy and sexual relationships diminish is difficulty in communication and silence around sexuality. Indeed, some studies highlight how couples "self-silence" as a way of coping or as a strategy to "protectively buffer" the other person from their distress (Manne and Badr 2010). This self-silencing or guarded communication between the couple made revealing fears and anxieties more challenging, which was often compounded by a lack of information and support by health professionals.

However, for others, despite an overall negative impact of illness, physical intimacy and sexual relationships were ways to convey mutual commitment. Many patients and partners reported improved communication, understanding, and emotional closeness and intimacy with their partner. The quality of the relationship prior to the diagnosis was a strong predictor of whether the couple was able to reframe their sexual identities and successfully incorporate changes into their relationship (Gilbert et al. 2011). There was some evidence that couples who had a broad sexual repertoire prior to diagnosis, were open to exploring alternative sexual activities and those who had an open style of communication were able to renegotiate the meaning of being sexual within the relationship. These couples were more successful in resisting the socially conditioned view of sexuality as penetrative intercourse (Reese et al. 2010; Gilbert et al. 2011; Tucker et al. 2016) and apply what Reese et al. (2010) termed "flexible coping" to learn new ways to appreciate each other's bodies and enact sexual intimacy and pleasure within the relationship. Developing alternative way of sexual expression beyond the "coital imperative" not only buffered both men and women against feelings of failure, but it reaffirmed their relationship, intimacy and sexual self-concept.

While the aforementioned studies included some people who were nearing the end of life, research that has specifically explored sexuality in palliative care contexts clearly indicates that the expression of sexuality continues to be an important part of people's lives, even in the last weeks and days of life (Taylor 2014a, b; Lemieux et al. 2004). For people with advanced life-limiting illnesses and who have complex care needs, there are many barriers to the expression of intimacy and the spontaneity of sexual activity, such as symptoms (dyspnea, pain, fatigue, and limited mobility) and the technologies of care (breathing equipment, catheters, tubes, drains, IV lines, and hospital beds). Nevertheless studies involving patients with motor neuron disease and cancer and their partners poignantly remind us that despite living in the "shadows of impending death," the need to connect in an intimate way remains a significant aspect of some couples' relationships (Taylor 2014a, b; Lemieux et al. 2004). Partners highlighted that despite the pain they experience as they live and cope with the impact of disease on their relationship, physical intimacy was a way to maintain a sense of normalcy and affirm life and was a means of mutual support and renewing of affectional bonds. Although over time connecting was experienced less through erotic sexual relationships and more through kissing, hand holding, and touching, several partners described a pattern of "physical reaching out" or not letting the spouse pass away without being touched in a tender or intimate manner. Affectionate touching helped partners to stay physically close and maintain their deep emotional connection until the end.

6 Addressing Issues of Sexuality in Practice

While the evidence suggests that some men and women restructure and reframe their ideas of sexuality, successfully incorporate body changes into their relationships, and find new and creative ways to express themselves sexually, many others struggle with the physical, psychological, and relationship changes. To move beyond the "safe horizons of medical expertise" (Horden and Streeet 2007:56) and venture into the hazards of a

conversation about love, relationships, loss, sex, and bodies requires the practitioner to view intimacy and sexual expression as a core aspect of identity and relationships and integral to personhood, irrespective of the stage of illness or context of care. In view of the fact that few people will be confident enough to raise their concerns with a member of the healthcare team, practitioners need to proactively legitimize sexuality as an aspect of care and convey a message early in their encounters that sexuality is a permissible subject to talk about. A necessary first step is the inclusion of sexuality as a normal part of care, which may start with a private, one-to-one conversation between the practitioner and the person around the impact of the illness on their lives, relationships, and intimacy needs. An important aspect of this process is to acknowledge that the person may be uncomfortable talking or answering questions about intimacy and relationships. The person will also need to be reassured that there is no pressure on them to answer questions; they may close the door on any line of exploration and are free to return to discuss issues at any time into the future. The use of reflective open-ended questions that allows for freedom of response is far less threatening than closed questions, which limit the person's range of responses and may imply judgments.

Should the person choose to talk, the practitioner's role is about facilitating the person to tell their story, grieve their loss, and talk about their feelings around loss of intimacy and their altered body image. Central to enabling the person to tell their story is the ability to live on the edge of "not knowing," to tolerate the anxiety and feelings of discomfort that are generated, while at the same time creating a context for telling through: embodied listening, "natural curiosity," gentle prompting, reflecting, using emotionally supportive statements, and the asking of interesting questions. Practitioners must also listen for the unasked questions or the often subtle unspoken cues that people may give; for example, the turn of the head away from the wound site, the reluctance to look in the mirror, or the withdrawal from social interactions.

Exploring the meaning of the illness and its impact on the person and their relationships in a compassionate way is central to building the trust and connection necessary to discuss sexuality and intimacy. While the same skills that are used to discuss other issues in palliative care are transferable to this context (e.g., seeking clarification, reflecting back, paraphrasing, and facilitating sensemaking), the caring process needs to be anchored in the principles of "being with," "engaging with," and "caring with" the person. At this stage, listening and bearing witness to the person's story and the meaning they attach to their experience needs to take priority. Practitioners who intervene too soon with premature reassurance or advice may close down the discussion by communicating to the person that their concerns are not permissible to talk about.

For some people sexual intimacy may no longer be desirable or part of their lives, and this needs to be accepted and respected. However, others may want information on symptoms associated with their illness and how to alleviate some of the problems they are experiencing, such as dyspareunia, pain, etc. Providing information and educating the person about alternative positions, touch techniques, or simple suggestions, such as the use of a lubricating gel where vaginal dryness is an issue, can make a major difference to the person's quality of life (see Table 3 for some suggestions). People often need permission to seek new ways of achieving sexual pleasure, to develop a repertoire of the less traditional sexual activities, and to be reassured that there is no right way. It may be helpful to remind people that while some sexual behaviors, such as intercourse, may undergo disruption, other aspects of intimacy and sexual pleasure, such as body caressing, kissing, massaging, mutual pleasuring, and masturbating, need not change. Irrespective of what suggestion is made, eliciting the person's perspective and reaction to the suggestion is central to crafting a plan of care that takes account not only of the physical dimension of sexuality but incorporates the psychological, interpersonal, and relational dimensions.

The interpersonal or relational model of intimacy proposes that ongoing reciprocal disclosures and responses to disclosures between partners is important to the development of

Table 3 Strategies to minimize impact of symptoms on sexual expression

Symptom	Possible strategies to explore
Pain	Explore strategies that may help minimize pain, such as pillows to support limbs, lying side by side, sitting on a chair Timing or temporarily adjusting medication to increase pain control Build in strategies that might help reduce discomfort such as massage, warm shower, and relaxing music
Fatigue	Select a time when less fatigued (morning as opposed to end of day) Provide time to rest before and after sexual intimacy Choose positions to minimize exertion (e.g., side by side)
Dyspnea	Experiment with positions that facilitate increased oxygenation, e.g., sitting up/ raise head of bed Using supplementary oxygen or inhalers before and during sexual activity Taking time and using slower movement to reduce oxygen demand Have partner adopt a position that requires greater physical effort (e.g., going on top)
Nausea	Review antiemetic medication Review timing and triggers that may provoke nausea to see if there is a time when less nausea exists
Mobility restrictions	Review pain control Use position to minimize discomfort Experiment with pillows to support limbs, lying side by side, sitting on a chair
Sore mouth	Identify cause (candidiasis, mucositis, mouth ulcer, cracked lips, coated tongue) and treat Review medication as some may cause dry mouth Refer to dentist if related to dentures or teeth Oral care using a soft toothbrush, fluoride toothpaste and water, after each meal and at bedtime
Dyspareunia	Assess location and type of pain to identify cause, such as infection, vaginal dryness Review medication as some may reduce vaginal lubrication Advise on use of water soluble vaginal lubricants, esthetic gels, or vaginal estrogen creams (VOC); however VOV is contraindicated for women with hormone-positive tumors Consider advice to increase foreplay, massage, and use of vibrator Advise patient to adopt a position where they can control force and pressure of penetration to help reduce pain Even after the original cause is resolved, some women may have difficulty relaxing due to anticipatory pain which may require relaxation techniques If pain persist, explore other ways of mutual pleasuring that does not focus on vaginal penetration
Erectile dysfunction	Medication such as Viagra Advice on other strategies such as vacuum devices or penile injections, although research suggest that many men do not wish to use these devices Explore other ways of

relationship intimacy, with studies supporting the idea that individuals who disclose more of their concerns to their partners experience more relationship intimacy (Manne and Badr 2010). Therefore, engaging in a conversation with the person and their partner, either alone or as a dyad, is important. Those unaccustomed to discussing their sexual and intimacy needs may need help communicating about their individual needs, preferences, and fears. They may also need time and support to explore and understand why each partner may be reacting differently to their changed circumstances. The therapeutic and emancipating value of the couple talking frankly to each other about feelings and experiences should not be underestimated. Providing support to people to open a conversation with their partner may be all that is required to help them to acknowledge their abilities that still exist and explore new ways of expressing love, affection, and pleasure.

While maintaining closeness and intimacy is important in relationships, Cort et al. (2004) remind us that there are also times when couples may need to redefine boundaries and create distance, and couples may need permission to withdraw from their previous physical relationship. Taylor (2014a) also highlights the importance of practitioners being aware of their desire to fix things, as some relationships cannot be repaired., In this context it is important that the practitioner

supports the people to make sense of their experiences and validate feelings of remorse, anger, and loss. If practitioners enable couples to communicate with each other, irrespective of the degree of intimacy within the relationship, not only is there an opportunity to create parting gifts and memories, but there is also an opportunity for couples to discuss feelings and changes in the relationship and resolve any misunderstandings that may have occurred.

The addition of a healthcare practitioner as a third guest into the privacy of a couple's relationship has the potential to create tensions. While the partner may be welcoming and experience great relief from the burden of care responsibilities, practitioners need to be mindful that as they become more involved in the intimate physical and emotional care of the ill person, their involvement may exacerbate ambivalent feelings within the well partner. Their involvement may also accentuate the emotional distancing that may have or be developing between the couple. It is important therefore to be mindful that the role of the practitioner is to facilitate the couple to communicate with each other, and not be drawn into a system, where they become the medium through which couple's communicate.

In a palliative care context, meeting and supporting intimacy and sexuality are not the prerogative of any one discipline, and the person will choose with whom they are most comfortable discussing and disclosing sexuality issues. As no one person within the team will have all the knowledge and skills required to respond to every eventuality, a team approach is required. A team that is not afraid to discuss sexuality in an open and non-hierarchical manner among themselves is also more likely to create and support a culture where sexuality is included in a proactive manner within the horizons of palliative care practice. However, such a team approach is not without its challenges. While a multidisciplinary team brings a range of skills and expertise enabling complex problems to be addressed, there is also the risk that problems become reduced to discrete elements and aligned with a particular discipline. For example, difficulties in maintaining sexual intimacy become viewed only in physical terms and addressed by one discipline through the use technical rational interventions, such as drugs with little acknowledgment of this as a core aspect of identity and relationships, and personhood. Yet, it should be clear from the discussion so far that the impact of a life-limiting illness on sexuality is multidimensional with physical, psychological, relational, and existential dimensions that are interrelated difficult to separate out from one another and greater than the sum of the parts.

7 LGBT Identities

What is interesting about the vast majority of research on sexuality and life-limiting illness is that sexuality is positioned within a heteronormative understanding of sexuality, with the research tools and questions framing sexual expression in the context of vaginal-penis penetration. Consequently, the evidence around the impact of life-limiting illness on LGBT people's expression of sexuality is sparse. Yet there is a growing awareness that, due to oppressive and discriminatory social contexts, people who identify as LGBT engage in more risky lifestyle behaviors, such as smoking and alcohol use, which are associated with higher rates of cancer (Fredriksen-Goldsen et al. 2013). Gay men are also more likely to be exposed to the burden of HIV-related cancers and have higher-risk factors for the development of anal cancers (Quinn et al. 2015). People who identify as LGBT are also more likely to delay accessing healthcare and screening services for fear of discrimination and stigma by health practitioners (Harding et al. 2012). Transgender men and women who have not undergone surgical transition may also find it psychologically difficult to seek help or address health concerns associated with reproductive organs that do not match their current gender (World Health Organisation 2015).

Although the impact of life-limiting illness on the intimacy and sexual needs of people who identify as LGBT is largely under researched, the limited evidence available suggests that they have additional concerns and worries that palliative care practitioners need to understand.

Research into the end-of-life needs of LGBT people suggests that many fear disclosing their sexual orientation or transgender identity and do not feel safe to be "out" within palliative care services, for fear that practitioners will be indifferent or hostile to their sexual orientation or gender identity and directly or indirectly discriminate against them (Marie Curie 2016; Harding et al. 2012; Almack et al. 2010). LGBT people may also have a deep distrust of services and practitioners (e.g., pastoral care worker) who may be perceived as being associated with a religious or church ethos that casts same-sex relationships as deviant, immoral, and sinful. This distrust may result in the person not coming out to the health provider or returning to the "closet" because of the need to rely on church-based services at the end of life. In addition to fears around coming out, those who have a same-sex partner express fears around demonstrating affection toward their partner and worry about receiving negative reactions from staff and other patients and families using the service they attend. People who identify as transgender may fear practitioners undermining and devaluing their identities by calling them by their birth name or by using incorrect pronouns in conversation and documentation. They also have concerns about being supported to live out their lives in their preferred gender and are fearful that, should they be hospitalized or admitted to a palliative care unit, they will be forced to use gender-specific bathrooms or bedrooms that do not align with their preferred gender. Without practitioners being proactive and communicating respect for sexual diversity, people may be reluctant to disclose their sexual orientation or transgender identity. Services, organizations, and care professionals must challenge anti-LGBT bias both within themselves and their service and demonstrate inclusiveness by ensuring that their mission statements, policies, and practices are LGBT affirmative (see Table 4 for LGBT-affirmative practices). At an individual level, practitioners demonstrate respect and acceptance by avoiding heterosexual assumptions and language that privileges heterosexuality. Opening a conversation in a nonjudgmental way and asking about partners and the gender of partners are critical to supporting disclosure. While attitudes toward LGBT people are changing and most people are out to someone about their sexual orientation, there are still some people who identify as LGBT who have not disclosed their orientation or gender preference because of fear or shame. For this small minority being in a palliative care service and feeling acceptance may create a context for this disclosure. On the other hand some people may have no desire to tell and this needs to be respected. LGBT people who are not out to family and friends may fear being inadvertently "outed" by practitioners or be concerned that due to practitioners' lack of knowledge, they will be exposed to intrusive questioning or have to repeatedly come out and/or provide each staff member with education on LGBT issues (Cartwright et al. 2012). Thus, practitioners need to have a conversation with the person on confidentiality, sharing information, and recording information.

LGBT people also worry about a lack of recognition of their relationships and partners during visits, medical decisions and advanced care planning, and decision-making in relation to funeral (Almack et al. 2010; Cartwright et al. 2012). People who identify as transgender have concerns about their wishes being respected after their death; in particular, they may worry that they may not be dressed in keeping with their preferred gender and wishes or fear being buried by their family of origin under their birth name and gender. Engaging in a conversation on living wills, advance care planning, or power of attorney may help avoid or minimize distress and conflict as the person is actively dying and nearing end of life. Such documentation will enable practitioners to give due consideration to the person's wishes, and care preferences should conflict arise. Without this documentation same-sex partners may have limited or no rights, especially if the biological family does not accept the relationship and wishes to exclude the partner (Rawlings 2012).

When it comes to end-of-life care, the research evidence around the needs of LGBT people and their families is sparse; however, in the context of supporting LGBT families, an important aspect is about understanding their differing family structures and relationships. Many LGBT people may

Table 4 LGBT-affirmative practices

Policies and service planning	Service policies make clear statements of inclusiveness of LGBT people and zero tolerance of discriminatory practices by staff and by people who use services Definition of gender within the policies moves beyond the binary division of male and female to include transgender and gender fluid identities Service planning and development informed by research evidence on LGBT issues
Organizational culture	Services display signs that highlight inclusiveness of LGBT people Service and programs (including bereavement services) are developed that address the specific needs of LGBT people All staff act as advocates by challenging heterosexism, homophobia, biphobia, and transphobia within the organization, irrespective of the source
Professional practice and interpersonal communication	Professionals acknowledge the person's sexual orientation and gender identity and promote safe and supportive relationships that are respectful of LGBT identities Care, treatment models, and structural design of services accommodate the realities of the differences between male, female, and transgender people Professionals work within a minority stress framework and recognize the different life experiences of LGBT people, their fears, and challenges in accessing support and being open about LGBT identities Language used is inclusive and affirming of LGBT relationships and reflects the individual's preference and family of choice Documentation and literature are inclusive of LGBT identities and avoids gender stereotyping and heterosexual norms Professionals interrogate their own stereotypes and language and have the confidence to challenge gender stereotyping and language within the team that is exploitative or harmful
Education and research	Professionals are informed and educated on LGBT issues, including LGBT issues as they relate to palliative care A process to address staff attitudes and practices that may be a barrier to LGBT-affirmative care is available Research into LGBT identities and palliative care is ongoing, including the impact of various models of care on outcomes for LGBT people and their families

Adapted from Higgins and Gill (2017)

have experienced rejection when they revealed to parents and siblings their sexual orientation or desire to transition, and consequently, they may be estranged from their biological family or family of origin. As a result of rejection within the biological family, many older LGBT relationships tend to be more friend-based, rather than family-based, and could include current and previous partners, biological or adopted children from relationships, and members of the wider LGBT community. For some LGBT people, the end of life is a time of reconciliation or reunions with estranged family. While some LGBT people may have no desire for a reunion, for others, irrespective of past hurts, reconnecting with, and being accepted by, family continues to be a priority. Practitioners need to be very sensitive and aware of the complex dynamics that such reunions can create, whether they are initiated by the person concerned or by a member of the family that is estranged. Such reunions may magnify the person's feelings of grief and loss, as some families may initiate reconciliation with the person in a way that denies the existence of the same-sex partner/spouse or family of choice (Harding et al. 2012).

8 Sexuality, Sexual Abuse, and Trauma

Sexuality for many is a source of pleasure, comfort, affirmation, connection, and identity; however, for others, sexuality is a site of pain, exploitation, violence, and trauma. Despite

evidence suggesting that sexual abuse (childhood sexual abuse (CSA)/rape/sexual violence (SV)) continues to be a feature of life, with high rates of men and women experiencing some form of sexual abuse in their life, the subject of sexual abuse is relatively nonexistent within the palliative care literature, except for a retrospective review of its prevalence within a palliative care audit (MacPherson 2009) and a paper involving a case study about a woman with a history of CSA and her family (Wygant et al. 2014).

Sexual violence has a lasting impact on a person's emotional, psychological, and social well-being and their quality of life. Evidence suggests that people who have been sexually abused experience low self-esteem, decreased self-worth, shame, stigma, and powerlessness; they have difficulty forming relationships, trusting people in intimate and sexual relationships, and maintaining sexual boundaries. Survivors of abuse frequently develop negative attitudes toward their own sexuality and either avoid all sexual contact or unconsciously enact aspects of early sexual abuse in subsequent sexual relationships. There is also evidence that people who have experienced sexual abuse in childhood are frequently left vulnerable to sexual re-victimization in adulthood. Although SV is both under-reported and under-acknowledged, high rates of sexual trauma have been reported among people who experienced depression, anxiety, self-harm, posttraumatic stress disorder (PTSD), personality disorders, eating disorders, and alcohol problems (Chen et al. 2010). For many these experiences may never have been disclosed because of stigma, self-hatred, shame, self-blame, and a fear that nobody would believe them.

In a paper exploring the intersectionality of terminal illness and unresolved PTSD, Feldman et al. (2014) argue that a diagnosis of a life-limiting illness, such as cancer, and healthcare encounters involving intimate physical examinations can mimic an original trauma, such as CSA. These events can reactivate memories of past CSA or rape, retraumatize the person, or even cause delayed-onset PTSD. As a result, the person may begin to experience hallucination-like flashbacks, intrusive trauma memories, nightmares, difficulty sleeping, dissociation, and hypervigilance with an exaggerated startle response (Feldman et al. 2014). As part of the dying process and preparation for dying, many people conduct life reviews, which may also trigger distress as the person revisits traumatic memories and periods of time.

As the illness advances and the physical body deteriorates, the person's capacity to manage their bodily functions lessens. For people who have experienced sexual trauma, having people violate social norms and conventions around touch, especially around touch of genital areas, can be profoundly distressing for the person, intensifying the suffering associated with the loss of function. In addition, dehumanizing touch and physical contact that treats the person as an "object" of care may trigger intense emotions, such as anger, panic, suspicion, and distrust of authority figures, or lead to the person withdrawing emotionally. Not only does this add to the person's psychological and existential distress, but it can lead to difficult, confrontational, or resistant styles of communication with the MDT team. Practitioners may also experience strong emotional reactions that may hamper the development of a therapeutic relationship, such as anger at the person's behavior or guilt over feeling responsible for the distress. If practitioners do not understand that the behaviors and emotions they are seeing in the patient are protective mechanisms, there is the potential that they label the person as uncooperative or aggressive and respond by avoiding or minimizing contact, thus creating a vicious cycle of avoidance and escalating hostility (Feldman et al. 2014).

While retraumatization can be unintentional, in a trauma-informed palliative care service, all staff (clinical and nonclinical) are mindful of the prevalence of sexual trauma in society and sensitive to the need to constantly work with the person's agenda, promote maximum control over decisions, and have a heightened sensitivity to the potential impact of procedures and touch on the person. They are also mindful of how the gender of the practitioner, power differentials within the relationship, and infantilizing interactions can impact the person.

The recall of sexual abuse can have a significant impact on the person, exacerbate physical symptoms, including pain, overwhelm them with distress close to the end of life, and have a negative impact on the quality of their death. While it is important to acknowledge and validate the significance of the abuse, and create a safe and non-judgmental space where the person feels safe to discuss their experience, both the person's wishes and the stage of the dying process will strongly influence the focus of care. For some people the time available is so limited that to engage in long-term therapeutic interventions is not possible; therefore, the focus of the care is on reducing the person's distress, containing emotions, and creating an environment where they feel safe, validated, and supported. Exploring with the person what coping strategies they found useful in the past may help them to identify their self-comforting skills and reactivate their strengths.

The family context and dynamics can also be highly challenging for practitioners for the following reasons: the abuser may have come from within the family circle or close family network; more than one family member may have been the victim of abuse; the person may have withdrawn from the family as a protective mechanism; the person may not have revealed their sexual abuse experience to the family and may not wish to do so; or the person may have revealed the abuse and was not believed. Therefore, responding to the needs of the person who has experienced sexual trauma whether in childhood or as an adult and the needs of the family requires a multidisciplinary approach, with input from clinicians who have had prior experience of working with trauma survivors and their families.

9 Sexuality and Sexual Disinhibition

Another aspect of sexuality and sexual behavior that has received limited attention in the palliative care literature is the area of sexual disinhibition. Yet it has the potential to cause immense distress to the person and disrupt relationships between the person, and partner, family, and the MDT. Sexualized behaviors and sexual disinhibition may also cause a conflict between the practitioner's ethical and legal responsibilities., Hindering sexual expression may be seen as a violation of the patient's autonomy, whereas failure to prevent sexual disinhibition or sexually inappropriate behaviors can place the patient and others at risk of mental and physical trauma.

As stated earlier in the chapter, the expression of sexuality involves complex brain functions that are influenced and mediated by psychological, cultural, and environmental factors. Altered sexual expression, in the form of sexual disinhibition, can result from damage to certain areas of the brain. Four brain areas or systems are thought to be implicated in the neurobiology of sexually disinhibited behavior, namely: the frontal lobes, the temporal limbic system, the striatum, and the hypothalamus. The frontal lobe of the brain is thought to be important for judgment, impulse control, and the regulation of insight and feedback regarding socially appropriate behaviors, including what might be called "sexual manners" (Higgins et al. 2004). Tumors of the frontal lobes are thought to remove the moral-ethical restraints that control our behavior resulting in decreased impulse inhibition. This may lead to indiscriminate sexual behavior, such as improper sexual remarks or gestures, and other sexual behaviors that may be considered "antisocial" or "inappropriate" to the time, person, or location, such as masturbation in public.

Similarly, dementia, although typically associated with sexual apathy, decline in sexual interest, and the loss of sexual relationships, may be accompanied by sexual disinhibition or "hypersexuality," with studies estimating that between 7 and 25% of patients with dementia exhibit some type of "inappropriate sexual behavior" (Higgins et al. 2004). Black et al. (2005, 156) divide sexually inappropriate behavior in dementia into three groups:

- Sex talk: this is the most common form and involves making sexually suggestive remarks or using foul sexual language that is not in keeping with the patient's premorbid personality.

- Sexual acts: these include acts of touching or grabbing the breasts, buttocks, and genitals of others, exposing genital areas, or masturbating in public areas.
- Implied sexual acts: these include openly reading pornographic material or requesting unnecessary genital care.

Addressing sexual disinhibition requires a team approach where there is an openness to acknowledge the distress and challenges for all concerned, including the person and family members. Exploring and understanding the reasons for, and all possible precursors to, the behavior is the first step in developing a person-centered plan that upholds the dignity and rights of all involved. This includes a systematic assessment of the person's cognitive/health status, their previous personality and sexual behavior, and their response to stress and the environment, including the behavior of staff and other people which might have influenced the person's behavior. Usually the sexual behavior is not confined to one particular relationship and is directed to a number of people. Behavior of people with cognitive impairment may be misconstrued as sexual when in fact it may have an entirely different meaning or purpose. The behavior may be a result of disruption to the neural pathways related to sex drive or may be due to cognitive impairment, where the person has forgotten sexual manners or has confused a person with a much loved partner. Therefore it may be a case of mistaken identity or misinterpretation of environmental cues. In other situations, the behavior may be simply the need for human contact and is the "acting out" of a strong need for intimacy and touch that has been sexualized. Practitioners, therefore, need to be guided by the principle that all human behavior is a form of communication and purposeful; thus key questions to consider is what is the purpose of the behavior and what is the person trying to communicate?

The typical educational, counseling, and behavioral approaches taken to solving these problems with people who do not have a cognitive impairment are not very useful when caring for people who have a continued deterioration in memory and learning ability. In many situations, what is required is a "low-key" approach toward reorientation and limit-setting that takes account of the person's need for human connection (Higgins et al. 2004). Within the literature the pharmacological model of treatment is sometimes advocated, when all possible environmental and psychological causes are assessed and treated. Although recommended, the lack of empirical evidence to support the effectiveness of drugs for sexual disinhibition, coupled with the side-effect profiles, poses professional and ethical challenges for practitioners.

Displays of sexual disinhibition can be very distressing for family members, who do not understand the reason for the behavior and may feel stigmatized, ashamed, and angry or may fear that their relative will be victimized or isolated by practitioners. Family members may also be concerned about the involvement of social or child protection services should the person have contact with children and young people. In an effort to protect the person, especially if they are being cared for at home, family members may restrict people visiting or confine the person to the house, thus isolating the person further (Black et al. 2005). Therefore, family members will need time and space to discuss their concerns, fears, and distress. They will also need education on the possible reasons for the behavior as well as reassurance that staff have seen similar behaviors before and are there to help and support. Involving family members in discussion and inviting them to participate with staff in problem solving are an effective way to build constructive and supportive relationships. This is especially important for partners/spouses who may be too embarrassed to tell practitioners that they are experiencing increasing demands for sex from the person with the cognitive impairment. Without practitioners creating a safe accepting space, and sensitively enquiring about relationships and relationship changes, partners/spouses may be left to cope alone, and feel sexual compliance is their spousal duty or fear that refusing may provoke anger or distress in the person.

10 Disenfranchised Grief and Loss of a Sexual Partner

The loss of a loved one through death is a universal human experience and is considered to be one of the most stressful life events that a human being can encounter. Although the experience of loss is universal, the experience of grief can vary enormously depending on the relationship with the deceased. The literature on grief is rich with information on how to navigate the intense emotional distress following the death of a spouse or partner; however, within this literature there is little reference to what Radosh and Simkin (2016) refer to as "sexual bereavement," the grief as a result of the loss of a sexual relationship. Published narratives and self-help books about the death of a spouse also reinforce this silence as they also fail to mention "sexual bereavement." One exception is Susan Wallbank's (2010) book "*The Empty Bed: Bereavement and the Loss of Love*," which breaks the conspiracy of silence and addresses, with sensitivity and insight, the distress of the loss of a partner with whom to sleep and make love and to physically hold. Within this book Wallbank recounts the stories of the pain of the bereaved person waking to the reality of their loss following vivid dreams of making love to their partner, the distress of being confronted with decisions around ceasing to continue with oral contraception or removing an intrauterine device, and the guilt and shame felt when the bereaved person experiences sexual feelings and desire for a sexual relationship. Despite this, there appears to be a lack of acknowledgment of the grief associated with the loss of a sexual partner by bereavement counselors, with participants in Radosh and Simkin's (2016) study reporting being too embarrassed to share this aspect of their grief experience with professionals. Consequently, practitioners, including bereavement counselors, need to create a context where this aspect of people's grief is spoken about, acknowledged, and validated.

The degree of distress and disenfranchised grief experienced by the person can be further increased if the person is in a same-sex relationship. Bereaved LGBT partners may be particularly vulnerable at this time, as research indicated that many LGBT people experience the pain of "silent mourning," often being deprived of the rituals of "communal sorrow" and other social/psychological supports that are present for heterosexual people. Although Bristowe et al.'s (2016) systematic review found that some LGBT people who had lost a partner were well supported by practitioners, others were not. Those who were in relationships that were not openly acknowledged or "hidden" from family, friends, work colleagues and practitioners were often left to cope and grieve alone. The fragility of biological family relationships or being estranged from the family of origin often meant that traditional sources of support and comfort were absent for some people. In some cases people's grief was exacerbated when they experienced overt exclusion by their partner's family or attended a bereavement support group where they experienced negative attitudes from people within the group.

As with any minority population, there is a need for sensitivity to the social and historical context of the lives of people who identify as LGBT when providing bereavement support. While, in many countries, legal changes have resulted in greater acknowledgment of same-sex relationships, practitioners, however, need to be mindful that many older people lived through a time when their identities were highly stigmatized or indeed illegal, and past experiences may inform their willingness to be open with practitioners. Consequently, practitioners need to be sensitive to the depth and nature of relationships, be mindful of the impact of a heteronormative culture on their assumptions about relationships, and ensure that literature on same-sex grief is openly available to people who use the service. In addition, for those who are out about their relationships, practitioners need to acknowledge the significance of the person's loss, not just as a friend but as a partner and lover, and demonstrate a willingness to develop the communicative space necessary to talk about their loss as well as providing appropriate bereavement support services. For some people this may mean a preference for attending a gay or lesbian bereavement counselor or attending services provided by gay and lesbian support groups.

11 Conclusion

Sexuality is an integral part of being human and being alive to the self that finds expression through body, mind, and spirit. Although sexuality is as unique to the person as their fingerprint, it is intimately bound up with the person's sense of identity, as well as their sense of self within relationships. Regardless of gender or sexual orientation, a life-limiting illness transforms every aspect of the person's life, including sexuality. Life-limiting illnesses can impact on sexuality in a manner that is all pervasive, permeating physical, psychological, relational, and existential dimensions of personhood.

For many people their expression of sexuality is so central to their life and is such a positive force that intimacy and sexual expression can preserve a sense of wholeness and "living well" in the face or shadow of death. For those within a couple relationship, the expression of sexuality can also embody emotional connection and comfort that is beyond language and penetrates the deepest part of their being. However, like a double-edged sword, for others sexuality it is a source of distress and loneliness. This distress may be connected to the loss of intimacy, relationships, and sexual contact that threatens the person sense of wholeness as they face the dying process. At the same time, painful experiences from the past and old traumas that have long been buried may reemerge. Unless the individual practitioner is mindful of sexuality and its complexity, and how the person's fears, embarrassment or self-stigma may impact on their willingness to discuss sexuality issues; "total pain" and suffering may be exacerbated. At the same time, without attention to their own value, judgments, and approach to care, they may desexualize and dehumanize the person adding to the distress experienced.

As person-centeredness or whole person care and "total pain/suffering" remains a defining characteristic that distinguishes palliative care from other care provided to patients in hospital, practitioners need to recognize the shared humanity that exists between themselves and the person, and connect with the person, not as a "patient" who is fighting for survival, but a living breathing sexual human being with a past, present, and future. By incorporating sexuality with the horizon of practice and opening an authentic communicative space that acknowledges the diversity of sexual expression, practitioners not only create an opportunity for the person to make sense of their distress and find meaning in their experience, but they also create opportunities for sexuality and sexual expression to be celebrate as a source of joy and affirmation in the living and dying process.

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Family-Focused Care Span

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_32

Abstract

A family-focused care approach in palliative care recognizes the fundamental role of families in contributing to the care of people with life-limiting conditions. It is essential that healthcare providers develop understanding of families' needs and the skills to collaborate effectively with families caring for people at the end of their lives. This chapter introduces the concept and components of family-focused palliative care. It continues with a discussion of what patients and families perceive to be the most important aspects of end-of-life care. This chapter provides information to assist healthcare providers who work with people with life-limiting conditions and their families in providing family-focused care and to identify gaps and challenges to providing such care.

1 Introduction

The increasing reliance on informal family caregivers ("carers") in today's healthcare environment mandates families to be actively involved in patient care and advocate for best practice. The Institute for Patient- and Family-Centered Care defines family-centered care as an approach to planning, delivering, and evaluating healthcare in the context of mutually beneficial partnerships among healthcare providers, patients, and families. It emphasizes collaboration with families who define their own membership and roles in care and decision-making (Johnson et al. 2008). The aim of this chapter is to increase palliative care healthcare providers' awareness of the needs of families to optimize their current and future well-being, including their bereavement outcomes.

After reading this chapter, you will be able to:

- Describe the components of family-focused care
- Discuss patient and family priorities for end-of-life care
- Identify opportunities to strengthen the provision of family-focused palliative care

2 Defining Family

The family is the basic unit of care, yet it comes in all shapes and sizes, compositions, and origins. Contemporary connotations of family extend beyond just people related to one another by blood or marriage. Divorce, same-sex partners, cohabitation, and

workforce globalization have ushered in a new era of family configurations that have superseded traditional nuclear family structures comprised of a husband, wife, and one or more children. Single parent families are increasing, and many children live with a stepparent or grandparent(s) at some point in their lives. In addition to traditionally termed extended family, close friends, companions, and others may all be considered to part of an individual's family. Family members may live in close proximity or at great geographic distances from one another, and as a result of changing work and previous life events, an increasing number of older people live alone. Global mobility and changing demographics mean that many family members may not be physically available to provide care and support in the context of a life-limiting illness and may have limited contact with one another. In this situation, neighbors and friends or distant relatives often step in to fill this void. As a result, who and what constitutes "family" has been evolving. While, some people continue to define family as the group of people they were born into (family of origin), others will define family as the group of close friends chosen to surround themselves with (family of choice) (Lawton et al. 2014). In this chapter, "family" is defined as whomever the patient describes or considers to be family (Torenholt et al. 2014) and/or who they identify as important and who influences their care and well-being (Wright 2007).

3 Family's Needs Throughout the Care Trajectory and Across Life Stages

The World Health Organisation (2018) has long championed the importance of assessing and addressing families' palliative care needs, as reflected in their current definition. This definition centers palliative care on providing relief from pain and distress, normalizing the dying process, providing holistic support using a team approach, and facilitating good quality of life and coping at all stages of the illness for the patient and their family (World Health Organisation 2018). By positioning families alongside patients, this definition highlights the needs of families as recipients of care, particularly in the provision of adjusting, coping, and bereavement support.

A progressive life-limiting illness diagnosis is a life-changing experience, for not only patients but also their families. This type of diagnosis is associated with significant physical, emotional, and social support needs as well as access to timely clinical support and information. Most patients will call upon various family members, often a partner/spouse, to assist them with their decision-making in relationship to treatment preferences, advance care planning, and legal and financial issues. The quality of life of patients with palliative care needs and their families depends on various factors that can change over the course of the illness. These fluctuating needs often occur during the transitions from curative to comfort care as the disease progresses. With each transition, families will have different information needs, and if they are active carers, their contributions to various activities of daily living is likely to increase as the patient's disease progresses, and they become less able to maintain their activity. The care and support that families require may differ according to their varied life stages and relationship to the patient. In some cases, patients are also carers for offspring, siblings, or older parents, which have implications for the family as the patients' own care needs increase. There are also some different implications for the individual and their family depending on whether the patient or carer is of working age (under 65 years old), has young children and/or teenagers, or is post-working age (over 65 years) and living with in-house or more distant family support.

3.1 Diagnosis Affects Families' Needs

Both malignant and nonmalignant diseases pose significant burden at the end of life. Some diseases, especially neurodegenerative conditions and/or primary or metastatic brain cancer, often cause more physical impairment and cognitive/personality changes. These devastating personality changes and disability also affect carers' capacity to manage (Pace et al. 2009; Arber et al. 2010; Gofton et al. 2012) and indicate significant support needs for carers.

Age can play a role in determining the type and level of needs of both patients and their families. For example, younger patients (≤70 years) generally have higher levels of overall unmet needs (McIllmurray et al. 2001), yet middle-aged patients (31–60 years) consistently display greater unmet needs than those age 70 years or older (Sanson-Fisher et al. 2000). These different needs have been attributed to cancer and its treatment having more of a psychosocial impact on younger people and the increased acceptability of younger people disclosing needs as compared to older patients (Sanson-Fisher et al. 2000).

3.2 Needs of Younger Working Age Families

Faced with a premature death during working age (ages 24–65 years) has its own inherent challenges related to life-stage commitments such as family, work, and financial responsibilities. A life-limiting illness has a profound impact on the family life of patients, their partners, and children. Family dynamics are often changed and normal life interrupted, which can be particularly burdensome for any dependent children, as their reality and day-to-day life often changes as the illness of their parent progresses. Families of working age patients have a range of needs at different time points across the illness trajectory (Kochovska et al. 2017), including:

Supportive care needs, which vary according to disease (malignant or nonmalignant) but typically for working-aged families, include assistance to effectively manage the patient's pain and other symptoms and dealing with feelings of loss (anticipatory grief), uncertainty, and fear of the patient and/or children suffering (Kochovska et al. 2017). The partner of working-aged person facing a premature death often have increased input into clinical, household, and financial decision-making and difficulty juggling multiple roles such as parenting, household duties, and family finances. This is all in addition to navigating the healthcare system, transporting the patient to/from hospital and/or appointments, maintaining family schedules, and minimizing the impact on other family members.

Information needs, for families are also significant and include diagnostic and disease information, financial and legal information, as well as end-of-life and spirituality information (Kochovska et al. 2017). This information is required at different stages in the illness trajectory, and healthcare providers should be both aware and prepared to meet families' specific information needs in a timely manner. *Disease and prognosis information* is most often sought at the initiation of treatment and transition from curative to palliative care but least wanted as death approaches. *Financial and legal information* from the time of diagnosis can help to manage anticipated reduced employment capacity for both the patient and carer. Financial advice is least wanted when completing treatment and when returning home from hospital. The need for financial/legal information related to death notification requirements and funerals is greatest immediately after the patient's death. *End-of-life and spirituality information* is most desired during a final hospital or hospice admission and least desired at the commencement of treatment.

Carers needs are significant, as most will need access to support services (such as respite and day care) and practical support (e.g., picking up children, preparing a meal, and other household tasks), especially in rural and remote areas (Kochovska et al. 2017). Balancing these competing demands while trying to maintain normality (especially when children are involved) is challenging, particularly for employed carers and/or those with young children.

Anticipatory grief and bereavement needs are experienced by patients, partners/spouses, and their children at various junctures and require an individualized and empathetic response that recognizes grief as normal but provides timely access to professional help for the minority who need it. Spending quality time with the deteriorating and/or dying person is important and can positively influence bereavement outcomes (Kochovska et al. 2017).

3.3 Maintaining Normality and Balancing Multiple Roles

For both the parent living with the terminal illness and their partner/spouse, maintaining normality is of paramount importance, as it acts as a coping mechanism that limits the adverse effects of the parent's illness on their children. Maintaining this delicate balance is challenging, and most families need practical advice about how best to describe in simple terms the patient's diagnosis, prognosis, and impending death; cope with their partner's/spouse's deterioration; and access practical help and resources, so as to minimize the impact on their children (Kochovska et al. 2017).

The interruption of family dynamics and the need to be able to maintain children's normal routines while managing escalating care demands is a frightening and stressful experience for many families (Kochovska et al. 2017). This is primarily because it requires the healthy parent to assume new roles within the family, deal with uncertainty and feelings of loneliness, balance everyone's needs (including the children, the patient, and themselves), and support their children. Access to specialist palliative care can mitigate many of these challenges and contribute to positive short-term and long-term effects, especially for carers of cancer patients (Kochovska et al. 2017).

Although dealing with a life-limiting illness is a demanding and stressful experience for everyone, there are some positive aspects for both parents with terminal illness and their children, which include strengthening the relationship and shifting perspectives on valuing the family and the important things in life (Kochovska et al. 2017). It is particularly important that children and dying parents remain connected during the terminal illness, and clinical care and support should be tailored to facilitate that (Kochovska et al. 2017).

3.4 Balancing Being Honest with Children, but Not Overburdening Them

Children of parents diagnosed with advanced cancer and/or who are dying need access to timely, age-appropriate information about their parents' disease that is sensitively communicated by people they trust both within and outside of the family (Kochovska et al. 2017). Children with parents living with a life-limiting illness (e.g., advanced cancer) display significant distress but also remarkable awareness and understanding of their parent's illness. While children of dying parents need support, they should not be protected from the truth of the situation, but rather, given accurate information as sensitively as possible (Kochovska et al. 2017).

Adopting a transparent approach helped children to make sense of their parent's impending death in their own way and grow through the experience. They also need an opportunity to spend quality time alone with their parent. While some children may welcome the opportunity to help care for a dying parent, they also need to have opportunities to engage in "normal" activities outside of their caring role both with their family and in contexts where they can temporarily "forget" their home situation (Kochovska et al. 2017).

Where children bear a significant caring responsibility, this may require respite care for the dying parent while the child takes a break. Similarly, adolescents and young adults are often required to assume more household responsibilities and have decreased social activity outside the home (Beale et al. 2004; Kennedy and Lloyd-Williams 2009) which can contribute to increased stress (Huizinga et al. 2003). Older children often take on more practical responsibilities, including picking up their younger siblings from school (Phillips and Lewis 2015). Adolescents also report feeling alone and alienated as family priorities shift and family roles are renegotiated within the family unit (Phillips 2015) and rely on routines to maintain a semblance of normality (Dehlin and Reg 2009). For adolescents, self-management and managing emotions through talking, thinking positively, and creating distractions and social support are also important (Phillips and Lewis 2015). Most adolescents try to maintain a positive attitude and facilitate communication within the family (Phillips and Lewis 2015), viewing the experience as

something that helps them mature and change their way of thinking about life, and reassess their values and relationship with other people (Dehlin and Reg 2009).

There are a growing number of adolescent and young adult carers, so considering their needs is crucial as they often have significantly poor quality of physical health (Hanly et al. 2015) and could be considered to be doubly disadvantaged because their carer role impacts on their educational opportunities and future earning capacity. Australian statistics show that the premature death of a parent can have a detrimental effect on the future wealth and employment of their children as adults (Australian Bureau of Statistics 2010).

4 Defining Family-Focused Care

A family-focused care approach recognizes the fundamental role of families and includes the following core concepts, namely, dignity and respect, information sharing, participation, and collaboration (Johnson et al. 2008). This method of care delivery supports the family in their carer roles and includes them in treatment decision-making. It positions the family as key members of the care team and privileges collaboration as a vehicle that increases trust and promotes more open communication between patients, families, and healthcare providers. When individuals perceive open communication, they are more likely to perceive fair processes, cope, and feel less frustration and confusion. Through collaboration, care provided to patients and families can be tailored to their individual needs, thereby demonstrating recognition of the uniqueness of each patient and family. Furthermore, the family is a valuable source of support for a patient and information on behavior and coping strategies of the individual (Bamm and Rosenbaum 2008). Preferences for communication, degree of involvement in caregiving activities, information provision and education, visiting, and counseling inform the way in which the family is supported and cared for by the palliative care team (Wright 2007).

5 The Most Important Elements of End-of-Life Care from the Family Perspective

Recent work undertaken by Virdun and colleagues (2015, 2017) synthesized 24 studies that described self-reported needs of palliative care patients and families in relation to end-of-life care in the hospital setting, with nearly all of these studies ($n = 21$) including a focus on family participants. This work included a systematic review of the quantitative studies, which included 3117 family members (Virdun et al. 2015) and a meta-synthesis of qualitative studies which examined 278 interview quotes from participating family members ($n = 672$) detailing what families considered the most important aspects of end-of-life care in hospital (Virdun et al. 2017). The 11 resultant themes of these studies structure the remaining sections of this chapter.

5.1 Expert Care (Good Physical Care, Symptom Management, and Integrated Care)

Family-focused care for the domain of expert care centers around concepts of excellent nursing care, excellent symptom assessment and management, holistic care delivered from a multidisciplinary team integrated in their care planning and delivery, and the need for healthcare providers to be knowledgeable about the patient they are caring for. While patients perceived many of these aspects of care provision as highly important for optimal end-of-life care, families specifically noted the importance of the following key aspects of care provision to enable quality end-of-life care:

- Careful attention to the personal hygiene and care needs of the patient both when family are and are not present in the hospital
- Excellence in core nursing as well as the ability to manage specialist patient requirements (e.g., colostomy care)
- Ensuring rapid and comprehensive assessment and management of symptoms with a particular

focus on staff prioritizing the patient's description of their symptoms
- The specific need to manage pain and agitation well
- Multidisciplinary care to support the patient physically, emotionally, and/or spiritually
- Integrated care inclusive of effective discharge planning and ensuring the patient could die in their location of choice
- That healthcare providers were knowledgeable about the specific condition of the patient and that it was clear who was in charge of care (Virdun et al. 2015, 2017)

5.2 Effective Communication and Shared Decision-Making

Family-focused care requires healthcare providers to have effective communication skills to be able to engage multiple members in different aspects of care. The ability to interview or converse with family members together is important to understanding interactions between family members (Denham 2016). Healthcare providers must ensure families understand the medical issues and clarify any technical language used. Plain language materials and providing opportunities for discussion and questions are recommended to address health literacy needs (Wittenberg et al. 2017). Effective communication is necessary to ensure that the patient, family, and healthcare providers have a shared understanding, which is dependent upon the compassionate delivery of understandable and honest information (Virdun et al. 2015, 2017). Being provided with the necessary information is important for families involved in end-of-life decision-making, because they want to understand the medical complexity and the emotional and financial implications of any decisions and be provided with sufficient and timely information to make the decisions that best reflect the patient's preferences (Virdun et al. 2015, 2017). Being actively involved in day-to-day care planning and having regular planned discussions with the healthcare team, including discussions with physicians, are considered by families to be essential for effective communication and shared decision-making (Virdun et al. 2015, 2017).

Families are equally responsible to provide accurate information to healthcare providers including medical and treatment history, patient preferences, and subtle changes in the patient that the provider may not see. Families, likewise, have an important and active role within the healthcare team as they have experience, insights, and knowledge about the patient that can contribute to their overall health and well-being (Johnson et al. 2008). Further, the family, as the unit of care, provides information about group values, supportive interactions, decision-making, relationships, caregiving, and health habits.

The delivery, content, and timing of end-of-life prognostic communication has a significant impact on the quality of life of spousal carers of patients with palliative care needs who have dependent children (Park et al. 2015). Families' preferences for honest and clear information communicated using nonprofessional language and with compassion help to foster a shared understanding of the clinical situation. The provision of adequate information throughout the admission helps support decision-making, decreases the families stress, and minimize surprises (Virdun et al. 2015, 2017).

An important outcome of family-focused care is patient and family coping, which can be facilitated by incorporating elements of family-focused care in practice (Wright 2007), such as:

- **Information Sharing**. The healthcare team communicate comprehensive, accurate, and balanced information for families in a timely, affirming, and useful manner to enable effective participation in both care planning and care provision.
- **Collaboration**. Valued collaboration with families in relation to policy and program design, implementation, and evaluation, the design of health facilities, and professional education and planning and delivery of care.
- **Participation**. Valued and supported participation in care planning and provision, inclusive of decision-making, to the level of the family member's choosing.

DiGiacomo et al. (2013) reported an example of how communication gaps can lead to protracted grief in a qualitative study of recently widowed older women. In the following excerpt, one woman described missed opportunities for healthcare providers to communicate with her regarding her husband's prognosis (refer Box 1). This is further confirmed by data reported by Virdun et al. (2015) where families noted the importance of being able to receive straightforward information about tests, treatments, and prognoses, as well as stating that being sheltered from honest information did not contribute to quality end-of-life care.

Box 1: Unintended Consequence of Ineffective Communication: Julie's Story

Family carer quote:

I definitely would have liked a realistic view. If somebody had said to me, "Julie, the end is nigh," you know? Nobody ever said that. The only thing was the young doctor and only about 3 weeks before he (my husband) died; he (the doctor) was in the room and he was always so lovely, and he said to me, "Julie, have you ever heard of sepsis?" And I said, "Yes, I have." End of conversation. Maybe if I'd answered no, he might have expanded. I remember thinking, "He hasn't got sepsis," but thinking, "Why did he ask me that question?" I thought about that as I drove home that night. I thought, did he know something more than I knew? Maybe I should have followed up on it. At that stage of an illness, I was waiting for them to give me information, not to have to solicit it. That's what I was waiting for. I actually really did think, why wasn't I given more information? All these doctors were coming around and nursing staff, but nobody was telling me anything. To go through the same thing again, I'd be asking a lot, lot more questions. I think I was a bit reticent to ask. I'd keep thinking, they'll tell me if there's something that I should know. I would have liked somebody to have come to me who knew the situation wasn't going to be good and sort of alerting me to what I was going to face. I think that would have been helpful to me...

I was coloured by what happened. I thought, what if I'd said more? I don't know in my case whether it would have altered the outcome, but I think I could have made things a little bit better for him. (Julie, age 71, wife and carer of patient who had cancer and died 12 months prior to interview)

Commentary: These excerpts reflect the interactions and the inner dialogue Julie experienced during her husband's final days in the hospital. Although her carer role had partially acclimated her to her husband's condition, she did not have enough knowledge to understand his illness trajectory. Julie was left ruminating over the experience after her husband's death with feelings of guilt and anger that culminated in a formal complaint to the health service. She had an expectation that information would be provided without necessarily having to seek it out. She wondered whether emphasizing her lack of understanding would have facilitated more and better information provision. This excerpt from an interview with a bereaved spouse depicts an example of the damage inflicted on family caregivers when they perceive that their loved ones have not received adequate care. Self-blame and sorrow for her husband's experience persisted.

5.3 Respectful and Compassionate Care

Families have identified that respectful, compassionate care that preserves the patient's dignity

and supports both the patient and family is vital. Family-focused care enables a welcoming environment where healthcare providers deliver tailored care for the unique needs of each patient and their family unit. Families desire helpful, empathic, affectionate, appreciative, comforting, gentle, considerate, and capable staff. They also spoke of the fact they want to be able to have physical contact with their loved one. Finally, individualized care provision is hugely important in enabling quality care with families noting the need for patients to remain a person and not become a number or illness within the healthcare system (Virdun et al. 2015, 2017).

5.4 Trust and Confidence in Healthcare Providers

Families consistently ranked trust and confidence in their healthcare providers as highly important. Therefore, family-focused care needs to explicitly focus on developing trust and confidence for both patients and families with their treating team. An explicit focus on the principles of person-centered care provision will support this aspect of care (McCormack and McCance 2016) (refer to ► Chap. 33, "Nursing and Palliative Care").

5.5 Adequate Environmental and Organizational Characteristics

Family-focused care respects the integral role of the family in care provision for patients with end-of-life care needs. In doing so, care providers should ensure hospital rules and processes both make sense and support optimal patient care. For example, families have described being asked to move their car while they were visibly distressed, patients not being given symptom relief while waiting formal admission, and visiting hour restrictions for dying patients (Virdun et al. 2017). Families also note the importance of privacy, cleanliness, and quiet within the care environment. Indeed, families noted that lack of privacy led them to feel disconnected from their loved one, unable to talk openly, and like they were simply observing. Family-focused end-of-life care ought to ensure these environmental and organizational characteristics are explicitly reviewed for each patient's care to identify which family members may require alterations to usual care practices. For example, alterations may include changed visiting hour allowances, quarantined time for privacy where staff do not disturb the patient/family member, and innovative thinking for enabling privacy in open-plan environments such as the intensive care unit. Finally, a family-focused care environment will also consider the availability of space to support cultural practices such as congregating family, chanting, or other rituals.

5.6 Recognizing and Supporting the Family Role in Care Including Valuing Their Expert Knowledge of the Patient and Advocating for Patient Needs

Families have outlined the importance of being recognized and respected as having expertise in the care of their loved one. It is essential that healthcare providers understand and respect that many families have been providing expert care to their dying family member long before palliative care is involved, so we need to draw upon their expertise and include them as authentic partners in care. Valuing and honoring families' contribution to care would ensure families were included as equal partners in care planning and provision and would enable their role as patient advocates to succeed. Failing to do this leads to family's feeling they are simply being an observer to care and their contribution is not valued. This challenges healthcare providers to consider approaches to communication and care both within usual care and also at times where care may be distressing with some data showing that removal of family members at times of distress may cause long-term harm into bereavement (Virdun et al. 2015, 2017).

5.7 Financial Affairs

Ensuring that the patients'/families' financial needs are identified and addressed in a timely manner is an often overlooked element of care. Families desire and need healthcare providers to proactively provide them with information about available financial supports, which helps to enhance comfort and decrease stress. They also want healthcare providers to create opportunities for financial issue discussions, at all stages of the patient's illness trajectory, not just during the final days of life (Kochovska et al. 2017). Taking the lead to initiate these conversations is important, as many patients avoid starting these conversations during the early stages of the illness, as they focus on understanding their diagnosis, treatment, and planning their recovery.

For most working-aged patients, an advanced cancer diagnosis is associated with loss of employment and/or their working partner/spouse also having to reduce their working hours. Studies consistently reveal few patients diagnosed with advanced cancer return to work after active treatment and consequently experience significant economic disadvantages, especially in the absence of universal healthcare or health insurance coverage (Kochovska et al. 2017). Cancer-related financial burden has adverse psychological consequences for both patients and their families, increasing the risk of depression, anxiety, and distress (Kochovska et al. 2017). Healthcare costs and out-of-pocket expenses add to financial stress, sometimes forcing families to reduce their discretionary spending and often affecting their medical treatment (Kochovska et al. 2017).

Taking on a caring role adversely impacts employment with many carers having to reduce their work hours and/or having to stop work. In working-aged families, the spouses/partners are often also caring for an aging parent and/or a young family. In this situation, taking on an additional carer role often impacts adversely on child care costs (Kochovska et al. 2017). Patient care cost and limited access to financial assistance are additional concerns of Australian carers, while unexpected costs, bereavement costs, and legal expenses also contribute to the financial burden (Kochovska et al. 2017). As well as imposing a significant financial strain (Gott et al. 2015), a carer role is associated with significant negative impact on quality of life (Williams et al. 2014). Younger patients and those with larger families are at greater risk of financial burden, while those without income seem to have significantly lower quality of physical health (Hanly et al. 2015).

5.8 Maintenance of Patient Safety and Prevention of Harm

Families identified the need for optimal end-of-life care to prevent harm and a feeling of being unsafe within a clinical environment. Aspects of care perceived to lead to a lack of safety included poor communication, lack of person-centered care, lack of identification of unique needs of people at the end-of-life, poor nursing care, lack of timely attention, and families feeling unsure of how to be involved in their loved one's care (Virdun et al. 2017). A recent study articulates that concepts of patient safety for those who are dying, and their family members, continue to focus on correct treatment, timely interventions, and appropriate infection control, just as would be the case for any patient, and therefore, careful attention to this is important for all patients (Collier et al. 2015). However, this same study asserts that patients with palliative care needs and their families also define patient safety quite broadly, inclusive of approaches to care, interpersonal communication, and the sociocultural context of care. Therefore, consideration of patients at the end-of-life and their families within usual patient safety parameters is required (as this patient population is not routinely considered within this forum) as well as consideration of broader contexts of safety, as articulated above. Finally, family-focused care also works to enable support and a feeling of safety for family carers to speak up without repercussions, as required (Virdun et al. 2015, 2017; Kochovska et al. 2017).

5.9 Preparation for Death

Family-focused care ought to ensure optimal communication and, in doing so, ensure families are aware of and prepared for a patient's imminent death so as they are able to say goodbye and assist their bereavement outcomes. Honest communication, delivered compassionately, is imperative as several family members described not understanding the extent of their loved one's illness or that they were imminently dying (Virdun et al. 2017). As healthcare providers, we need to ensure such conversations have been held and understood by families and to plan for and/or facilitate their support throughout this time.

5.10 Duty of Care Extending to the Family After Patient Death

Families have described their need for follow-up after a family member's death so as to avoid their feeling disconnected and rushed away from the hospital at such an important time (Virdun et al. 2017). If the healthcare provider team truly partner with family members in care provision, then it stands to reason that the duty of care would extent to them, following the patient's death. Systems and processes may hinder this aspect of care, and therefore, needs should be considered within a policy and quality improvement framework.

While the majority of palliative care services focus on contacting the decedents' family, usually their documented next of kin, this approach may fail to identify informal caregivers, who, despite their intensive caregiving role are not listed as the patient's next of kin because their relationship falls outside of these parameters. Given the complexities and nuances of modern relationships, an important area of inquiry is to develop the evidence base for palliative care services to systematically determine more broadly the patients' kinship network (Phillips et al. 2018).

Grief is a normal response to loss during a period of bereavement. Spousal bereavement has been associated with increased mortality and longer hospital stays and negative effects on employment (Stephen et al. 2015). Psychological or social support (e.g., talking to family members and friends during the grieving process) and practical support (e.g., with funeral arrangements, legal and financial help) are commonly identified needs of bereaved persons (Stephen et al. 2015). When the bereaved prefers to speak to others or when family networks are dysfunctional, help is sought from professionals closer to the time of death and shortly after (Benkel et al. 2009). Children and teenagers who experienced the death of a parent to cancer have a range of psychosocial anticipatory grief and bereavement needs (Macpherson and Emeleus 2007a, b). These include maintaining contact with the dying parent; being prepared for their death; holding on to meaningful memories; maintaining privacy, normality, and continuity in family and school life; escaping the intensity and stressfulness of the home situation; being understood and supported by others; and better understanding death (Macpherson and Emeleus 2007a, b). Children and teenagers desire support and understanding from others to help them cope with feelings of grief, anger, and depression and need access to information and opportunities to talk with others who have had a similar experience (Patterson and Rangganadhan 2010).

Although grief is a normal response to loss, a subset of bereaved individuals may experience "persistent complex bereavement disorder." It affects approximately 10–20% of bereaved people and causes significant functional impairment and symptoms that last 6 months or longer (Lobb et al. 2010; Shear et al. 2011). Complicated grief requires early intervention (Lobb et al. 2010).

5.11 Enabling Patient Choice at the End of Life

Family-focused care requires healthcare providers to be aware of and follow the patient's advance care directive. Given recent debates about legalized euthanasia for people with advanced and critical illnesses, legal support in relation to enabling patient choice (both in relation to advance care planning/directives and legalized

euthanasia) needs to be understood within each care jurisdiction with global variances notable within this aspect of care. However, the principle of care ought to remain focused on supporting patient choices, within legal parameters, is fundamentally important and forms an important aspect of family-focused end-of-life care.

5.12 Summary

The above domains of care have been consistently reported by families as contributing to optimal end-of-life care for more than 30 years, yet few healthcare systems and services have been able to effectively address these priorities (Virdun et al. 2017). However, services currently lack the ability to measure the quality of such care provision which hinders careful and targeted quality improvement strategies. Strategies focused on education, quality improvement, policy development, and research are required to truly see family-focused care realized for all patients with end-of-life care needs, irrespective of care setting (Virdun et al. 2017).

6 Strategies to Optimize Outcomes for Families

There are a number of important and cost-effective strategies that healthcare providers can implement to optimize palliative care outcomes for families, as detailed below:

6.1 Need for Healthcare Provider Self-Awareness

It is important for healthcare providers to be aware of assumptions they may have about families. Common assumptions may involve the perceived altruistic nature of family members, such that they always have the best interests of the patient at heart, when this may not be the case and/or that the family is close, supportive, and loving. Another assumption is the belief that children, particularly female children, are obliged to care for chronically ill or older family members. We all bring our own assumptions about the structure and function of families, but not all families are the same, and they all bring their experiences from the past. Activities to facilitate self-awareness can help healthcare providers to acknowledge and reflect on their own assumptions and biases to facilitate their ability to provide family-focused care (Acquaviva 2017).

6.2 Interdisciplinary Team

A key strategy underpinning the provision of family-focused interventions is the active engagement of a cohesive team of healthcare providers who are able to respond to the needs of patients and their families during the palliative phase of the patient's illness. It is important to recognize that the focus of care should be on an interdisciplinary approach that enables and supports shared decision-making that includes the family as a core team member. Using this approach, all members of the team are able to contribute and to share their expertise in providing care to the patient's family and in making decisions that are responsive to family issues and concerns (Haugen et al. 2015). The team's focus should be on responding to the family's needs, issues, and care, rather than basing their decisions on the imperatives of healthcare providers (Speck 2006).

6.3 Effectively Engaging and Supporting Families

One of the most important aspects of engaging and supporting families is to respond to them with respect and compassion, in a manner that is non-judgmental and preserves the dignity of their personhood. It is important to recognize the unique qualities of each individual and their unique ways of behaving and responding in the palliative care phase. Chochinov (2007) outlined key elements of preserving dignity for the patient, which could equally be used in the care of families. He emphasized the importance of attitude, behavior, compassion, and dialogue. He describes each element

with examples. Attitude focuses on the healthcare providers' attitudes and assumptions so that they do not adversely affect the rapport that needs to be created and maintained with the patient. Behavior can include the necessity for honest, open, and easily understood communication, with the availability of time to answer questions and clarify information provided. Dialogue encompasses the individuality of a person and seeking to gain an understanding of the person beyond their disease or circumstances. Chochinov poses a key question in relation to the patient:

> "What should I know about you as a person to help me take the best care of you that I can?" (Chochinov 2007)

This same question and the key components of the dignity-preserving model can be equally applied to the family. These principles can provide the foundation for engaging in a relationship with the family to provide effective support during the palliative care phase. Effective engagement of the family using this framework will guide the support that families require. Information about the patient's condition, what to expect at this time, explanations of what a service provides, and the roles of the different healthcare providers are fundamental to families. Information needs to be tailored to the needs, language, and culture of the family. It is important to understand the family's current understanding of the patient's condition and their degree of acceptance or denial of the situation, so that information can be provided in non-threatening and empathic manner. Information that may seem self-evident to healthcare providers concerning dying and death may be totally foreign to a family who has never previously experienced the death of someone (Kristjanson and Aoun 2004).

Acknowledgment of the physical demands and caregiving roles of families is important in providing adequate support. Practical issues such as ensuring that families have access to sustenance can be provided with overnight facilities toward the terminal phase of the patient's illness; gentle reminders to take "time-out" or obtain some relief for their caring roles are also important.

Support for the emotional needs of the family members is also critical. The witnessing of a relative's deterioration, the impending loss, and a sense that they may be relatively alone in confronting this existential challenge require careful assessment and appropriate emotional, psychosocial support, and spiritual support (Cahill et al. 2017). Attending to these needs and preparing the family for the impending loss may alleviate some of the distress of bereavement (Fineberg and Bauer 2011). Engaging the family in preparatory grieving can be ultimately therapeutic for individual family members and the family unit as a whole.

6.4 Undertaking a Family Assessment

A thorough understanding of the patient's family is fundamental to providing family-focused interventions. To ensure that this occurs, a comprehensive assessment of the family should be undertaken (Fineberg and Bauer 2011). This assessment will involve both psychosocial and other healthcare providers on the team. The assessment should include the identification of key family members and any other people considered "family" by the patient. To ascertain the important family member(s) to a patient, a healthcare provider can ask the patient who is important to them or who they consider their family to be and who they want at the bedside or to have present at a meeting about care. The way a healthcare provider asks this question can convey the provider's openness to different family configurations. To normalize this phenomenon of bringing an accompanying person, the healthcare provider can explain that patients often find it helpful to invite one or more people to participate in the meeting with healthcare providers (Acquaviva 2017).

The role of family members in relation to the patient's illness and his/her care should also be delineated, for example, caregiving duties. Identifying all the people who constitute the patient's family ensures that no family member is excluded from the support needed during the palliative care

phase (Kristjanson and Aoun 2004). It is also prudent to obtain information about any estrangements in the family, and to identify family members who are not readily available to the patient, or for the important interactions that need to take place. Documenting the family structure in the form of a genogram may help to ensure that this information is easily accessible to the entire interdisciplinary team. In the course of the patient's care, different family members will often encounter different members of the interdisciplinary team. Recognition by the team of all family member(s) provides a context that is most likely to enhance communication and good relationships between the family and team members. It is also important to gain an understanding of the patient's current illness and its impact on the family as whole and on individual family members (Lethborg and Kissane 2015). Previous significant life events, as well as important events likely to occur in the future (e.g., the birth of a child), should be documented. Particular note should be made of any history of mental illness, substance abuse, or any intra-family abuse (Fineberg and Bauer 2011). In addition, the possible impact of the patient's illness, according to the life stage of individual family members should be considered. Social aspects of the family unit such as culture, language, financial, and employment issues should also be recorded (Lethborg and Kissane 2015). Religious practices and an understanding of spiritual beliefs should be assessed. The particular sources of meaning and purpose for family members will be relevant, given the context of dying and death of their family member.

6.5 Identifying and Understanding Family Patterns of Communication and Cohesiveness

A specific area for family assessment relates to an understanding of how family relationships work, the sources of strength within the family structure, and the family members' preferred communication style(s). Previous ways of relating to each other, and managing challenging family situations, may influence and provide the team with guidance as to how the family might respond and confront the life-limiting illness of their family member (Lethborg and Kissane 2015). Any previous or current issues that have provoked conflict should be identified, particularly those affecting the patient at this final phase of his or her illness. This information and any major concerns articulated by individual family members, or by the family in its entirety, will assist the interdisciplinary team to respond with suitably family-focused interventions (Lethborg and Kissane 2015). The resolution of family conflict may not be possible. However, appropriate family-focused interventions and support may improve family relationships. Such interventions may also foster more open communication and enhance decision-making so that the family's cohesiveness is optimized at this time (King and Quill 2006).

6.6 Engaging Families in Decision-Making

Decision-making in the palliative care context will be influenced by the communication styles of the family and the family's previous ability in making decisions. It may be that the family do not routinely make joint decisions or they may have a preference for one family member to make decisions on their behalf (Wellisch 2000). In addition to understanding previous decision-making patterns, the interdisciplinary team requires an understanding of the degree to which the family unit and individual family members wish to be involved in this process. Some families are content to forego input into decision-making and to allow all decisions to be made by the healthcare team. Alternatively, other families and family members require regular information, consultation, and involvement in decision-making (Isaac and Curtis 2016). It is important to elicit from the family where they are placed on this continuum of decision-making and which decisions are of particular concern to them. For instance, the family may be comfortable for the interdisciplinary team

alone to make decisions about the patient's care. However, they may require the team to consult with them about all decisions that affect both the patient and the family. Families may often have a preference to engage with specific team members in the decision-making process. This preference should be shared with other team members. It is essential to establish and document to what degree family members are surrogate decision-makers for the patient or if one particular family member is the primary spokesperson and surrogate decision-maker (Isaac and Curtis 2016). Patients and families also value the naming of a decision-maker as a contingency plan for situations in which the patient may be unable to make decisions (Cahill et al. 2017). Recognition of these key factors will guide the team to respond effectively and will enable the provision of family-focused care in relation to decision-making.

The processes required for decision-making are likely to involve sharing of information with families and individual family members, in either one-on-one conversations, informal consultations around the patient's bedside or at home, or during a family meeting. Decision-making is likely to be an iterative process and although it is time-consuming, it is integral to family-centered care. In the era of enhanced communication, telephone and electronic devices can facilitate discussions and decision-making when family members are not physically available (Fineberg and Bauer 2011).

Evidence supports the importance of decision-making by family members in the palliative care setting, not only from the family perspective but also for the patient (Cahill et al. 2017). It should be recognized that decision-making may not only focus on clinical issues. Decisions about everyday activities such as going to the hospice garden or having a pet visit may be just as vital for the patient and family. This type of decision-making enables the patient and family to experience some degree of control in their life at a time when this may be limited. It is incumbent on the interdisciplinary team to recognize and support such decision-making to ensure family-centered care (Cahill et al. 2017).

6.7 Undertaking a Family Meeting: Purpose, Roles, and Responsibilities

Cahill et al.'s (2017) systematic review of family meetings highlighted research indicating effective communication is essential to understanding and responding adequately to family needs and concerns. Bringing together patients, family, and interdisciplinary team members for a focused discussion has been advocated as a method to facilitate effective patient-family-team communication in the specialist palliative care setting (Cahill et al. 2017). These formalized conversations are usually referred to as a "family meeting" or a "family conference," and these terms are often used interchangeably in clinical and research settings. In the palliative care context, a family meeting may be defined as a one-off meeting that includes the patient (when possible), family members, and healthcare providers to discuss an issue related to the health and care of the patient and family (Fineberg et al. 2011).

Family meetings can provide a forum for sharing of information concerning the illness experience, goals of care, current treatment, and end-of-life care. The adoption of an open style of communication by the interdisciplinary team members can help build consensus about the goals of care and management plans and promote a shared understanding of the current clinical situation and its uncertainties. These meetings can also increase the patient's and family's involvement in decision-making. Facilitating expression of family concerns, issues, and needs provides the family with a sense that their concerns are being heard and addressed (Cahill et al. 2017). Discussion at these meetings will inevitably include clinical issues; however, psychosocial issues, preparation for death, and other key areas of importance for that patient and family may be paramount and should also be addressed. It will be an important task to establish the best way to communicate with the patient, family, and the clinical team, and with whom, during this phase of the patient's care.

Conflicting perspectives may emerge between the patient and family members, especially when

certain family members are not able to be present. Family participants (or significant others) may also raise contentious issues and unresolved concerns or indicate pre-existing family conflict. In all cases, it is important to address the specific issues (if possible) or to give voice to concerns as expeditiously as possible so that the meeting's focus remains on the patient and the family (Cahill et al. 2017). In some cases, it may be prudent to acknowledge these concerns but to offer an alternative time to deal with them more fully, either with both patient and family present or with the family in the absence of the patient. Significant conflict between the patient and a family member, such as the existence of an abusive relationship, is not conducive to the patient or family member being able to honestly discuss their concerns and issues. In such situations, a family meeting may not be possible or may even be contraindicated.

The practical aspects of arranging, organizing, and convening a family meeting are important if one is to achieve the maximum benefits for all participants in terms of communication, information sharing, and decision-making (Kissane and Hempton 2017). Key components include who will participate and where and how the family meeting will be conducted. The patient and the primary family support person including any additional family members who wish to participate or whom the patient requests to attend. The patient's palliative care consultant and/or registrar and social worker should routinely attend the meeting. Other members of the team, including pastoral care, nursing, and allied health staff attend as required according to the agenda or the specific issues to be discussed. Patients and families may also request the presence of particular team members during the preparation phase of the meeting. Prior to the meeting being convened, one of the attending healthcare providers will be designated to facilitate the meeting based on mutual agreement with other team members. A co-facilitator of the meeting may also be considered (Kissane and Hempton 2017). Ideally, the lead healthcare provider should have had prior experience in facilitating family meetings in the palliative care setting. All participants should be informed in advance of the date, time, and place for the meeting and commit to being present for the entire meeting, with the exception of unanticipated crises. This will ensure that the "flow" of conversation and discussion are not disrupted nor are participants distracted. The meeting focuses on the patient and the family.

Given that the agenda will influence the goals of the meeting, it is important to recognize that the process by which the agenda is set varies considerably in the reported literature. Some authors suggest that healthcare providers set the agenda. However, the Australian Guidelines for Conducting Family Meetings in Palliative Care (Hudson 2004) recommend that the primary family carer should be the one to identify the main issues and concerns; if the patient attends, he/she also should attempt to identify key issues. Whichever method is used, a prearranged agenda shared with all participants is preferable to an ad hoc arrangement.

A private, comfortable space with adequate seating and ventilation is preferred for the meeting. Meetings should not be held in a shared room within inpatient units unless there is no other option physically possible. The space for the meeting should be prepared in advance so that the meeting can commence in a timely and unrushed fashion. The family meeting begins with the facilitator ensuring that all participants introduce themselves and indicate their relationship to the patient and to each other. The participating healthcare providers are reminded of the importance of "open listening" and to refrain from interrupting the patient and family discussion or directing the discussion away from those issues raised by the patient and family members. Occasionally, however, clarification of an issue or point will need to be made to provide information requested by the patient and/or the family. Kissane and Hempton (2017) describe specific details of communication skills required in the context of family meetings.

The agenda should guide the family meeting, although it is likely that the patient and/or their family may raise additional issues or concerns. It is important that the facilitator acknowledges and facilitates discussion about the issues raised.

However, clarification of information about the patient's illness, prognosis, goals of care, and management plans will usually be required (Kissane and Hempton 2017). Patients and family members should be supported when raising anxieties or fears so that these can be heard by all present and addressed in a timely manner (Cahill et al. 2017).

Once the discussion has been completed, the facilitator summarizes the agreed goals of care. Other key points that have been discussed or agreed to, any matters of disagreement, and any actions required to be undertaken following the meeting are confirmed. Endorsement for the decisions made and the actions to be undertaken is sought from the patient, family, and healthcare providers (Hudson et al. 2008; Kissane and Hempton 2017). The facilitator concludes the meeting by emphasizing the positive results from the meeting; acknowledging the patient, family, and clinical contributions to the meeting; and thanking all the participants.

Guidelines for Conducting Family Meetings in Palliative Care were developed in Australia (Hudson et al. 2008) based on available literature, various theoretical models, expert opinion, and the results of focus groups. These consensus guidelines provide a planned approach for preparing, conducting, and documenting the agreed decisions resulting from a family meeting. An evaluation to assess the effectiveness of these *Guidelines* (Hudson et al. 2009) demonstrated a significant increase in families' unmet needs being satisfied as a result of participating in such meetings. Family members also reported that the meetings were useful because they gained a better understanding of the patient's illness and what to expect in the immediate future.

7 Conclusion and Summary

While caring for a family member with a life-limiting condition can be distressing, it can also be a positive and rewarding experience. Carers have reported positive experiences from caregiving to include a strengthened relationship between carer and care recipient, personal growth, increased self-efficacy, and recognition of personal strength through adversity, acceptance, and necessity (Hudson 2004; Wong et al. 2009). However, family-focused care is critical in supporting positive care experiences and more healthy adjustments to grief and bereavement, where possible. Challenges to family-focused care include individual healthcare provider practice that fails to prioritize working in partnership, a lack of policy and infrastructure support with often-exclusive focus on patient needs, and a lack of open, innovative, and creative thinking to facilitate and partner with families caring for people at the end of their lives. Meeting these challenges through education, policy reform, quality improvement initiatives, and research provides enormous opportunity for improved family-focused end-of-life care into the future.

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Grief and Bereavement

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Contents

Abstract

In spite of grief and bereavement being fundamental to high-quality palliative care, grief and bereavement care is often under-resourced and haphazard and fails to reflect contemporary evidence. This chapter will examine a number of approaches to evidence-informed bereavement care and explore some of the seismic shifts that have taken place in our understanding and response to the grieving and bereaved. The chapter will conclude with an examination of complications in bereavement and what might be considered best practice in providing bereavement support in the palliative setting.

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_33

1 Introduction

Loss and grief are the ever-present companions along the trajectory from the appearance of symptoms, diagnosis, treatment, palliation, and death. It is important to remember that both death and non-death losses punctuate this journey. These include a loss of physical strength and well-being, independence, role and professional identity, sexual function and intimacy, a sense of control and safety, mental integrity, and life expectancy. The experience of loss may be subtle or overwhelming. These losses may or may not be recognized by family, friends, or health professionals. What matters are the subjective appraisal and experience of these losses.

Loss and grief are fundamental to human life. Grief can be defined as the response to the loss in all of its totality – including its physical, emotional, cognitive, behavioral, and spiritual manifestations – and as a natural and normal reaction to loss. Put simply, grief is the price we pay for love and a natural consequence of forming emotional bonds to people, projects, and possessions. All that we value we will someday lose. Life's most profound losses disconnect us from our sense of who we are and can set in train an effortful process of not only re-learning ourselves but also the world. In recent decades, we have seen a broadening of attention from a traditional focus on emotional consequences, to one that also considers cognitive, social, cultural, and spiritual dimensions to the study of grief. There is also a growing awareness that losses can also provide the possibility of life-enhancing "post-traumatic growth" as one integrates the lessons of loss and resilience. Personal growth following even seismic experiences of loss is common. While loss and grief are fundamental to human life, the course and consequences of bereavement will vary for each individual. For highly resilient individuals, acute grief may be limited to a few weeks, and for most people, their grief subsides over time (Bonanno and Kaltman 2001).

Over the past two decades, the field of grief and bereavement has undergone significant change in terms of how the human experience of loss is understood and how the goals and outcomes of grief therapy are conceptualized. Long-held views about the grief experience have been discarded, with research evidence failing to support popular notions, which construe grief as the navigation of a predictable emotional trajectory, leading from distress to "recovery." We have also witnessed a shift away from the idea that successful grieving requires a "withdrawal of emotional investment" and a "letting go" of the deceased and a shift toward a recognition of the potentially healthy role of retaining continued bonds with the deceased. Recent research evidence has also failed to support popular notions that grieving is necessarily associated with depression, anxiety, and PTSD or that a complex process of "working through" or engagement with "grief work" is critical to recovery. The absence of grief is no longer seen, by definition, as pathological. How we adapt to these deprivations shapes who we become. While recognizing that grief reactions are universal, they are shaped by the reciprocal impact of loss on families, organizations, and broader cultural groups.

While loss and grief are fundamental to human life, the course and consequences of bereavement will vary for each individual. For highly resilient individuals, significant grief may be limited to a few weeks (Bonanno and Kaltman 2001), though a more typical trajectory involves readjustment to life over the course of a few years (Bonanno et al. 2004).

This chapter will explore a number of theoretical approaches to bereavement which has seen a move from simplistic generalizations of these phenomena to more evidence-informed and nuanced descriptive and explanatory frameworks. Attention will be given to some of the current controversies in the field, such as complicated grief as a mental disorder and the management of clients with complex bereavement needs. The chapter will conclude with a consideration of what best-practice bereavement care in the palliative care setting might look like.

2 Theoretical Perspectives

The first major theoretical contribution on grief was provided by Freud in his paper *Mourning and melancholia* (1917/1957) and profoundly shaped

professional intervention for over half a century. For Freud, "grief work" involved a process of breaking the ties that bound the survivor to the deceased. This psychic rearrangement involved three elements: (1) freeing the bereaved from bondage to the deceased, (2) readjustment to new life circumstances without the deceased, and (3) building of new relationships. Freud believed that this separation required the energetic process of acknowledging and expressing painful emotions such as guilt and anger. The view was held that if the bereaved failed to engage with or complete their grief work, the grief process would become complicated and increase the risk of mental and physical illness and compromise recovery. The grief work model stresses the importance of "moving on" as quickly as possible to return to a "normal" level of functioning. It is ironic that Freud maintained that mourning ends within a relatively short time, because, as a bereaved father, he wrote about his strong attachment to his daughter some 30 years after her death. In his private correspondence, he was acutely aware of the long-term nature of grief and a parent's ongoing connection to their dead child (Shapiro 2001).

Several later grief theorists conceptualized grief as proceeding along a series of predictable stages, phases, and tasks (Kübler-Ross 1969; Bowlby 1980; Parkes and Weiss 1983). Perhaps the best-known model is that postulated by Kübler-Ross in her 1969 text *On death and dying*. Based upon her clinical work with the dying, her model was one of anticipatory grief, how an individual responds to a terminal diagnosis. Over time this model transformed into the five stages of grief – (1) shock and denial; (2) anger, resentment, and guilt; (3) bargaining; (4) depression; and (5) acceptance – and was subsequently applied to both the bereavement experience and many other forms of change. The model implied that failure to complete any of these stages would result in a variety of complications. Kübler-Ross's perspective, although capturing the imagination of both lay and professional communities, has been widely criticized for suggesting that individuals must move through these stages and has been empirically rejected.

Stage theories have a certain simplistic appeal – they bring conceptual order to a complex process; however they are incapable of capturing the complexity, diversity, and idiosyncratic quality of the grieving experience. Stage models do not address the multiplicity of physical, psychological, social, and spiritual needs experienced by the bereaved, their families, and intimate networks. Since the birth of these theories, the notion of stages of grief has become deeply ingrained in our cultural and professional beliefs about loss (Stroebe et al. 2017). These models of grieving, albeit without any credible evidence base, have been routinely taught as part of the curriculum in medical and nursing programs (Downe-Wamboldt and Tamlyn 1997).

Prospective studies of spousal bereavement have identified the most common trajectories of adjustment to loss (Bonanno et al. 2002) and made the compelling finding that resilience is the most common pattern and that delayed grief reactions are rare. Five distinct trajectories covered the outcome patterns of most participants: (1) common grief or recovery (11%), (2) stable low distress or resilience (46%), (3) depression followed by improvement (10%), (4) chronic grief (16%), and (5) chronic depression (8%). Bonanno identified, within the depression followed by improvement group, individuals who improved in functioning after the death of their spouse. This was most prevalent in those who experienced relief following a period of considerable caregiver burden or who suffered oppressive relationships (Bonanno et al. 2004).

In Bonanno's research, those who experienced the highest levels of distress tended to exhibit high levels of personal dependency prior to the death of their spouse. For those not depressed prior to the loss, dependency was an important predictor of grief reactions. A lack of expectation or psychological preparation for the loss also contributed strongly to increased distress. The distinction between chronic grief and chronic depression, which this study illuminates, is of critical importance. Relationship conflict was predictive of chronic depression but not chronic grief. Chronic grievers reported greater processing of the loss and searching for meaning

compared to chronically depressed individuals. Both groups evidenced elevated pre-loss dependency. What is clear is that there is no single set of stages or tasks in adapting to loss but instead qualitatively distinct paths through bereavement, which calls for a closer understanding of both patterns of complication and resilience. Further work is required to explore strategies to promote resilience, which includes factors and mechanisms that impact on an individual's level of protection against adversities. Resilience is not only a result of an individual's personal attributes but can be impacted by a variety of community and cultural factors.

The early stage theories of grief became unpopular because they were considered to be too rigid. There are, however, new models that succeed in identifying definite patterns and relations in the complex and idiosyncratic grief experience. Phasal conceptualizations have been enormously influential. Two of the most comprehensive and influential grief theories are the dual process model of Stroebe and Schut (1999) and the task-based model developed by Worden (2008). These models serve both counselors and clients by offering frameworks that guide interventions and enhance clients' self-awareness and self-efficacy.

The dual process model of grief (Stroebe and Schut 1999), developed from a cognitive stress perspective, describes grief as a process of oscillation between two contrasting modes of functioning. In the "loss orientation," the griever engages in emotion-focused coping, exploring, and expressing the range of emotional responses associated with the loss. At other times, in the "restoration orientation," the griever engages with problem-focused coping and is required to focus on the many external adjustments required by the loss, including diversion from it and attention to ongoing life demands. The model suggests that the focus of coping may differ from one moment to another, from one individual to another, and from one cultural group to another.

Worden (2008) suggests that grieving should be considered as an active process that involves engagement with four tasks: (1) to accept the reality of the loss, (2) to process the pain of grief, (3) to adjust to a world without the deceased (including internal, external, and spiritual adjustments), and (4) to find an enduring connection with the deceased in the midst of embarking on a new life.

Worden also identifies seven determining factors that are critical to appreciate in order to understand the client's experience. These include (1) who the person who died was, (2) the nature of the attachment to the deceased, (3) how the person died, (4) historical antecedents, (5) personality variables, (6) social mediators, and (7) concurrent stressors. These determinants include many of the risk and protective factors identified by the research literature and provide an important context for appreciating the idiosyncratic nature of the grief experience. Issues such as the strength and nature of the attachment to the deceased, the survivor's attachment style, and the degree of conflict and ambivalence with the deceased are important considerations. Death-related factors, such as physical proximity, levels of violence or trauma, or a death where a body is not recovered, all can pose significant challenges for the bereaved.

A stigmatizing death, such as that by suicide or AIDS, can "disenfranchise" the griever (Doka 2002) and complicate the bereavement experience. Disenfranchised grief refers to grief that persons experience when they incur a loss that is not or cannot be openly acknowledged, publicly mourned, or socially supported. The concept of disenfranchised grief recognizes that societies have sets of norms – in effect, "grieving rules" – that attempt to specify who, when, where, how, how long, and for whom people should grieve. Disenfranchised grief can be a result of the circumstances of the death but can also extend to the relationship not being socially recognized, the griever being excluded (such as a child), or the way the individual expresses their grief, particularly with regard to the level of emotional distress which is publicly displayed.

Those who help bereaved people must recognize the unique reactions, needs, and challenges as individuals and their families cope with loss.

Subscription to a stage theory can lead to a failure of empathy, where we fail to listen to and address the needs of the bereaved.

3 Continuing Bonds

There has been a paradigm shift from the idea that successful grieving requires "letting go," with writers such as Klass et al. (1996) and Klass and Steffen (2018) offering an alternate approach where they argue that after a death, bonds with the deceased do not necessarily have to be severed and that there is a potentially healthy role for maintaining continuing bonds with the deceased. This idea represents recognition that death ends a life, not necessarily a relationship. Rather than "saying goodbye" or seeking closure, there exists the possibility of the deceased being both present and absent.

The development of this bond is conscious, dynamic, and changing. The expression of this continuing bond can be found in a variety of forms. The deceased may be seen as a role model, and the bereaved may turn to the deceased for guidance or to assist them in clarifying values. The relationship with the deceased may be developed by talking to the deceased or by relocating the deceased in heaven, inside themselves, or joined with others whom they predeceased. The bereaved may experience the deceased in their dreams, by visiting the grave, feeling the presence of the deceased, or through participating in rituals or linking objects. Many people build the connection out of the fabric of daily life. Frequently this continuing bond can be co-created with others. A number of studies have found that approximately half of the bereaved population experience the sense of presence of the deceased (Datson and Marwit 1997) although the true incidence is thought to be much higher, given a great reluctance among the bereaved to disclose its occurrence to clinicians for fear of ridicule or being thought of as "mad or stupid."

Ongoing research is still examining when continuing bonds are helpful and when they are not. Continuing bonds must always be considered within a cultural context, and there needs to be assessment of the ways the bond influences adaptation to the loss. Recent literature has attempted to distinguish the conditions under which it is adaptive from those where it is maladaptive. Field (2006) identified a type of continuing bonds expression that represents failure to integrate the loss due to extreme avoidance in processing the implications of the loss. In keeping with Bowlby's (1980) early work, growing evidence suggests that individuals who experience insecure styles of attachment are more prone to chronic grief trajectories (Bonanno et al. 2004), contributing to maladaptive rather than adaptive forms of continuing bonds with the deceased.

In essence, continuing bonds expressions that are indicative of unresolved loss imply disbelief that the other is dead. An important factor distinguishing adaptive versus maladaptive continuing bonds expression is whether the given expression reflects an attempt to maintain a more concrete tie that entails failure to relinquish the goal to regain physical proximity to the deceased. This can be compared to a more internalized, symbolically based connection, which suggests a greater acceptance of the death.

4 Meaning Reconstruction Following Loss

For many the desire to "make sense" and "find meaning" in the wake of loss is central. Neimeyer and Sands (2011) have emphasized that the reconstruction of meaning represents a critical issue, if not the critical issue in grief. In stark contrast to earlier modernist or positivist views which focus on breaking bonds and universal symptoms and stages of adaptation to loss, the postmodern social constructionist approach views continuing bonds as resources for enriched functioning and the oscillation between avoiding and engaging with grief work as fundamental to grieving (Neimeyer 2001). These later models see grieving as a process of reconstructing a world of meaning that has been challenged by loss. The experience of loss, particularly if it is sudden and unexpected, can interfere with a bereaved

person's ability to rebuild his or her assumptive world, particularly when the death assaults the survivor's notion world that life is predictable or that the universe is benign. A bereaved individual may have no mental constructions to help them with the meaning-making process to incorporate the loss into a new worldview. When people indicated that they could not make sense of the loss, they often indicated that the death seemed unfair, unjust, or random. If the loss is consistent with existing worldviews, then making sense does not appear to represent a significant coping issue.

Across a variety of different losses, a body of research indicates that the failure to find meaning following the loss, especially in terms of "making sense" of the death itself, is associated with higher levels of complicated grief symptoms. An intense and protracted search for meaning is likely to accompany losses that are unexpected and premature, as in the death of a child, and that a ruminative preoccupation with the loss is an indicator of long-term depression, anxiety, anger, and grief. A failure to find spiritual or secular meaning in the loss accounts for nearly all of the heightened symptoms of complicated grief following suicide, homicide, and fatal accident, as opposed to natural anticipated deaths (e.g., cancer) and even natural sudden deaths (e.g., heart attack).

Most definitions of meaning encompass two concepts: (1) making sense of the loss (e.g., the death had been predictable in some way; it was consistent with the caregiver's perspective on life; or religious or spiritual beliefs provide meaning) and (2) finding benefits from the loss (e.g., it led to a growth in character, a gain in perspective, and strengthening of relationships). Data suggests that sensemaking and benefit finding are two distinct processes and represent two distinguishable psychological issues for the bereaved person. It is not so much making sense of the loss that alleviates distress, as it is becoming less interested in the issue. The finding of benefit on the other hand grows stronger with time (Davis et al. 1998). Meaning-making is a highly iterative and interactive process, and the significance of a loss can be affirmed or disconfirmed, congruent or discrepant, and supported or contested within families and other reference groups (Nadeau 1998).

4.1 Complications of Bereavement

A century ago, Freud (1917/1957) wrote:

> Although mourning involves grave departures from the normal attitude toward life, it never occurs to us to regard it as a pathological condition and to refer it to a medical treatment. We rely on its being overcome after a certain lapse of time, and we look upon any interference with it as useless or even harmful. (p. 243)

Research has proved Freud largely correct, although not completely. A small proportion of bereaved individuals experience severe and prolonged grief that has an ongoing and negative impact on their lives.

For a subgroup of individuals, around 10%, the symptoms of distress following the death of a family member or friend are more intense and persistent (Prigerson et al. 1996; Latham and Prigerson 2004). Known variously as complicated grief (Shear et al. 2001) or prolonged grief disorder (Prigerson et al. 1996; Boelen and Prigerson 2007), this condition can be associated with severe mental and physical health problems such as insomnia, substance misuse, depression, depressed immune function, hypertension, cardiac problems, cancer, suicide, and work and social impairment. Bereaved individuals in this cohort report higher use of medical services and more frequent hospitalization than people with similar losses whose grief is less intense and of shorter duration. These effects have been observed for as long as 4–9 years after the death (Neimeyer and Burke 2012).

Neimeyer and Burke (2012), in a summary of the clinical literature on pre-loss risk factors for the development of complicated grief, identified three groups of factors – background factors, death-related factors, and treatment-related factors, which were predictive of adverse outcomes:

1. **Background factors** – these include close kinship to the dying patient, being female,

minority ethnic status, insecure attachment style, high pre-loss marital dependence, religion, and spirituality.

2. **Death-related factors** – these include bereavement overload, low acceptance of pending death, violent death (suicide, homicide, accident), finding or viewing the loved one's body after violent death, death in the hospital (vs. home), and dissatisfaction with death notification.
3. **Treatment-related factors** – these include aggressive medical intervention (e.g., ICU, ventilation, resuscitation), ambivalence regarding treatment, family conflict regarding treatment, economic hardship created by treatment, and caregiver burden.

Most people ultimately adapt well to bereavement, typically regaining their psychological equilibrium after some weeks or months of acute mourning, although they frequently will continue to miss their loved one for a considerably longer period of time (Bonanno et al. 2002). Studies show that for most people grief intensity is fairly low after a period of about 6 months. This does not imply that grief is completed or resolved but rather that it has become better integrated and no longer stands in the way of ongoing life. Acute grief is a normal response to loss, with symptoms that should not be pathologized.

Two main diagnostic criteria for disordered grief have been proposed – complicated grief (Shear et al. 2001) and prolonged grief disorder (Prigerson et al. 2009). Both describe intense distress; a range of cognitive, emotional, and behavioral symptoms; and functional impairments, all persisting for at least 6 months. The American Psychiatric Association (2013) drew from both in proposing persistent complex bereavement disorder, with the criterion that the symptoms must persist for more than 1 year.

Complicated grief (CG) is characterized by a relentless period of profound grieving that continues for at least 6 months beyond the death of the loved one, in which the survivor suffers marked and disruptive separation distress and psychologically disturbing and intrusive thoughts of the deceased. Additionally, CG frequently entails a sense of emptiness and meaninglessness about life and/or the future, trouble accepting the reality of the loss, and difficulty moving forward in making a life without the deceased (Holland et al. 2009; Prigerson and Jacobs 2001). (Stroebe et al. 2007) found that grievers, especially spouses, have an increased risk of early mortality merely as a result of being bereaved, and other investigators have found CG in particular to predict a variety of concerning conditions, including impaired quality of life and social functioning, substance abuse, immune dysfunction, cardiovascular illness, and suicide (Latham and Prigerson 2004; Prigerson et al. 1996, 2009). Clinicians should be alert to these symptoms as they evaluate the longer-term adjustment of clients to the loss of a loved one, as both self-report (Keesee et al. 2008) and neurophysiological (O'Connor et al. 2008) data suggest that time alone does little to diminish CG symptomatology. Once identified, however, prolonged grief is clearly amenable to treatment (Shear et al. 2001).

Population-based studies reveal the clinical threshold for complicated grief to be 2.4% in a Japanese sample (Fujisawa et al. 2010) to 6.7% in a German sample (Kersting et al. 2011). It is now clear that grief, at least for a subset of approximately 10% of the bereaved, can be intense and chronic for many months or years. Individuals bereaved as a result of deaths that are unexpected, violent, or untimely (e.g., the death of a child) tend to be overrepresented in this cohort. This condition, termed complicated grief (CG) or more recently prolonged grief disorder (PGD), has received increasing attention in both the psychiatric and psychological literatures over the past decade. An estimated 7–10% have a complicated grief syndrome – currently called persistent complex grief disorder. More broadly, an estimated 10–20% have some form of complicated response to loss, which includes a full range of mental and/or physical reactions and illnesses. Taken together, 7–20% of all grievers may experience complications which are associated with several mental and physical health problems such as sleep disruption, substance abuse, depression, compromised immune function, hypertension, cardiac problems, cancer, suicide, and work

and social impairment. Bereaved individuals in this cohort report higher utilization of medical services and more frequent hospitalization than people with similar losses whose grief is less profound and extended. These effects have been observed for as long as 4–9 years after the death.

In addition to those who experience complicated grief, a significant proportion of all people caring for someone in palliative care will experience poor psychological, social, financial, spiritual, and physical well-being. When grief is complicated and prolonged, evidence suggests that intervention is both indicated and effective (Currier et al. 2008). Directing scarce resources at the groups that will benefit most from them is critically important. The available evidence suggests that while many bereaved people will benefit from bereavement support, only a minority of people will require and benefit from specialist bereavement interventions.

5 Prolonged Grief Disorder and the DSM-5

In the late 1990s, two research teams independently published a set of diagnostic criteria to assess CG (Horowitz et al. 1997; Prigerson et al. 1999). Recently, these two diagnostic entities were integrated, and the concept of CG was renamed as prolonged grief disorder (PGD). This incapacitating disorder is defined as a combination of separation distress and cognitive, emotional, and behavioral symptoms that can develop after the death of a significant other. The symptoms must last for at least 6 months and cause significant impairment in social, occupational, and other important areas of functioning.

The addition of complicated grief (CG) to the DSM-5 (American Psychiatric Association 2013) received significant support. Findings confirm the proposition that professional assistance is indicated for only a subgroup of the bereaved, namely, those who show CG reactions. CG symptoms have been shown to be different from other symptoms and disorders, such as normal grief reactions, mood disorders, and anxiety disorders including post-traumatic stress disorder.

It is essential that we do not consider bereavement complications simply as a relabeling of conventional psychiatric conditions. Bereavement is a severe stressor that can trigger the onset of both physical and mental disorders such as major depression, post-traumatic stress disorder, anxiety, and sleep disorders. These comorbidities require identification, clinical attention, and treatment. It is noteworthy that antidepressant medication has been found to do little to address the core symptoms of bereavement complication, even when it usefully reduces symptoms of depression (Pasternak et al. 1991).

Although prolonged grief disorder failed to be included in the DSM-5, the most recent edition has included persistent complex bereavement disorder (PCBD) as a condition that merits further study. The criteria for PCBD have been established to encourage future research and are not designed for clinical use.

5.1 Grief Interventions

With the support of friends and family and the mobilization of their own resources, most bereaved individuals adapt well following loss. Unsolicited help based on routine referral and delivered shortly after loss has not been found to be effective. Schut and Stroebe (2005) summarize their review of the literature with the conclusion that:

> Routine intervention for bereavement has not received support from quantitative evaluations of its effectiveness and is therefore not empirically based. Outreach strategies are not advised, and even provision of intervention for those who believe that they need it and who request it should be carefully evaluated. Intervention soon after bereavement may interfere with 'natural' grieving processes. Intervention is more effective for those with more complicated forms of grief. (p. 140)

The general pattern emerging is that the more complicated the grief process, the better the chances of bereavement interventions leading to positive results. When grief is prolonged

or complicated, evidence indicates that interventions are both effective and indicated (Currier et al. 2008). A large body of evidence supports the value of grief counseling as long as clinicians undertake careful assessment and interventions are carefully tailored. Given the idiosyncratic nature of grief, the most effective grief support offers a range of options including psychoeducation, online support, individual counseling, group support, community support, bibliotherapy, and rituals. There are a wide range of publications which provide detailed information on clinical interventions from constructivist (Neimeyer 2001), cognitive (Malkinson 2007), attachment (Kosminsky and Jordan 2016), and family systems perspectives (Nadeau 1998; Kissane and Parnes 2014). Neimeyer (2012) provides comprehensive details on a range of bereavement interventions that are drawn from a range of theoretical perspectives. Fortunately, several research-informed treatments exist, both for use prior to the loss and afterward. The following are examples of grief-specific interventions:

6 Cognitive Behavioral Therapy (CBT) for Complicated Grief

The CBT conceptualization of complicated grief proposes three processes: (a) problems with properly integrating the loss into the bereaved person's existing knowledge about themselves and their relationship with the dead person stored in long-term memory, (b) the presence of unhelpful thinking patterns such as negative global beliefs and misinterpretations of grief reactions, and (c) anxious and depressive avoidance. The CBT approach assumes that these three factors that play a key role in the development of complicated grief, with the first, poor integration, being mainly a disturbance of memory, and that this accounts for the fact that bereaved people can be preoccupied with their loss and, at the same time, continue to feel, think, and act as if the loss is reversible. The second factor, negative cognitions, is primarily a disturbance of thinking, which contributes to yearning and related emotions of sadness, depression, and anxiety. The third process, anxious and depressive avoidance, represents a disturbance in the behaviors of mourners that blocks adjustment as they attempt to deal with the internal demands of their loss (painful feelings and memories) and the external demands (adjusting to a changed situation).

From the perspective of CBT, (a) the loss needs to be integrated with existing knowledge, (b) unhelpful thinking patterns need to be identified and altered, and (c) maladaptive avoidance behaviors need to be replaced by more helpful ones. Various cognitive behavioral interventions can be used to achieve these changes. Imaging techniques, cognitive restructuring, and behavioral activation have been identified as beneficial (Boelen et al. 2006).

7 Family Focused Grief Therapy

Family focused grief therapy (FFGT; Kissane and Bloch 2002) is an approach that has been developed within the palliative care setting. Kissane makes the case for family-centered care, which is based on two premises: families in palliative care can be classified according to the quality of their relational functioning, and this functioning is highly predictive of individual functioning.

Based on the Family Relationships Index (FRI), families are classified as either well-functioning (i.e., supportive, showing a high level of cohesion, or conflict resolving, permitting and accepting each others' differences and dealing with discord constructively) or dysfunctional (hostile, families characterized by high conflict, low cohesion, and poor expressiveness, or sullen, families characterized by poor communication, depression, and muted anger). A final intermediate group shows some impairment in communication and teamwork, although conflict is less intense than in the hostile group (Kissane and Hooghe 2011). Supportive and conflict resolving categories reflect about 53% of families entering palliative care. Those considered sullen and hostile represent about 15–30% of families entering palliative care. Another 20–30% are mid-range, with mixed outcomes if left untreated.

Family focused grief therapy is a brief, focused, and time-limited intervention typically comprising four to eight sessions of 90 minutes' duration, which are arranged flexibly across 9–18 months. The intervention aims to prevent the complications of bereavement by enhancing the functioning of the family, through exploration of its cohesion, communication (of thoughts and feelings), and handling of conflict. The story of illness and related grief is shared in the process. Family focused grief therapy has three phases: (a) assessment (one or two weekly sessions) concentrates on identifying issues and concerns relevant to the specific family and on devising a plan to deal with them, (b) intervention (typically two to four sessions) focuses on the agreed concerns, and (c) termination (one or two sessions) consolidates gains and confronts the end of therapy. The frequency and number of sessions in each phase are modified to meet the needs of each family.

Families that function best under any type of stress tend to be the 3 Cs: communicative, cohesive, and conflict resolving. In clinical practice, one can screen for these characteristics with three simple questions:

> How openly and effectively do you communicate?
> What is your family's teamwork like?
> How do you manage differences of opinion and conflict in your family?

Once a family has been identified as at-risk, members are invited for a family meeting. The goals of FFGT are to increase the three Cs and to promote sharing of grief and mutual support. FFGT deliberately focuses and refocuses the family on:

1. Their strengths and coping skills
2. Transgenerational mapping of patterns of relating and ways of coping with loss
3. Encouraging the family to take responsibility for change

A goal of the therapy is to help the family reconstruct shared meaning. Defining the value and legacy of the dying or deceased person in the family and examining or creating family mottos are also crucial to this meaning-making process. Assessment and treatment typically last six to ten sessions and take place before and after the death of the family member. Outcome studies suggest the FFGT approach (compared to standard care) reduces individual depression and the incidence of complicated grief at 6 months post-death.

8 Complicated Grief Treatment

Complicated grief treatment (CGT; Shear et al. 2005) is an individual treatment protocol which has been specifically designed to identify and resolve complications of grief and to facilitate adaptation to loss. Rigorously tested in three large studies funded by the National Institute of Mental Health (NIMH), the intervention consists of ten modules that include psycho-education about complicated grief as well as a range of techniques derived from interpersonal therapy, motivational interviewing, positive psychology, and cognitive behavioral therapy. The treatment is administered in 16 weekly sessions with introductory, middle, and termination phases. The treatment includes two key areas of focus: restoration (i.e., restoring effective functioning by generating enthusiasm and creating plans for the future) and loss (i.e., helping patients find a way to think about the death that does not evoke intense feelings of anger, guilt, or anxiety). A portion of each of 16 weekly sessions is allotted to each area of focus. Grief monitoring and other weekly activities are assigned at the end of each session. Research indicates that CGT outperformed a more general psychotherapy for carefully diagnosed bereaved people and was particularly helpful for those whose losses were traumatic (Shear 2006).

9 Meaning Reconstruction Approaches to Grief Therapy

Meaning reconstruction refers to a cluster of processes that include sensemaking about the loss (Neimeyer 2000), finding some kind of existential benefit or life lesson in the loss, and then

also reconstructing one's sense of identity as a social being in the wake of that loss. A fundamental tenet of this approach is seeing adaptation to loss as an attempt to rebuild or to reaffirm a world of meaning that has been challenged by the loss experience. Bereavement and loss propel us into unanticipated or unwanted transitions, which we are forced to make sense of both our changed life and identity.

10 Online Support

Internet-based communication has changed the way people communicate and provides an alternative to conventional face-to-face interactions. Online services can overcome some of the restrictions of access posed by geography, disability, and privacy. Studies have found no difference in impact between face-to-face and online interventions (Barak et al. 2008).

While still in its infancy, research is also beginning to investigate the efficacy of online interventions for complicated grief. One study which used a series of tailored writing assignments delivered over the Internet that helped people express and explore their stories of loss significantly reduced symptoms of complicated grief relative to a no-treatment control group (Wagner et al. 2006).

10.1 Palliative Care and Bereavement Support

Although grief and bereavement support is central to palliative care, studies have demonstrated that it is often under-researched, under-resourced, and not systematically applied (Stroebe and Boerner 2015). In the palliative care setting, bereaved persons have frequently undertaken caregiving roles that can have both positive and negative consequences, with caregivers prone to physical and psychological morbidity, financial disadvantage, and social isolation (Hudson et al. 2011). Depression rates of between 12% and 59% (Hudson et al. 2011) and anxiety rates of between 30% and 50% have been reported (Grunfeld et al. 2004; Hudson et al. 2011). Meeting the needs of bereaved persons with complicated grief can be a complex, specialized task requiring input from appropriately trained staff (Guldin et al. 2015), particularly when supporting those from diverse cultural and linguistic backgrounds (Arthur et al. 2011).

In one study (Hudson 2013) almost half of family carers met the criteria for psychological distress when measured at the commencement of palliative care provision. Research indicates that preparing family caregivers for the role of supporting a person with advanced disease has valuable psychological and social sequela including lessening the propensity for distress during bereavement (Hudson et al. 2015). This preparation can include how to support the person with advanced disease, self-care, support services, and considerations for impending death and bereavement. Pre-bereavement levels of psychological distress are predictive of post-bereavement maladjustment (Stroebe and Boerner 2015); pre-existing conditions seem to be most important in explaining the occurrence of complicated grief (Bruinsma et al. 2015).

When grief is complicated, evidence suggests that intervention is both indicated and effective (Currier et al. 2008). However, providing universal bereavement services is unnecessary, and offering therapy to resilient individuals is known to be of limited benefit (Schut and Stroebe 2005; Wittouck et al. 2011).

A tiered or layered approach to bereavement care has been advocated based on meta-analyses of clinical trials (Schut and Stroebe 2005). However, there appears to be a dearth of contemporary practice standards that explicitly articulate what resources palliative care services should allocate, when they should allocate them, how, and by whom. Findings from the USA and Australia indicate that bereavement coordinators and counselors are not available in the majority of hospice or palliative care services, bereavement support is highly variable, and there is insufficient evidence-based guidance (Demmer 2003; Mather et al. 2008). Recent data from Europe also indicates a lack of guidance on bereavement support and a reliance on intuition over evidence

when responding to bereavement care needs in palliative care (Guldin et al. 2015). Alarmingly almost one-fifth of palliative care services provided no bereavement support (Guldin et al. 2015). Furthermore, services may not formally recognize family carers as "clients" consequently bereavement support needs for many may go unmet.

Given the variability in the adaptation to bereavement, it is often difficult to make confident predictions in terms of longer-term functioning of bereaved individuals before a minimum of 6 months post-death. At this point, tools such as the PG-13 (Prigerson and Vanderwerken 2008; Prigerson and Maciejewski 2012) have been found to have effective predictive validity and reliability for identifying a prolonged and complicated grief disorder.

Provision of bereavement support is an essential component of palliative care service delivery and is explicitly acknowledged in several national and international publications (National Institute for Clinical Excellence (NICE) 2004; World Health Organization 2016; National Coalition for Hospice and Palliative Care 2013; De Lima et al. 2012; Hall et al. 2012) that have established recommended standards which are recommended as a minimum level of bereavement support to be provided to primary carers and bereaved individuals by specialist palliative care services. The guiding principles underpinning these standards are:

Standard 1: Access

All primary carers of clients cared for by a specialist palliative care service are eligible to access palliative care bereavement services regardless of age, gender, culture, sexual orientation, socioeconomic status, religious beliefs, and physical or other disabilities or abilities to pay.

Standard 2: Coordination of bereavement services

Bereavement programsin palliative care services should provide coordinated services.

Standard 3: Training and support

All staff in a palliative care service, including administrative staff, will come into contact with bereaved people and will therefore require training and support in dealing with bereaved individuals. Staff and volunteers who have contact with bereaved individuals are required to achieve appropriate competencies in delivering bereavement support.

Standard 4: Screening and assessment

Screening and assessment for the presence of psychosocial and spiritual distress and risk of complicated grief is a continuous process undertaken from the time the client enters the palliative care service to many months after the client's death (where pertinent). These assessments are multidisciplinary and interdisciplinary as clients may disclose different information to different staff at different times.

Pre-death screening and assessment

Several tools are recommended for screening for psychosocial distress such as the Distress Thermometer (National Comprehensive Cancer Network 2013) and the General Health Questionnaire (McCabe et al. 1996; Goldberg et al. 1997). The PG-13 (Prigerson and Vanderwerken 2008; Prigerson and Maciejewski 2012) has been found to have effective predictive validity and reliability for identifying problematic bereavement experiences. Where pertinent the screening should be followed up with a comprehensive holistic assessment and/or referral to a suitably qualified professional. However, there is insufficient empirical evidence to support the validity of one particular tool to screen for risk of complicated bereavement prior to the person's death. For this reason, in addition to the use of a tool, a structured assessment should be undertaken through a conversational exploration of risk factors and strength/resilience factors.

Post-death screening and assessment

Due to the variability in the adaptation to bereavement, it is difficult to make safe predictions in terms of longer-term functioning of bereaved individuals before a minimum of 6 months post-death. There are several different tools available to screen for risk (Sealey et al. 2015); tools such as the PG-13 (Prigerson and

Maciejewski 2012) appear to have predictive validity and reliability for identifying a prolonged and complicated grief disorder.

Standard 5: Bereavement support strategies

The recommended bereavement supports include two types of strategies:

1. Universal strategies that are targeted at all carers and bereaved individuals.
2. Specialist bereavement support strategies targeted at those with elevated risk of developing prolonged or complicated grief or with current psychosocial and/or spiritual distress.

Universal strategies include:

(a) Screening and risk assessment

Screening to identify bereavement support needs does not need to be arduous or overburden already struggling palliative care services. We need to move beyond merely identifying risk factors for CG and toward an understanding of mediating factors. In this way, we can move beyond just identifying those at risk but also minimize the development of grief complications.

(b) Best-practice symptom management of the terminally ill client to reduce the impact of traumatic death on carers as well as the client themselves.

(c) Provision of structured information and support at various points along the grief trajectory including at admission to the palliative care service, when death is imminent, immediately following the death and at regular intervals following the death such as 3, 6, and around 12 months (and beyond if appropriate).

(d) Provision of access to support strategies such as participation in a bereavement information session and opportunities to review and reflect on the experience of loss and activity-based programs such as walking, meditation, and music and art groups.

Specialist bereavement support strategies may include:

Bereavement counseling and psychotherapy using evidence-informed specialist interventions for complicated grief such as:

- Cognitive behavioral therapy (CBT) for complicated grief (Boelen et al. 2006)
- Family focused grief therapy (Kissane and Bloch 2002)
- Complicated grief treatment (Shear et al. 2005)
- Meaning reconstruction approaches to grief therapy (Neimeyer 2000)
- Online support (Wagner et al. 2006)
- Bereavement support groups

In general, the more complicated the grief process, the greater the efficacy of specialist bereavement interventions. The empirical evidence underpinning these interventions should be explored comprehensively prior to implementation.

Standard 6: Clinical handover and referral to specialist services

Where provision of bereavement support falls outside the skills and competencies of palliative care staff, referral to external specialist agencies or practitioners is undertaken.

Standard 7: Community education and health promotion

The importance of promoting community awareness of bereavement issues and acceptance of the bereaved is recognized and acted upon. Information regarding grief and bereavement is available for general practitioners, employers, and other groups.

Standard 8: Privacy, confidentiality, and consent

The palliative care bereavement program ensures the privacy and confidentiality of its bereaved clients.

Standard 9: Integration with the health and support system

The bereavement support program is part of a general health and support system working to promote the health and well-being of bereaved individuals and the wider community.

Standard 10: Resource allocation

One study highlighted that less than 5% of the palliative care budget is directed to bereavement services (Breen and O'Connor 2007). Resources should be allocated in a systematic manner that allows the palliative care service's bereavement program to respond to the changing needs of clients and staff.

A key measure of quality palliative care should be the well-being of family carers in the years after relinquishing the role (Hudson 2013). Accordingly, bereavement support should be targeted, evidence based, and systematically applied. However, the development of bereavement services has lagged behind other palliative care initiatives (Morris and Block 2015), and scientific inquiry into meeting the needs of bereaved family caregivers has received insufficient attention (Stroebe and Boerner 2015).

11 Conclusion

Bereavement support is core to palliative care, yet the rhetoric is not always matched by the reality. Bereavement care is often haphazard and under-resourced and frequently does not reflect contemporary evidence.

Bereavement care is an integral component of palliative care as clinicians sustain continuity of care in assisting the bereaved. Knowledge and competency in assessing grief is essential to enable recognition of the significant minority of the bereaved who can benefit from additional assistance. Routine assessment of the bereaved for risk factors for complicated grief provides a reliable method through which clinicians can intervene preventatively to reduce unnecessary morbidity. Effective therapies are available to assist in the management of complicated grief, and palliative care practitioners should be skilled in their application or understand the circumstances when referral to more specialist practitioners is most appropriate.

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End of Life Care

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_46

Abstract

This chapter aims to tackle end of life issues for patients and their families. It will reflect on the process of disease to understand when "end of life" begins and what this stage entails. It will also address adjusting expectations and treatments, symptom management, and emotional and spiritual care at this stage of the disease. Care for end-of-life patients who are dying and their families will additionally be addressed, as well as the attention that healthcare professionals provide to patients and their families in consideration of different religious perspectives.

1 Introduction

Palliative care also involves caring for people who are nearing death and is referred to as end of life care. End of life care occurs in the last part of a patient's life, but the timeframe can be difficult to predict. Typically, it happens in the last few months, depending on the underlying diagnosis and clinical course. End of life care is an important part of palliative care for people who are nearing death.

End of life care aims to help people live as well as possible and to die with dignity. It is not just about the practical and technical delivery of medical care, but rather also involves supporting and providing available information both to patients and the people who are important to them.

Healthcare professionals should ask about patients' wishes and preferences and take them into account as they work with patients to plan their care.

2 Beneficiaries Of End Of Life Care

People in a variety of situations can benefit from end of life care. Some may have a life expectancy that does not go beyond the next few hours or days. Others receive end of life care over many months. This includes people whose death is imminent, as well as people who (NHS Choices 2015)

- Have an advanced, incurable illness such as cancer, dementia, or motor neuron disease
- Are generally frail and have co-existing conditions whose diagnosis gives them a life expectancy of less than 12 months
- Have existing conditions that make it possible for them to die from a sudden crisis in their condition
- Have a life-threatening, acute condition caused by a sudden, catastrophic event, such as an accident or a stroke

3 Changing The Goals Of Care

End of life care can be provided at home, in care homes, hospices or hospitals, depending on a patient's needs and preferences. The important thing is to have the goals of care clear.

End of life care aims to help people live as well as possible and to die with dignity and to help patients, and the people most important to them, to maintain the best quality of life possible. Holistic assessments of the patient and global care are essential for providing high quality care that prioritizes achieving patients' comfort and wellbeing, as well as that of the people closest to them, until the last days of life.

A number of healthcare professionals can be involved in care at the end of life in order to achieve the goals of care. For example, hospital doctors and nurses, general practitioners, community nurses, psychologists, hospice staff and counselors, as well as social care staff, chaplains (of all faiths or none), physiotherapists, occupational therapists, and complementary therapists, may all be involved. The healthcare professionals involved in a given care plan need to appropriately coordinate and to consider patients and families' previous experiences, including their cultural and spiritual backgrounds.

4 Diagnosis of Impending Death

Predicting the prognosis of advanced diseases can be **complex**. Patients and their families often ask for specific timeframes, which are difficult to set. But when a patient is in his last days of life, several signs help to identify this situation and, in general, healthcare professionals are more precise when the prognosis is shorter rather than longer. Professionals should be alert and prepared to detect these signs and be able to inform the family, the patient and the rest of the team about the impending end. Palliative care professionals must incorporate this responsibility into their work, which is valuable for patients and other professionals (Pontin and Jordan 2013).

4.1 The Importance Of Knowing How To Diagnose Dying

A correct diagnosis allows patients to adjust their expectations and treatment objectives during their last days.

For the family, knowing in time allows them to call upon other family members that may be farther away, to finalize preparations and pending issues, to organize religious rites according to the patient's beliefs and culture, and even to say goodbye.

For the medical team, identifying an impending terminal prognosis helps to focus all care on the patient's comfort, eliminating elements that do not contribute thereto and that may interfere with or tarnish a person's last moments. Healthcare professionals carefully review the patient's surroundings, starting with medical orders and specific and individualized care plans. They change the focus of attention to the patient's comfort in all senses, thus taking care of and accompanying him.

If an impending death is diagnosed in time, the patient can be transferred to the place where she prefers to die if it is suitable, whether that be at home or in hospice. If the situation is not properly identified, a patient may die in a place or under conditions that do not line up with their desires, or they may be on the receiving end of inappropriate or invasive measures during their last days. The task of adapting the care plan is easier for everyone if good prior communication – including a full understanding of the patient's wishes before the crisis (advanced care planning) – was established beforehand.

4.2 How to Diagnose Impending Death

This requires taking into account certain signs that the patient presents (Hui et al. 2014), some measures that can help guide, as well as the team and companions' perceptions. It is a clinical diagnosis that requires an overall view of the patient and his evolution.

4.2.1 The Signs

The most frequent signs include a marked **functional deterioration** and **dysphagia**, with patients gradually losing the ability to swallow liquids, or said task becoming very difficult, although they may still retain the ability to take

small sips. Decreased levels of **consciousness** or, occasionally, terminal delirium may be accompanied by moaning that originates in the vocal cords, including grunting or groaning, which are a sign of neurological changes. **Distal cyanosis** and lividity in the knees or thighs are easily recognizable during physical examination. It may also be impossible to feel the **radial pulse** and coldness in the hands and feet is frequent. In addition, we find changes in breathing, including periods of **apnea**, sometimes a few seconds but sometimes lasting for about a minute, or **Cheyne-Stokes** respiration (growing and decreasing periodically, with intermediate periods of apnea), superficial respiration, noisy or **rattling breathing** with jaw movements or out of breath. One of the most obvious signs is **oligoanuria**, and sometimes edema. All this can be accompanied by tachycardia and a tendency towards hypotension (Hui et al. 2014).

4.2.2 Prognostic Scales

In patients with cancer, the use of prognostic scales can be useful, such as the Palliative Performance Scale (**PPS**), which measures several parameters, including evidence of disease, the ability of patients to walk and care for themselves, and their ingestion and awareness levels. The lower the PPS score, the shorter is the prognosis. A recent study concluded that a PPS of 20% or less associated with **drooping of nasolabial fold** is a reliable predictor of a 3-day life expectancy (Hui et al. 2015). Other scales, such as the Karnofsky index or the PPI (Palliative Prognostic Index), may also be helpful in determining prognosis.

4.2.3 A Global View and Communication

When a patient is thought to be in his last days, and the above points have been reviewed, it is time to share this information with the multidisciplinary team that cares for the patient, thus facilitating adequate coordination and comprehensive care. Doctors tend to overestimate patients' prognosis, while nurses often realize the end is near first (Pontin and Jordan 2013). Sometimes, the patient himself may feel that the end is approaching. If there is a close and preestablished relationship with the patient, it is time to convey this impression and share it with the family.

4.3 How to Respond to Situation of Impending Death

The patient's last hours and care objectives should be recorded in the clinical history.

4.3.1 Emotional, Social, and Spiritual Support

The end of life has a high emotional impact in patients, their relatives, and caregivers. If a medical professional only visits the patient occasionally, it may be more appropriate for their main doctor to talk to them about the situation. The medical professional in question should begin to review and clarify the patient's wishes and their needs, which are physical, social, spiritual, and emotional, in an attempt to find out if the patient has the means and sufficient support to face the diagnosis.

The family should be informed about the signs as they present themselves, including those that will manifest in the future and their meaning and treatment. **Exploring relatives' fears and previous experiences** may help to accompany them in the process. The doctor can delicately tell the family and patient about the availability of spiritual support in accordance with their beliefs.

4.3.2 Review Medical Records

Occasionally, patients with advanced diseases accumulate medications in the last year of life (McNeil et al. 2016).

(a) Necessary treatments should be determined, which include excluding possible treatments that do not contribute to the patient's wellbeing or that could even diminish their level of comfort. This is often easy, for example, with primary prevention guidelines and more difficult with secondary prevention guidelines in patients who have already had problems like ischemic heart disease or seizures. If the patient cannot eat, the risk of hypoglycemia secondary to insulin should be assessed. Treatments that are unanimously

considered superfluous should be taken away first. In general, the **minimum** level of necessary medication should be maintained for symptomatic control to avoid side effects and interactions.

(b) Medical professionals should review how to deliver medication to the patient. If he or she has lost oral functioning, or is expected to lose it in the next few hours, the practitioner should make sure that alternative routes are identified. The intramuscular route is considered the last option, while the intravenous route is an option if already in place; otherwise, the first option is the **subcutaneous** route, which is also safe and accessible outside of the hospital context. The transmucosal or sublingual routes may be damaged by xerostomia. Adult patients and family members react poorly to rectal administration of medication in the presence of viable alternatives.

(c) Other medications should be maintained or prescribed to **prevent** undesirable situations, such as antiepileptic medicine or benzodiazepines in patients at risk for seizures. Certain prescriptions should be left to be administered **according to the nurse's assessment** taking into account that some symptoms may appear when doctors are absent. Indications, dosage, and frequency of administration should be clearly specified.

(d) The benefits and possible disadvantages of artificial **hydration** in each case should be discussed. It is sometimes necessary to relieve symptoms related to dehydration, but it can worsen others such as rales, edema, and dyspnea. Artificial calorie intake does not improve energy, extend survival, or increase comfort in the last days when the patient cannot **feed** him or herself. These issues must be delicately addressed with the patient and family, allowing them to express their opinions and emotions.

4.3.3 Increased Focus on Specific and Individualized Care

(a) Attempts should always be made to include the patient's preferences and the family's participation. Active involvement helps both parties maintain a close relationship and a helpful disposition on the part of family member(s) or loved one(s). Instructing and educating the family in care is one of the essential missions of at-home care.

(b) Special care should be taken of the **skin** by attempting to maintain adequate hydration and preventing ulcers related to pressure. This includes postural changes when the patient can tolerate them. Healthcare professionals should also attempt to maintain the patient's personal **hygiene,** adapting it to the maintenance of general comfort.

(c) Practitioners should ensure adequate care of the **mouth**, which is usually dry and can be painful, seeking to moisturize, moisten, and clean it carefully if the patient tolerates care and it brings him or her relief. For the lips, fatty preparations are better than glycerin, and sprays and swabs soaked or prepared in gel can be used for inside the mouth. **Oral ingestion** should be limited according to the patient's level of consciousness and ability to swallow because of the risk of bronchoaspiration. If feasible, the patient can enjoy cold, thick foods.

(d) If the patient is unable to move to go to the bathroom or has lost all or part of his or her **sphincter control**, practitioners should seek the most appropriate and comfortable way to meet these needs, recognizing the need for privacy and the difficulty of adapting to the loss of autonomy. A bladder catheter can be considered in some cases.

(e) The patient's **surroundings** should be taken care of, respecting natural light, but avoiding sound and excessive stimuli. Practitioners should facilitate the family's presence. The **monitoring** of vital signs will become less frequent in an attempt to respect the patient's need for rest and so as not to alarm those present. Instead, monitoring signs of suffering should be intensified and the practitioner's presence in this sense should be frequent, appropriate, and calming.

5 General Symptoms Near the End of Life

The end of life requires careful and expert management of symptoms, in addition to gentle and humane treatment at all times. Families should receive the message that this is a priority to which effort and resources will be devoted, which may comfort them and encourage them to transmit their concerns or perceptions of suffering (Blinderman and Billings 2015). Family members help healthcare professionals to detect changes in the patient's facial expression and restlessness.

The following includes a description of the most frequent symptoms and their treatment. In the context of the end of life, practitioners should seek to implement the best possible symptom control in accessible and noninvasive ways, taking into account that the patient probably cannot swallow or experiences much difficult doing so, and that a hospital is not the only place where care can occur (Kehl and Kowalkowski 2013; Bartz et al. 2014).

5.1 Pain

Pain is frequent at the end of life; 40% of hospitalized patients present moderate or severe pain in the last 3 days of life. If the patient complained of pain previously and is incapable of expressing it in his or her current state, practitioners should assume that pain medicine is still necessary and treatment should be adjusted accordingly.

Expressions associated with pain should be closely monitored; relatives and other healthcare professionals are to be asked if they detect signs of pain in the patient's movements or gestures. Careful physical examination in search of pain that cannot be verbally expressed is unavoidable; therein, healthcare professionals should look at the patient's facial gestures and his body position, trying to locate suspected pain points with palpation and any skin alterations or deformities that may cause pain.

Pain management should be effective and quick; thus, the administration of opioids is usually necessary. Oral slow release or transdermal administration is not appropriate in this situation because patients tend to eliminate waste less effectively and thus have more side effects from accumulation of metabolites. Rapid and short acting prescriptions should be used, preferably subcutaneously.

Recommended starting doses:

- Subcutaneous Morphine (consult the formulation available in each country and the recommended doses)
- Oxycodone, 2 mg, subcutaneous
- Hydromorphone, 0.4–0.8 mg, intravenous or subcutaneous

The dosage and frequency of administration should be periodically reviewed because the patient's needs may change quickly. Prophylactic doses should be prescribed for procedures known to cause pain.

5.2 Dyspnea

Dyspnea can be accompanied by weakness or anxiety and is stressful for the patient's loved ones. It is easy to recognize if the patient cannot express himself with words. It is not difficult to identify because the patient tries to open his airway as wide as possible by opening the mouth or using auxiliary muscles. Opioid management is similar to pain management, although the required doses are less and morphine is the best choice. The use or maintenance of oxygen therapy should be evaluated individually; if symptomatic hypoxemia presents itself, oxygen administration through the nasal cavity is preferable to a mask because it is tolerated better (Campbell et al. 2013). Other more general measures are effective in relieving the patient and they encourage caregiver participation. Use of a hand or small battery operated fan near the nose and mouth, thus maintaining fresh air, as well as raising the head of the bed, leaving the patient space and trying to convey a sense of tranquility, help the patient to adopt a good breathing posture.

5.3 Delirium

Once reversible causes of delirium have been ruled out, this state is referred to as *terminal delirium* during the end of life. It is often associated with other symptoms and decreases in intensity when treating pain appropriately, for example. The treatment of choice for terminal delirium is haloperidol (0.5–1.5 mg subcutaneous or intravenous), and other atypical or second generation antipsychotics may be used (Boettger et al. 2015). If the patient does not respond to these medicines, it is useful to administer benzodiazepines subcutaneously or intravenously (lorazepam or midazolam). Appropriate prescriptions include the following:

- Haloperidol, 3–6 mg, subcutaneous or intravenous over 24 h
- Olanzapine, 5–10 mg, over 24 h

The patient's surroundings must first be adapted to facilitate his or her bearings and need for rest, avoiding excessive stimuli. Professionals should explain what is happening and the treatment objectives to the family. The main objectives are to ensure calm, to prevent falls or other harm to the patient, and to alleviate the suffering it generates. Sedation is not the primary goal, although it is a frequent side effect of the most frequently used medicines.

5.4 Anxiety

In a patient's last days, it is difficult to distinguish anxiety or anguish from agitation. If healthcare professionals know the patient and have ruled out delirium, anxiety can be treated with benzodiazepines on demand or in perfusion. Doses are lower than those used for other situations and are usually sufficient with 10 mg of midazolam or 1.5 mg of lorazepam over 24 h. These doses, however, may be higher if the patient was previously treated with benzodiazepines for a prolonged period.

5.5 Nausea

As with every stage of illness, healthcare professionals should always think about possible causes to recommend the most successful treatment. At the end of life, there is an additional possibility that respiratory secretions or constipation may rarely cause nausea, although patients do not usually vomit at this stage. At times, in conjunction with postural changes, for example, patients can involuntarily expel secretions or food remains. It is likely that the cause of nausea is not specifically treatable, such that careful symptomatic management should be undertaken. Medication is chosen based on the suspected etiology and sometimes it is necessary to combine two medications to achieve adequate control.

- **Metoclopramide** is the first choice, between 30 and 60 mg over 24 h subcutaneously or intravenously.
- **Haloperidol**, if a central cause is suspected, 1.5–2 mg of haloperidol subcutaneously over 24 h.
- **Dexamethasone**, 4–8 mg subcutaneously or intravenously every 24 h, as adjuvant or in cases with clear cerebral edema or bowel obstruction; if bowel obstruction is clear and established, add Octreotide 300-600mcg over 24 h subcutaneously or intravenously.

5.6 Seizures

For patients with a history of seizures who were already being treated with antiepileptic medicine, an attempt will be made to continue administering the same medication, although the delivery method may change in accordance with the patient's state. There is evidence that supports administering some medicine subcutaneously, like phenobarbital or levetiracetam (Remi et al. 2014). For crises or patients who present seizures for the first time in their last days or hours of life, benzodiazepines are the most appropriate treatment.

5.7 Fever

Some patients have a fever at the end of life. If no obvious infection is present, it is typically associated with oncologic disease or brain damage. If a patient is unable to swallow, intravenous administration of paracetamol is effective, especially if the patient or family wishes to avoid rectal administration. If the only possible means of administration is subcutaneous, ketorolac may be used. Physical interventions help improve levels of comfort.

5.8 Rales or Death Rattle

Noisy breathing (bubbling or rales) is due to the accumulation of bronchial secretions and saliva, usually in the bronchi, trachea, and oropharynx. It may be unpleasant for the family and companions, but it is important to let the family know the person is not "drowning." Practitioners should take into account the impact that these noises have on caregivers and try to treat them when possible.

Some general measures work very well, such as postural changes, raising the head of the bed 30 degrees or the gentle aspiration of secretions if the patient is unconscious.

Depending on the availability and commercialization of some pharmaceuticals, different guidelines are used in different countries. They can cause sedation, worsen dry mouth, and even favor urinary retention. The use of pharmaceuticals that require oral administration is not feasible because patients have usually lost the ability to swallow when they have rales (Kintzel et al. 2009).

There is not enough evidence to show that any intervention is superior to placebo in the treatment of noisy breathing, and there are insufficient data (Wee and Hillier 2008).

The tested pharmacological alternatives include the following:

- **Hyoscine butylbromide (buscopan)**, 60–90 mg every 24 h or more, subcutaneously or intravenously

  It does not cross the blood-brain barrier and is less sedative.

- **Hyoscine hydrobromide (scopolamine)**

  It can be used subcutaneously, transdermally or intravenously and the usual subcutaneous dose is 1.5 mg/24 h.

  It may cause sedation and confusion or worsen delirium.

- **Glycopyrronium bromide.**

  The subcutaneous dose is 0.6–1 mg / 24 h; an oral dose can be used sublingually reducing the dose to 0.4–0.6 mg every 24 h.

  It does not produce sedation or confusion.

  A recent study advocates for the use of **atropine** (in ophthalmic form) administered sublingually (Protus et al. 2013).

  There is not enough evidence about the cardiac effects it can produce (Protus et al. 2013).

6 Holistic Care

As explained in the section above, patients experience physical changes, as well as emotional and spiritual ones, as they approach the end of life. All of these changes are part of the natural way in which the patient prepares himself for this final stage of life. The emotional and spiritual process is individual since each person is unique and needs to do things his or her own way. However, some general considerations of common emotional and spiritual processes are explained in what follows.

6.1 Emotional Care

The following includes an overview of some of the most common emotional reactions at the end of life, aiming to help understand them and to offer some suggestions on how to deal with these reactions. Hope, anger, maintaining control and dignity, and meaning-making will be discussed as part of the process of coping with and adapting to the end of life.

6.1.1 Hope

The concept of hope has been linked with treatments and cure. At initial stages of disease, patients may manifest hope for a cure, but, as the disease worsens and the end of life approaches, patients may feel that all hope is gone. This state of hopelessness can be associated with intensifying depression and a desire to die (Rodin et al. 2009). In a study involving advanced cancer patients, 48% reported at least some sense of hopelessness (Wilson et al. 2004).

Hope is present throughout the illness trajectory and changes accordingly. Palliative care certainly includes hope, though with a slightly different perspective (Nekolaichuk 2005); it identifies other things to hope for that are more achievable and involves hope for the individual. The therapeutic value of hope when it comes to life-threatening illnesses is documented. Hope has been positively linked to effective coping. Living with meaning and hope is one of the six essential elements for psychosocial and spiritual well-being (Lin and Bauer-Wu 2003). Several papers highlight the need to intentionally incorporate hope within end of life care (Sullivan 2003). This can be done by jointly identifying other things to hope for – e.g., good symptom control, staying at home, being with family – and developing realistic plans to achieve them. In addition, some interventions focused on hope for terminally ill patients (e.g., viewing a video on hope and choosing one of three hope activities to work on over a week) could be used given that there is some evidence that hope offers a statistically significant improvement of quality of life for the intervention group versus the control group (Duggleby et al. 2007).

6.1.2 Anger

Anger may arise from fear or feelings of impotence and is a reflection of one's response to the loss of control. During illness, the patient is forced to deal with a series of losses such as the loss of his or her role in life, of functional capacities, of independence and even the awareness of dying. Approaching death leads to another loss that can be expressed with inadequate demands or complaints. Anger can temporarily give a dying person the sense of being in control and block out the emotion of fear. Expressing this anger can be a process towards accepting reality and should be understood as the inability to deal with the situation at hand.

Family members may also become angry because of perceived inadequacies in care and struggles to accept that their loved one is dying.

This feeling is difficult for health professionals and requires a team response. Anger, no matter its cause, can obstruct effective interaction between the patient and the caregiver. If dealt adequately, the patient usually moves on; a painful experience full of fear can become an opportunity for forgiveness and meaning-making.

There are several steps to be taken into account when approaching anger (Philip et al. 2007). The first one involves preparing oneself for the fact that the patient is angry and seeking out an adequate atmosphere that transmits openness and allows for time to discuss. Professionals ought to clearly demonstrate being fully present with eye contact, body language, and verbal response and avoid responding with advice, critique, or reassurance. They should also offer therapeutic validation by identifying the underlying emotions and responding in a way that demonstrates an understanding of them. And they can demonstrate empathy with phrases such as, "I am sorry to hear that." It is important to listen and to engage with the patient in respectful communication, avoiding taking anger personally by remembering that anger can be a coping strategy that contains a different worldview.

In conversation, the angry person can be invited to redirect his or her emotions, encouraging reflection with questions like, "How do you manage to cope?" "What keeps you going even though you have endured so much?" "What do you think you need right now?" "How can I be most helpful to you?"

Anger can be an expression of the patient or the family's suffering. If anger persists, the care team needs to support each other when dealing with them (Philip et al. 2007).

6.1.3 Maintaining Control and Dignity

The experience of living and dying with a terminal illness shocks and shakes aspects that are

otherwise taken for granted. The patient may feel more vulnerable and question his identity, future, worth and even change his perception of dignity. In this situation, the patient is looking to gain some control over his life and death; some patients even express a desire to die in order to demonstrate some measure of control (Monforte-Royo et al. 2012).

One's perception of dignity can also be affected. The dignity of the person has become increasingly relevant in recent years in the healthcare field. A critical review of dignity models in healthcare concludes that all models consider dignity an intrinsic feature of human beings, but at the same time contemplate a subjective dimension that depends on personal experience. This subjective dimension of dignity is influenced by the person's own view of himself, the repercussion that the disease has on this view, the context, and even healthcare professionals' behavior (Errasti-Ibarrondo et al. 2014). These aspects acquire special relevance during terminal illness because the patient may feel more vulnerable. The review points out that Chochinov's Dignity Model is one of the most empirically based models applied to clinical practice (Chochinov 2002) (see ▶ Chap. 42, "Dignity in Palliative Care" for further study). It is important to highlight the concept of care tenor, which refers to the attitudes and behaviors of people who interact with the patient, which is especially applicable to healthcare professionals.

Research points out that relationships and the way in which healthcare professionals care for a terminally ill person make a difference in that patient's experience. Patients convey that authentic relationships with their nurses make them feel valued and dignified and alleviate inner loneliness (Errasti 2015). The way patients perceive of their care echoes dignity-conserving care, which promotes "being there" for the patient and interacting not only according to respective roles, but also as unique persons.

In this framework, clinical interventions have been developed to preserve and promote the patient's perception of dignity, which can be useful at the end of life. To this end, the Patient Dignity Question (Chochinov et al. 2015) stands out. It is a brief intervention to promote the patient's perception of self-value and recognition. The Patient Dignity Question proposes developing a conversation with the following questions:

What should I know about you as a person to help me take care of you?

What are the things that concern you most?

Who else is affected by what's happening with your health?

Who should be here to support you?

This kind of short intervention allows healthcare providers to get to know their patients and incorporate their values and perspectives into the care plan. A review suggests that this novel intervention is useful in approaching and getting to know a patient as a person (Arantzamendi et al. 2016). The TIME questionnaire (Pan et al. 2016) has also been developed and includes a set of questions based on identifying primary themes that emerge from the PDQs qualitative responses in order to elicit personhood and enhance dignity.

6.1.4 The Search for Meaning

The diagnosis of advanced disease and the possibility of dying often involve reprioritizing values and points of views. The patient often "opens his eyes" and sees what is really important in life. This situation leads to rethinking priorities and focusing more on what is really important as the reality of life's finiteness becomes more patent. The patient desires to achieve reprioritized goals and create a bearable or meaningful existence in the face of death.

Forgiveness may be one of these goals and may entail forgiving people who have hurt the patient, as well as asking for forgiveness from the people that the patient wronged. This is a way to diminish negative emotions and to generate well-being and calm (Mickley and Cowles 2001). This process helps re-establish relationships, close pending issues, and achieve a sense of transcendence.

Another goal entails meaning-making, even if this process is sometimes unconscious. Patients draw on their underlying beliefs, personal identities, moral principles, and religious beliefs to make sense of their situation. And, in so doing,

they search for meaning. The meaning left in their lives often corresponds to caring for others, resolving pending matters, and doing what they can to improve the lives of those they leave behind.

Valued relationships become even more important and relationships that were previously taken for granted, often with partners, children, and grandchildren, become more cherished (Sand et al. 2009). This sometimes entails saying goodbye and transmitting gratitude and love to loved ones. In this process, in cases where there are small children, the patient may aim to help them understand the situation and to transmit messages they consider vital. This can be seen as a luxury, since, as one patient said, "*Saying farewell to my children has been hard, but it is a luxury. Yes, yes, I said goodbye to the relatives that matter most to me and my best friends... It was a truly beautiful and fantastic experience that meant a lot to me because I could say goodbye to my wife, my children, my mother, my brothers, my friends ... to all the people that matter to me! I told them that probably not even Onassis or Rockefeller or anyone else had the opportunity I had. And that, to me, is a luxury*" *(Garcia 2017).*

Some people find meaning themselves, while others may benefit from specific interventions such as meaning-centered therapy (Breitbart et al. 2010; Breitbart 2002), dignity therapy (Chochinov et al. 2005; Aoun et al. 2015; Chochinov et al. 2011) (Martinez et al. 2017), or life reviews (Ando et al. 2010) that enhance a sense of meaning, peace, and purpose in their lives as they approach the end of life. Spirituality can be another source of meaning for people at the end of life and indeed constitutes an integral part of human life, which will be explored in what follows.

6.2 Spiritual Care

An acknowledgment of spirituality is necessary at the end of life, as well as throughout the advance of illness (Balboni et al. 2007), and influences decision-making when it comes to care (Silvestri et al. 2003).

From its origins, palliative care has included spiritual care as an essential part of caring for patients (Saunders 2001; Saunders 2003) (see ▶ Chap. 41, "Spirituality in Palliative Care"). It is one of the eight domains of quality palliative care and, as the consensus report developed by 40 health-related Canadian national leaders states, it is crucial (Puchalski et al. 2009).

The term spirituality has different connotations in relation to different backgrounds (e.g., Roman Catholic, Protestant, Eastern religions, or those with no faith at all). Herein, a broad definition is employed. Spirituality is understood as "the dynamic dimension of human life that relates to the way person[s] (individual and community) experience, express and/or seek meaning, purpose and transcendence, and the way they connect to the moment, to self, to others, to nature, to the significant and/or the sacred" (Leget et al. 2014).

Spirituality is a movement of personal searching in three directions: towards the innermost self in search of meaning, towards one's surroundings in search of connection, and towards the beyond in search of transcendence (Gomis et al. 2017). In this movement, many people who are confronted with a life-threatening illness begin to ask themselves "big questions," such as "What did I do wrong?" "Why do I have to suffer?" "Why should I go on living?" "Am I not just a burden to others?" This line of questioning can be called **spiritual** or **existential questions**.

Whether or not a person has expressed spirituality at other moments, the end of life experience will often lead to further exploration of this realm. Many people seek answers from within their life view or religion.

6.2.1 The Natural Course of A Spiritual Process

On life's path, everyone goes through a kind of spiritual process by which the uncertainty of existence is replaced by a kind of purpose or meaning. In this natural process, a number of themes can be distinguished (Leget et al. 2014).

- **Awareness of finiteness**: The moment that disease poses a threat to existence, the patient becomes aware of his or her finiteness. Some

people struggle with it, while others panic. This awareness may also cause the patient profound loneliness as they struggle to deal with and talk about it.

- **Loss of grip on life**: Being aware of one's finiteness causes the patient to feel as if he has lost his grip on life. The constructs of meaning he regularly relied upon no longer suffice for many aspects associated with a threat to existence.
- **Loss of meaning:** When death approaches, a sense of the future is lost. The patient often perceives his experience as unreasonable and meaningless.
- **Bereavement process**: The bereavement process begins when an awareness of all the things one must let go of, such as loved ones and plans, sets in.
- **Experience of connectedness**: This term is used to distinguish it from ways in which the patient previously searched for and found meaning. This experience may be new for the patient and therefore difficult to verbalize.
- **Integration of meaning and the experience of connectedness**: This happens when the search for meaning and the experience of connectedness are again integrated. When finiteness has been integrated into a system of meaning, the patient focuses more on the here and now and usually undergoes a shift in priorities.

6.2.2 Healthcare Professionals and Spiritual Care

During this natural process, the patient is searching and sometimes struggling to find his or her way. Healthcare professionals should be open to considering the spiritual dimension. What should healthcare professionals do specifically?

It is indispensable for healthcare providers to be open, which facilitates an appropriate atmosphere and attitude. Next, healthcare professionals should seek to offer some spiritual accompaniment, understood as the practice of recognizing, welcoming, and giving space to the patient's inner dialogue, such that he himself can give voice to his questions and life to his answers (Gomis et al. 2017). This spiritual accompaniment is part of palliative care's dynamic of interdisciplinary teamwork. It requires detection, exploration, and intervention.

- **Detection** is the responsibility and task of all team members; it consists of using various indicators or "warning signs" to detect the emotional expressions, values, and ethical conflicts, etc., that accompany spiritual experience. One must be attentive to expressions of hopelessness, to phrases like "I do not feel prepared to face the end" or "I think it's time to throw in the towel," and to objects that support a spiritual practice (e.g., certain books the patient is reading or religious icons in the room).
- **Exploration**: Some suggest that the relevance of spirituality for patients should be systematically evaluated. Instruments have been developed to this end, such as FICA (Borneman et al. 2010) or SPIRIT (Taylor 2006).

  From a different perspective, the beginning of spiritual exploration requires establishing a relationship of trust and a therapeutic link to identify suffering and its perceived causes or threats and to try to resolve or neutralize problems that can feasibly be dealt with (Gomis et al. 2017). In this preliminary part, exploration of the experience of suffering as a problem is fundamental, as well as being aware that people define existential suffering differently (Boston et al. 2011). Subsequently, variables in the experience of suffering are seen as a mystery, as an existential condition. In this approach, three levels are involved in spiritual exploration (Gomis et al. 2017).

  The **general level** explores worries, as well as the degree of difficulty in facing them, resources where help can be found, and the patient's expectations about the extent to which healthcare professionals can help. Questions that may be useful are: Is there something that, in this situation, worries you? In your current situation, what is most helpful to you? Is there something more that you think we could do and that could help you? The **intermediate level**

explores the resources and/or concepts that help patients through the process of dying, as well as the existence of certain questions (which express unresolved needs) and the degree to which they influence the patient's process. Some useful questions include other patients in situations similar to yours tell us that, in order to better support illness and everything associated with it, it is very useful to have a certain meaning in life, a way of understanding illness, relationships, your personal story, and so on. Do you have something like that? The s**pecific level** explores more explicitly the spiritual and/or religious realm, its potential benefits, one's desire to deepen therein, and the need to search for another interlocutor. Some questions that may be useful for this exploration include: Do you have any spiritual or religious beliefs? If so, how are they helping you in your situation?

These questions may be useful for exploring spirituality in a natural and nonthreatening way, but should not be used as a questionnaire, thus respecting the patient's personal dynamics. In fact, depending on the patient, third-level questions may appear in the conversation associated with the first level.

- **Intervention:** The mere fact of exploration has a therapeutic element and supposes – in some way – a potential first-level intervention because the patient perceives that someone cares about his person in its entirety. In addition, exploration already has a therapeutic edge because it facilitates a clarification of the internal world (Gomis et al. 2017).

  Specific guidelines have been published addressing the issue of spiritual support or accompaniment (Lo et al. 2002) (Rodin et al. 2009), and interventions have also been developed (Boston et al. 2011), such as a life review, meaning-centered therapy, or dignity therapy, which were mentioned earlier as therapies that promote meaning.

In the process of accompanying a person at the end of life, there may be conversations about death and about how he or she envisions and wants to prepare for it. The patient may appreciate having someone to talk to about this and patients often choose healthcare professionals to have this conversation with. In this type of situation, the practitioner must take a deep breath and stop to really listen to the patient, taking into account that, although death is a universal fact, not everyone faces it in the same way since one's history and culture strongly influence this realm. Listening attentively and responding to concerns, as well as taking about the patient's wishes at the end, are key elements of this conversation (National Institute for Health and Care Excellence 2017).

Reaffirming that the patient will be cared for until the end and that the medical professionals involved will accompany him and help him through the process of death is vital for the patient to feel comforted and recognized as a person. In some situations, various interventions meant to adequately relieve end of life suffering fail and palliative sedation may be considered (see ▶ Chap. 87, "Palliative Sedation: A Medical-Ethical Exploration").

7 Caring for the Family

As mentioned previously, the end of life affects patients, as well as their families. The concept of family is in constant evolution. It has cultural, legal, and sociological definitions – and different cultures define family in a variety of ways. Traditional definitions of family include what is referred to as the nuclear family – including a father, mother, and one or more children – or the extended family that includes grandparents, aunts, uncles, and cousins. Here, family caregiver is broadly defined and refers to any relative, partner, friend, or neighbor who has a significant personal relationship with and provides a broad range of assistance to a person with a chronic or disabling condition (Blum and Sherman 2010).

Palliative care includes caring for the family through the disease process, including at the end of life. The patient's family is like an important ally whose power must be recognized. Family members know the patient better than anyone and can help healthcare professionals do their

jobs. However, the end of life is an emotionally demanding time for the family and they also require the attention of healthcare professionals, taking into account the family's beliefs about health and illness, the culture they belong to, as well as the family's dynamics.

7.1 Preparing the Family for Impeding Death

A loved one's last days has an important emotional impact on the family. Healthcare professionals should consider who they are, as well as their family culture and history (especially religious/spiritual leanings) when caring for the patient and family. Healthcare professionals should consider the following:

- Provide the patient's family with **accurate information** about the prognosis, explaining any uncertainty and how it will be managed and, in so doing, avoiding false optimism (National Institute for Health and Care Excellence 2017). The disease progresses and the patient experiences functional decline. The family perceives that the situation is worsening and that their loved one is becoming weaker, but sometimes is not aware that death is so near. Healthcare professionals can help the family adapt and understand that their loved one is close to death.
- Provide family members an opportunity to talk about their fears and anxieties and to ask questions.
- Provide **information about how to contact healthcare professionals** – especially if the patient is at home – including contact details for relevant after-hours and emergency services.
- Explore the family's fears and previous experiences, since they sometimes make demands that do not line up with the patient's situation based on previous negative experiences.
- Explore whether the patient has prepared a written statement or has verbally stated **preferences about their care during the last days of life** (including any anticipated prescriptive decisions, advance decision to refuse treatment in certain cases, or details about any legal power of attorney for health and welfare).
- Explain that you will continue to care for the patient, prioritizing her comfort and wellbeing. This is an emotionally intense situation for the family, making it advisable to explain that healthcare professionals are on their side and will continue to care for both the patient and the family. In this phase, family members pay close attention to the interactions between healthcare professionals and the patient; it is thus essential to continue providing respectful and quality care that conveys that the patient is truly valued.

7.2 Caring for a Dying Person's Family

Healthcare professionals are supposed to witness and support the family's growing awareness of their loved one's deterioration and medical issues, including what these revelations mean for the family's future. Healthcare professionals have two important roles: to support family-patient interactions and taking care of family members.

The dying process is a roller coaster of emotions for the family too. **Sometimes family members do not know how to interact with a dying person**. Staff should suggest that family members remain themselves as the dying person continues to need intimate, natural, and honest relationships. The family should understand that they do not have to hide their tears, as crying is a way of showing love.

Healthcare professionals should promote discussions with the family about the role they want to play in the patient's care, remembering that it is very important to treat this topic delicately. Some family members may want to be involved in simple activities such as mouth care, while others may not feel comfortable being involved in direct patient care.

Healthcare professionals can encourage the family to think about and **discuss how they want to spend the final weeks and days**, taking advantage of the time that remains with their

loved one. They can decide to spend time together talking, simply being, or recalling old memories. It is important to promote meaningful interaction for the current situation and for future memories.

Healthcare professionals can also explain to relatives the importance of being thoughtful and that the patient feels their love and care. It is important to **show kindness,** as well as convey care and acceptance, thus building trust and enhancing self-esteem. It is helpful for family members to hold the patient's hand, listen to his stories, or just be with him, which will mark the family's future memories. It is not the time to try to change a loved one, but rather a time for full acceptance, support, and comfort.

It is also important to explain to the family the importance of **talking about death** when both parties are ready. While it is difficult to talk about, discussing death can ultimately alleviate fears and foster stronger emotional bonds between the patient and the family. It can help the family reflect on the importance of understanding their loved one's final wishes, so that they can carry them out as fully as possible. Some suggestions for this conversation include the following (Family Care 2016):

- Always use language about death that everyone is comfortable using. Try not to avoid using the word, but feel free to use metaphors or softer words (e.g., "pass away") as long as the fact that death has occurred is clearly explained.
- Do not rush the conversation. Make time for your loved one and realize that you might have to do so on a flexible schedule – predicting when someone will feel comfortable discussing death is often difficult.
- Do not discredit any of the emotions that you, or your loved one, feel. Be sure to acknowledge that these emotions may influence both parties' words and behavior. This will help your loved one to better understand.
- If a loved one brings the topic up and it scares you, do not shut the individual down by saying something like, "don't say that." Instead, even if you are not ready to talk about it, let your loved one discuss his/her feelings. Keep the conversation going by saying things like "really?" or by rephrasing what he or she has already said.
- Finally, talk about your loved one's current condition and his/her hopes or fears for the future.

Saying goodbye is an important part of the patient-family interaction at the end of life. Staff can facilitate it by highlighting its importance and suggesting it as a final gift of love since it contributes to closure and makes the final release possible. It may be helpful to suggest that family members sit close to the patient, take his hand, and say everything they need to say. It may be as simple as saying things like I love you or thank you; or it may involve recounting meaningful shared moments or saying sorry for whatever contributed to any difficulties in the relationship. Tears are a normal, natural part of saying goodbye and should be understood as an expression of love. Healthcare professionals should, in turn, promote an environment that facilitates saying goodbye. This includes adequate symptom control, giving the patient and family privacy by allowing them to be alone and ensuring a pleasant environment.

Healthcare professionals need to address caregivers' needs in a sensitive way, supporting them emotionally. Some suggestions include the following (Centeno et al. 2009):

1. Recognizing the family's suffering and taking an interest in how they are, may be enough for them to open up, improve their attitude toward professionals and share their concerns. It is important to use room visits to assess the family's needs, asking what help they need and how they perceive the patient's state.
2. Be willing and accessible so that the family can express their emotions. Reiterate your offer to help with any of their current needs.
3. Explore with the family the role they wish to have in caring for their loved one. This serves as a manifestation of affection and helps them to feel useful.

4. Explain that you cannot know exactly when the end is near, but do explain the patient's possible course to the family. In particular, it is important to explain, as mentioned previously, possible cognitive changes, the progressive decrease of consciousness, and respiratory difficulties. The impending death of a loved one is always a difficult emotional time, but knowing what to expect can help the family prepare.
5. In the case of families with children, it is important to help children situate themselves and prepare for their loss. The sooner children know what is happening, the better. It is important to reassure children that they did not cause this loss. When adults do not explain things to children, they are faced with drawing their own conclusions, which tend to be much worse than the facts. Ultimately, children are flexible and resilient and can deal with reality.
6. Allow the family to participate in decision-making, ensuring that the family agrees to and understands any changes to the care plan and that said changes are recorded in the clinical record.
7. Offer spiritual support to the family according to their beliefs. Spiritual care as a component of palliative care is also important for those close to the patient since their loved one's impending death can evoke spiritual questions for them as well.
8. Help the family prepare for the death of their loved one, as they may be prepared for the dying process but not for the actual moment of death. It may be helpful to encourage the family to think about and discuss what they want to do at death (i.e., funeral home, prepare the body). They may have talked with their loved one about it or they may know what he or she would like.
9. At the right time, the professionals in charge of the patient's care should discuss with the family the paperwork that needs to be done when the patient dies. Planning a funeral is a complicated process, which is made even more difficult by the emotional stress that accompanies the death of a loved one. Thinking ahead of time about these arrangements decreases the burden on those left behind.
10. Healthcare professionals should support family members who arrive after the patient has lost consciousness or has died, and thus have missed the opportunity for meaningful interaction. They may benefit from information about the patient's state, such as skin temperature and color change, or the jaw being relaxed and the mouth slightly open. Professionals should support them in having private time with the patient should they wish. This might not be an intuitive step for families, and encouragement from staff may be needed.
11. When the patient dies, the family should be supported and, without rushing anything, should be given a few moments of privacy if they wish. After this, the care needed in this situation can be performed, which will be explained later.
12. Help the family with the bereavement process. This can include a phone call to see how the relatives are doing or a condolences letter. There are also a variety of interventions specific to bereavement care, as shown by a systematic review (Forte et al. 2004).

8 Impact of End of Life Care on Healthcare Professionals

Working with patients who have incurable diseases and those in the process of dying exposes professionals to the physical, psychological, and spiritual suffering of patients and their relatives (Hanks 2009). This exposure means that working in palliative care can be challenging, rewarding, and stressful (Bruera et al. 2015). Professionals face a difficult reality that contains different kinds of suffering, a mix of feelings, and questions without answers. This reality may also force professionals to deal with their own mortality, fears, vulnerability, and the meaning they draw from life.

8.1 Definition and Overview of Distressing Experiences

There are a number of distressing experiences that palliative care professionals have to deal with. The most frequently researched are stress, burnout, and compassion fatigue.

8.1.1 Stress

Stress is defined as the body's physical, mental, or emotional response to change (Selye 1980). The European Agency for Safety and Health at Work has defined work-related stress *"in terms of the 'interactions' between employees and (exposure to hazards in) their work environment. Within this model stress can be said to be experienced when the demands from the work environment exceed the employee's ability to cope with them."*

Some studies have found that staff working in palliative care have less stress than other professionals working with patients (Bruera et al. 2015; Berman et al. 2007), but this does not mean that stress does not occur.

8.1.2 Burnout

Burnout is defined as "*the progressive loss of idealism, energy and purpose experienced by people in the helping professions as a result of the conditions of their work*" (Edelwich and Brodsky 1980). In addition, "*The root cause of burnout lies in people's need to believe that their life is meaningful, and that the things they do- and consequently they themselves- are important and significant*" (Pines 1993). It is a response to work-related interpersonal and emotional stressors and has three key dimensions: (1) overwhelming emotional exhaustion (EE), which is the basic individual stress dimension of burnout, (2) feelings of cynicism and detachment from the job, i.e., depersonalization (DP), which is the interpersonal context dimension of burnout, and (3) a sense of ineffectiveness and lack of personal accomplishment (PA), which is the self-evaluation dimension of burnout (Pines 1993). Yet, recent research shows that staff working in palliative care may in fact experience lower levels of burnout than professionals from other disciplines (van Staa et al. 2000; Hospice Friendly Hospitals Programme 2013).

8.1.3 Compassion Fatigue

This fatigue refers to an acute onset of physical and emotional responses in relation to work that culminate in a decrease in compassionate feelings towards others (Sinclair et al. 2017). It is considered a significant stress response in healthcare providers. The signs and symptoms of compassion fatigue can be classified as physical, behavioral, psychological, and spiritual and are thought to have a global impact on healthcare providers wellbeing (Sinclair et al. 2017).

Six occupational areas are associated with the factors that add to distressing experiences, including: (1) workload and intensity of work, (2) lack of autonomy, (3) social climate at work, (4) emotional demands on staff associated with multiple bereavements and grief, as well as exposure to patients and families' distress, and personal discomfort with suffering and death, (5) conflicting values and meanings that arise between the employee and health institution, and (6) working conditions (Bruera et al. 2015).

8.2 Facing Difficulties: Resilience

Resilience is an individual's ability to adjust to adversity, maintain equilibrium, retain some sense of control over one's environment, and continue to move on in a positive manner (Jackson et al. 2007). About resilience nature, Jackson (Jackson et al. 2007) believes that individuals can develop and strengthen personal resilience by developing strategies that reduce their own vulnerability and the personal impact of adversity in the workplace.

8.2.1 Strategies Against Professional Distress

A recent literature review (Hospice Friendly Hospitals Programme 2013) presented five elements that are effective in promoting resilience and avoiding distressing situations: (1) self-care strategies, (2) the creation of support groups, (3) the cultivation of supportive inter-professional relationships, (4) education and skill-building, and (5) meaning-making through ritual or commemoration.

1. ***The four dimensions of self-care***

   Caregivers cannot meet their patients' needs if their own needs are not met (Huggard and Nichols 2011) (Cohen et al. 2001). Self-care is associated with lower levels of stress and burden (Merluzzi et al. 2011) and emphasizes the obligation to take time for self-care (Cohen et al. 2001). This dimension includes maintaining one's health and wellbeing and exploring the feelings derived from being surrounded by difficult situations.
2. ***Inter-professional or specialty-based support groups***

   Inter-professional support groups are based on the idea that supporting the needs of professionals working with incurable disease may improve job satisfaction and prevent compassion fatigue (Hospice Friendly Hospitals Programme 2013) (Huggard 2012) (Wenzel et al. 2011). Several types of support groups are recommended depending on the characteristics of the person in need of support (Huggard and Nichols 2011) (Le Blanc et al. 2007) (van Staa et al. 2000).
3. ***Building supportive teams***

   Teamwork is the central idea of palliative care. This strategy is found in the idea of becoming a supportive team instead of just practicing teamwork. Some studies show improvements as a result of becoming a supportive team (Le Blanc et al. 2007) (Wenzel et al. 2011).
4. ***Education and skill-building***

   There is a need for continuing education focused on developing strategies that enhance professionals' coping skills (Wenzel et al. 2011) so that they can effectively assist in daily patient care. One study argues that end of life care providers "need to be taught a rational concern, which allows the expression of feelings without impairing the ability to make decisions, rather than a detached concern" (Le Blanc et al. 2007).
5. ***Meaning-making.***

   Spending "therapeutic time" with patients can be beneficial for both the patient and the caregiver (Cohen et al. 2001). This can help the professional to consolidate his or her experiences into meaning structures; the individual ability to make or find meaning can transform intensely stressful situations into positive experiences and can serve as a "profound motivational force" that improves quality of life (Desbiens and Fillion 2007).

9 After a Patient's Death

Procedures after death may vary locally so practitioners should be aware of local regulations, considering that they may differ depending on if death occurred at home or in the hospital.

9.1 Tasks to Be Completed After a Patient's Death

In today's hospital environment, it is clear that some relatives do not know what to do after their family member dies, so it is necessary for healthcare professionals to guide the family in the tasks to be completed, including:

(a) Tell the health professional to certify the death.
(b) Contact a funeral service.
(c) Specify the conditions, time, and place of burial/cremation.
(d) Write a notice for dissemination, indicating if a religious funeral will take place and the place of burial/cremation.
(e) Talk to the people close to the deceased and invite them to attend the funeral(s) and burial/cremation.
(f) The deceased's religious creed and his last wishes in this regard must be respected. The funeral chapel and the family and friend gathering' will accommodate the deceased's traditions.
(g) After a few days, it is recommended that relatives respond to the condolences they received.

Although the patient has passed away, healthcare professionals still have other things to deal with, including caring for the family, caring

for other patients who were close to the deceased, as well as caring for the medical team and for the deceased patient (corpse) (Centeno et al. 2009).

9.2 Caring for Family Members

The death of a loved one affects relatives emotionally, which is why the medical team must employ special tact. Family members can react very differently immediately following a loved one's death, and professionals need to know how to understand and respect all of these reactions. Professional must be available and must act naturally, displaying certain closeness. Words may be superfluous at this time and the family is often just grateful for the company (Centeno et al. 2009).

9.3 Caring for the Team

The death of a patient affects caregivers and, when it happens on a daily basis, caregivers' moods can be affected. It is therefore important to develop protective mechanisms for both individuals and for palliative care teams. In this context, it helps to share lived experiences, to review how the patient was cared for, and to recognize the work completed (Centeno et al. 2009).

9.4 Postmortem Care

Once the patient has died, death should be confirmed through available techniques by checking unmistakable signs, usually by means of an electrocardiographic record at the time that the doctor responsible for certifying the death of the patient deems necessary.

Professionals must take into account that sedated patients may have prolonged apnea pauses before dying, so they must rule out any confusion with a situation of apparent death.

After the health professional has verified the patient's death and confirmed it with the family, they should be allowed to remain as long as they need with the deceased, so that they can express their emotions.

Once the family has stayed with the patient as long as they need, they will be invited to move to another unit while health professionals proceed with the postmortem care of the deceased. This care consists in hygiene, withdrawal of clinical devices, and arrangements so that the deceased is in adequate conditions to be seen by relatives who wish to say goodbye. The corpse must be wrapped in a clean sheet or shroud. The deceased's privacy and right to professional secrecy should still be protected.

9.5 Farewell Rituals

A wake involves caring for and accompanying the deceased, and traditionally happened at night. Previously, the wake took place in the deceased's home since people usually died at home. Today, most deaths occur at a hospital, so the deceased is usually transferred to the hospital's mortuary or to the morgue (Centeno et al. 2009).

The deceased's religion and customs determine the relevant funeral rites. Today, different cultures and religions coexist and the rites involved in each case should be respected.

10 Religion and the End of Life

Care for dying patients has always existed in one form or another, but the modern hospice and palliative care movement is intimately associated in its origins with religious orders that cared for those suffering from life threatening illnesses and nearing the end of their lives. In fact, by the middle of the nineteenth century, a number of institutions and hospitals started establishing centers uniquely devoted to care for dying patients (Clark 2016).

Nowadays, even in the most commonly used definitions of palliative care, the spiritual component is included as a key element. The World Health Organization defines palliative care as "an approach that improves the quality of life of patients (adults and children) and their families who are facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification

and correct assessment and treatment of pain and other problems, whether physical, psychosocial or spiritual" (WHO 2017). After all, palliative care supports the person as a whole, which necessarily includes the spiritual dimension.

The importance of religion in palliative care is thus evident, and when reviewing current literature, there is a reasonably large body of research on this topic. Most existing studies have evaluated different religions and their impact on perceptions of palliative care (Steinberg 2011); they commonly note that most palliative care patients have spiritual needs that palliative care providers do not properly address (Richardson 2014). Similarly, in another study, under the assumption that "attending spiritual needs ensures that a dying patient has the chance to find meaning in the midst of suffering," a list of beliefs and traditions from Judaism, Islam, and Christians are presented, along with the way in which they portray dying and mortality (Puchalski et al. 2004). The idea of spirituality being a fundamental element of human experience is deeply established, along with how – viewed in this sense – "spirituality can be a key factor in how people cope with illness, and achieve a sense of coherence" (Puchalski et al. 2004).

Religion is also important during end of life care because it influences ethical (and therefore medical) decisions, which suggests that physicians and nurses should understand religion and spirituality in order to understand people's choices and "to respect their conscience and worldview" (Broeckaert 2011).

The importance and existence of diverse religions suggests the need to better understand them and how they consider issues related to dying since views associated with different religions can be essential knowledge when treating patients. Different religions hold diverse premises that most certainly influence the way a patient should be cared for. There are a few manuals/guides that present information on each religion, focusing on doctrinal elements and beliefs in relation to the concept of illness and death, as well as morality, behavior and commitments, practices and rites, prayers, organization, etc., which are all related to and closely conditioned by the specific religion (Unescocat et al. 2013).

Table 1 presents the most relevant considerations on illness, rituals, and death associated with the world's major religions (Unescocat et al. 2013), but a deeper reading is recommended when

Table 1 Considerations by religion (Unescocat et al. 2013)

	Illness	Rituals before death	Death and other considerations
Catholicism	Pain, disease, and death are all part of life Everyone should care about the sick, seeking to heal them and alleviate their suffering	Anointing of the Sick: The sign of the anointing of the oil gives "a special grace to the Christian experiencing the difficulties inherent to the state of serious illness or old age." The priest prays for the patient's health that he may be granted "strength, peace, encouragement, and the forgiveness of sins"	Death is perceived of differently by thinking of Jesus Christ on the cross and of the difficulties that other saints went through Even though the body ceases to have life, the soul survives and appears before God to be personally judged. The corpse must be treated with respect
Islam	Illness is considered a test of faith and not a punishment. The sick are encouraged to find healing and doctors to thoroughly seek a remedy. But ultimately God allows for healing; doctors and remedies are only means	When death nears, place the patient on his side, with his head facing the Qibla. If that is not possible, then place him lying on his back with his feet towards the Qibla. When suffering becomes intense, people in the room recite the Surah Ya-Sin and recite the profession of faith	Death is the beginning of another phase of existence, the return to God Each person dies at the appointed time and place After death, the eyes are closed and the body is covered. The corpse should be moved with the utmost respect, especially keeping in mind that private parts should remain covered

(*continued*)

Table 1 (continued)

	Illness	Rituals before death	Death and other considerations
Buddhism	Illness is inherent in the nature of living beings. It is the result of negative actions in the past and, at the same time, an opportunity to be free of them	The patient should be in an atmosphere that supports peace of mind. Sometimes, Buddhists give up painkillers to preserve a certain lucidity of conscience before death, which allows them to meditate	Death is the end of current bodily life, but not of individual existence The body must be wrapped in a plain sheet free of symbols. The body must be respected in this state for 72 h
Hinduism	Some consider Western medicine to numb the mind and pollute the body. Thus, they may resist treatment	When death is imminent, the patient is placed with his head facing eastward and the family may request that a lamp be lit near his head, asking those around him to focus on his mantra. The body is left in the foyer or on the floor of the hospital facing south	Death is a natural phenomenon of a life. It is a cyclical transfer from one vital state to another Once dead, the body and the religious objects adorning should not be touched. If you need to touch the body, you should check with the family
Chinese traditions	The rupture of the harmony in human relationships (Confucianism) or of human beings with nature (Taoism) manifests itself in disease since, in Chinese medicine, health is a state of physical and spiritual harmony with nature	Before death, the dying must see each of his relatives. Death is announced in community. The body is bathed in fresh water to make the trip to the next world comfortable. Relatives light an oil lamp at the feet of the body to illuminate their loved one's way to heaven and immortality	Confucianism does not tout the existence of another life after death For Taoism, death is a door to immortality and a release of the body

caring for patients of each religion or a patient of another minority religion.

The implications for medical practice are subsequently based on the fact that spirituality is an essential dimension of integral attention and that death and dying is interpreted depending on specific religious or personal convictions when facing the end of life. Thus, in the end, we aim not only to be respectful of everyone's beliefs, but also to know or at least have material on hand that provides information about the different religions and their associated convictions.

11 Summary

This chapter has explained the context of end of life care and its goals in caring for the patient and family. Palliative care prioritizes comfort, wellbeing, and dignity until the end.

The text additionally highlights the importance of diagnosing impending death such that healthcare providers are able to offer personalized quality care for the patient and the family as the end nears. Recognizing that a patient is nearing death helps professionals adapt physical care and symptom control, in addition to helping them accompany the emotional and spiritual process that facing death involves, whether as the patient or a family member.

Caring for patients and their families at the end of life is challenging, and it is important that healthcare professionals incorporate activities that promote self-care and resilience to avoid falling into burnout or compassion fatigue.

For reflection

The way in which the end of life unfolds leaves an indelible mark on those who

(*continued*)

accompany the dying, thus healthcare professionals have a fundamental role in ensuring that companions' memories are full of peace and, as much as possible, the absence of suffering.

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Palliative Care Education: An Overview 49

Lis Latta and Roderick D. MacLeod

Contents

Abstract

Education has been a core function of all practitioners in palliative care since the birth of the modern hospice movement. Much progress has been made since palliative medicine was first recognized as a discrete medical specialty. In order to understand the complexities of education in this area, this chapter provides a broad overview of issues related to palliative care education from undergraduate students to continuing and postgraduate training and to the

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_95

needs of family carers and staff who work in residential aged care facilities.

The chapter initially outlines some of the principles of adult education by drawing on the work of several key theorists and then discusses the sociopolitical context of palliative and end-of-life care with due consideration to the changing needs of society. Evidence of progress in undergraduate and continuing education is presented and discussed as well as opportunities for advanced specialty training.

The learning needs of family carers and staff who work in residential aged care facilities are addressed with examples of the types of education and training that is available for these essential providers of palliative care and whose needs are often overlooked in traditional educational settings.

Finally, we provide examples of the many and varied educational methods that are currently in use including simulation, interprofessional education, and learning in the clinical setting.

I never teach my pupils, I only attempt to provide the conditions in which they can learn.
–Albert Einstein

1 Introduction

The development of palliative care as a discrete and recognizable medical specialty in the UK in 1987 presented new challenges to educators in the health professions. Until that time, the main focus of health professional education had been on knowledge and skill acquisition that was focused on cure, which was unsurprising given the advances in medical science and technology that occurred in the first half of the twentieth century. However, this single-minded focus on curative treatment denied many people a peaceful and dignified end to their life and replaced it with aggressive and invasive treatments that carried little if any benefit. The modern hospice movement grew out of an awareness that the care of people who were dying fell far short of what many people in modern society deemed acceptable, and as such, a new dimension to the training of healthcare professionals for the future began with the introduction of teaching in palliative care.

Because of the technological advances in medicine toward the end of the twentieth century, medical education in palliative care tended to focus primarily on techniques for the control or management of symptoms, and there was a real fear by some that palliative medicine would merely become synonymous with symptom management. From an educational point of view that has some attractions, it is far easier to gain knowledge of drugs and how to use them than it is to try and understand the lifeworld of someone close to death. However, symptom management is but one important area of palliative care. It is equally important to learn how to *be with* patients and families who are facing death and how to respond to and relieve suffering in all its guises.

It is impossible to overemphasize the importance of palliative care education, particularly in light of the changing needs of a rapidly aging population with a high prevalence of noncommunicable diseases. In order to be able to provide high-quality care at the end of life and avoid unnecessary suffering, the people who provide that care must be equipped with the necessary knowledge, skills, and experience to be able to do so. Palliative care education must therefore be widely available in the community and accepted as a core component of learning in the health and social care professions. This chapter begins with an overview of relevant adult learning theory before going on to discuss particular issues related to palliative care education and training.

2 Understanding Adult Learning

Once qualified in their chosen speciality, much of health and social care professionals' learning is self-directed, which requires individuals to be reflective, self-aware, and self-motivated learners and practitioners. All of these skills are essential attributes in the provision of high-quality patient care. Self-directed learning can be described as a process in which individuals take

the initiative, with or without the help of others, in diagnosing their learning needs, formulating goals, identifying human and material sources for learning, choosing and implementing appropriate learning strategies, and evaluating learning outcomes.

Self-directed learning takes a variety of forms ranging from informal and unstructured activities to intentional formal educational endeavors based on identified learning needs. Many hospices around the world offer continuing education programs for healthcare professionals with St Christopher's Hospice in London being an outstanding example as the pioneer of the modern hospice movement (www.stchristophers.org.uk/). Conferences, seminars, and workshops also provide a useful avenue for further learning, keeping up to date with recent research, and networking with colleagues who share similar interests. While many countries have excellent national palliative care meetings, notable international palliative care conferences include the International Congress on Palliative Care, the European Association for Palliative Care Conference, and the Asia Pacific Hospice Conference.

There are various types of self-directed learning, all of which are employed by healthcare and social care professionals at various times depending on their learning needs and professional requirements.

2.1 Informal Self-Directed Learning

This is seen as part of the normal day-to-day activity of professional development. There are no specific objectives, but it is rather an attempt to keep abreast of recent developments. The sort of activities included here are journal reading, ad hoc conversations with colleagues or experts (known as educational influentials – professional peers who are deemed to be experts in their field and therefore influential), attendance at regular continuing education meetings (grand rounds, journal clubs, etc.), preparation for lectures, or writing. Often these activities are not documented and are difficult to quantify, evaluate, and assess.

2.2 Semi-structured Self-Directed Learning

These activities are based around specific clinical problems. The clinicians have specific learning needs and objectives that can be related to current clinical problems. Commonly this sort of activity is in the form of discussions with colleagues (educational influentials), literature searches, medical informatics or reading.

2.3 Formal Self-Directed Learning

These are intentional efforts to learn specific topics, usually through a formal course or program, delivered locally or online by distance education and assessed formally with a qualification awarded on successful completion. Additional methods may include learning contracts, formal traineeships, informal traineeships, educational consultants, or specifically tailored plans. These activities are usually self-assessed. Typically, healthcare professionals draw on differing types of educational activities to meet their needs and draw on multiple resources. It is now commonplace in most parts of the world for these activities to be recognized as an essential part of professional development, and many healthcare professions including medicine and nursing are required to undertake continuing education in order to reaccredit for practice.

2.4 The Role of Reflective Practice in Learning

One of the central tenets of professional development is enhanced performance. Perhaps the most relevant work is that of Donald Schön (1987) who used experience as the critical piece of performance to understand how a professional's knowledge changes with what he termed "reflective practice."

Professionals develop a specific knowledge base that informs their work. Experience allows that knowledge base to expand in ways that cannot readily be linked to traditional teaching

methods. Reflective practice proposes that problems are often not clearly identified, and it is through a process of critical reflection that problems can be clarified and solutions or new strategies for future action identified.

Formal interdisciplinary team debriefings following a critical incident and mortality and morbidity meetings are good examples of formal reflective processes that enable individuals to gain an understanding of events from others' perspectives, support one-another, identify issues, and make changes for improved practice.

In Schön's model, learning is directed by performance-related problems, and teaching is seen as guiding or coaching performance rather than the more traditional telling of facts and theory. Learners work on specific professional problems standing alongside a professional as teacher or mentor in that area. Schön also talks of the "right kind of telling" that takes place when students work closely with their teacher or mentor to learn how to frame the questions and to respond in an appropriate manner. By this he means helping learners to see on their own behalf and in their own way what they most need to see and learn about.

It is essential to recognize that individual reflection in, on, and about professional knowledge and practice can be a powerful way of enhancing our understanding of it. Shared reflection with others who understand and can empathize with our experience and life world is especially valuable. This is why mentors, preceptors, professional supervisors, and critical friends (peer mentors) of all sorts are particularly valuable. When nonjudgmental conversations occur between or among collaborative practitioners where experience is reflected upon, it can be a profound and powerful learning experience for all concerned. Finding ways of encouraging and supporting collaborative, interdisciplinary reflection is an important professional development task.

2.5 Motivation in Adult Learning

The ability to make or set goals characterizes much of adult education, which tends to be driven out of curiosity or related to a specific self-identified learning need, otherwise known as intrinsic motivation. On the other hand, extrinsic motivation is an equally common motivator and is driven by external sources such as professional bodies and work-related requirements. Whatever the source, motivation drives learning, and in a modern society with vast resources of ever-changing knowledge, technology and skills, a common goal for educators is to help students become lifelong, self-directed learners in order to respond effectively to the changing needs of the population.

Important educational theories have contributed to our understanding of adult education. Schön (1983) described professionals' self-directed learning as an interaction with the environment in a reflective process which he calls "reflection in action." In this process, the learner becomes aware of a learning need when a "surprise" is encountered (also described as a discrepancy) through a process called "knowing in action." This is thought to be the embedded knowledge that makes up most of the activities of the clinician. Schön makes the point that it is not possible for a professional to work effectively if they do not have this embedded knowledge. In effect, knowing in action represents those activities that are routine and automatic – so deeply learned that they require little reflection or effort. An example of this is the recognition of a diagnosis of a commonly seen problem. This is the level that practice is based on fact and science. The development of a new problem or a doubtful diagnosis produces "surprises." When a surprise occurs, the clinician is caused to pause and reflect on what has happened and on previous actions. This process of reflection may lead to the selection of a solution. This process takes place during the patient-clinician interaction. This may then produce a response that may be appropriate during the patient encounter. The next stage of Schön's model is the "experiment." These experiments reflect the ability of the clinician to reconstruct the information, knowledge, and skills needed to accommodate what it was that was unusual about that encounter. The outcome of that action may then produce the opportunity for "reflection on action." This is when the new learning is

incorporated into the new body of knowledge and becomes part of the new knowing in action. This then is the closing of a loop that brings learning from previous experiences to bear on general procedures and develops new frames of reference for future problems. It is believed that this is one way in which healthcare professionals navigate through the maze of conflict, difference, and uniqueness that characterizes much of their work.

Julian Rotter's work on locus of control (1966) is particularly relevant to educational theory, especially when considering an individual's belief in their ability to effect a positive outcome or achieve learning goals. Individuals with an internal locus of control believe their actions have an effect on the world around them, whereas those with an external locus of control believe outcomes are due to forces outside of their control (e.g., people in authority or fate) and would occur independently of his or her actions (Rotter 1966). In social learning theory, a positive outcome that occurs as a result of an individual's actions reinforces the behavior, which creates an expectation of a similar outcome given similar actions in the future. However, if the outcome is not based on a person's own behavior (i.e., outside of the person's control), there is no such expectation, hence the power of positive reinforcement. On the other hand, a negative outcome or an identified gap between standards and performance has the opposite effect when upon reflection the practitioner learns to avoid certain activities to prevent further negative outcomes. Such experiences often motivate the individual to correct the deficit in their knowledge, skills, or behavior. Albert Bandura's social cognitive theory of the role of self-efficacy in learning and behavior (1977) explains this phenomena as an *outcome expectation* which he describes as "the conviction that one can successfully execute the behaviour required to produce the outcomes" (p.193). Self-efficacy refers to a person's belief in their ability to perform a specific behavior or skill and influences how people think, feel, motivate themselves, and behave and can be positively influenced by education. The greater an individual's self-efficacy, and the more rewarding the outcome expectancy, the more likely they are to be successful in their chosen endeavor (Mason and Ellershaw 2004). Bandura describes efficacy expectations as being based on four main sources of information:

1. Performance accomplishments – opportunities to achieve mastery through practice, e.g., simulation activities and successful clinical encounters
2. Vicarious (observational) experience – opportunities to observe experts in action, e.g., role modeling from senior clinicians and competent peers
3. Verbal persuasion – feedback and encouragement provided by respected clinicians who are knowledgeable and whose opinion can be trusted
4. Emotional arousal – physiological and psychological states that can impair or enhance performance, e.g., negative mood or attitude (e.g., fear and anxiety) may impair performance, whereas positive mood/attitude (energized and enthusiastic about the task) tends to enhance performance (Bandura 1977).

Interestingly, Bandura noted a significant difference between having the required knowledge and skills and the ability to use them in stressful situations. He suggests our ability to perform well in a given situation is determined by our self-efficacy or confidence in our ability to undertake a particular task or activity, which is in turn heavily influenced by the learning process. This confidence is independent of our knowledge and skills, which means that people who have achieved the same level of knowledge and skill tend to perform better or worse depending on their self-efficacy (Bandura 1993). Confidence in our ability to perform well in a given situation suggests we have had opportunities to develop the required skills, which demonstrates a higher level of learning than simply having knowledge of it. For example, knowing the theory of CPR does not mean we can apply it in a cardiac arrest unless we have had opportunities to observe and practice this skill and demonstrate competence in a supervised setting. Such examples suggest that in order for individuals to feel confident in their ability to care for people who are dying, they not only need

knowledge and skills but opportunities to interact with people and families receiving palliative and end-of-life care and critically reflect upon and receive feedback from experienced clinicians about their performance. It follows that if these experiences are lacking, learners may lack confidence and avoid being involved in caring for people who are dying, i.e., an expression of death anxiety. It is therefore important that educators take these factors into consideration when designing curricula and provide opportunities that build self-efficacy. These theories have important implications for undergraduate teaching in the health professions as well as for continuing professional development activities.

Ultimately, all theories require certain personal characteristics for individuals to be effectively motivated to learn. These include:

- The ability for forethought (to perceive a desired outcome)
- The ability to learn from experience (to be reflective practitioners)
- The ability to set goals to achieve the desired outcome
- A sense of curiosity or a perceived gap or need for learning
- A belief in their capability to undertake the required task
- The ability to recall previous success in learning

3 Palliative Care: The Sociopolitical Context

Advances in the management of chronic diseases combined with an aging population have led to an increasing prevalence of people with complex life-limiting conditions and an increasing demand for palliative care. Diseases such as ischemic heart disease, stroke, dementia, chronic respiratory disease, cancer, and diabetes are now the leading causes of death in the 60+ age group accounting for a large majority of deaths in the developed world. This is driven largely by the aging population and behavioral risk factors and is forecast to increase substantially (World Health Organisation 2003). Responding to this need is a global health challenge which requires government-led initiatives to support the provision of palliative care and increase workforce capacity across all healthcare settings.

The World Health Organization defines palliative care as "an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual" (Sepúlveda et al. 2002, p. 94). This definition has been instrumental in guiding the development of palliative care services around the world with increased public awareness and government-led strategies to improve the availability and quality of palliative care.

The 2015 Quality of Death Index (The Economist Intelligence Unit 2015) rates the provision of palliative care across the world with rankings based on income as a predictor of the availability and quality of services. Countries with higher incomes are more likely to have a national palliative care strategy, higher levels of government funding, and palliative care training resources. The UK currently ranks at the top of the scale due to the extensive integration of palliative care into the National Health Service, a comprehensive national strategy that includes undergraduate healthcare education and a strong well-developed hospice movement. Australia and New Zealand come in second and third places, respectively. Other high-income countries such as Ireland, Belgium, Taiwan, Germany, the Netherlands, USA, and France are also listed in the top 10. However, even the highest ranked countries are not able to cater for the palliative care needs of every individual with geographic isolation, late or lack of referral, or an unwillingness to accept palliative care services indicating there is still much work to be done. Barriers to accessing services also exist within the healthcare community where death is often perceived as medical failure, where curative treatment is prioritized over quality of life, and where palliative care tends to be considered the sole domain of hospices for people with cancer in

the last days of life. However, this perception is changing with an increasing recognition that palliative care is relevant in all life-limiting conditions with early integration in the course of illness alongside disease-modifying treatment to improve quality of life. Consequently, palliative care is becoming a more common component of undergraduate education and continuing professional development programs with increasing recognition of the importance of a primary palliative care approach, with support from specialist services for those with complex needs (Gott et al. 2012).

The Quality of Death Index (2015) carries a timely warning that countries without sufficient training resources are likely to face a shortage of specialist staff, while nonspecialists (primary palliative care providers) may lack the skills to provide quality care if adequate educational preparation is not provided.

4 Undergraduate and Continuing Education in Palliative Care

Death and dying is a universal human experience and an inherent part of healthcare. Death occurs in all healthcare settings, and as such, it is difficult for healthcare professionals to avoid. In developed countries where people have access to high-quality healthcare, death is often perceived as an extraordinary event. This is especially true in hospital settings where care is oriented toward providing curative treatment, with palliative care being considered a specialist role. However, caring for people with life-limiting illnesses is part of everyday clinical practice for most health and social care professionals, so it is essential they are well prepared to do so with training beginning in undergraduate programs through into postgraduate and continuing education.

Unfortunately, death and dying have not traditionally been part of undergraduate curricula until relatively recently (Worldwide Palliative Care Alliance 2014; Lloyd-Williams and MacLeod 2004), which reinforces death-denying attitudes. This oversight meant new graduates were left to rely on their colleagues for guidance and support, which was not always readily available and meant that the quality of care depended on graduates' unguided instincts and their colleagues' level of experience and attitudes toward caring for people who are dying. Unsurprisingly, both medical and nursing graduates consistently report feeling inadequately prepared to care for people at the end of life, which not only compromises patient care but may also undermine graduates' self-efficacy at a critical point in their professional development.

A systematic review undertaken by Lloyd-Williams and MacLeod in 2004 reported that despite widespread acknowledgment that learning about palliative care should be included in undergraduate curricula, there was a lack of rigorous research in palliative care education. Teaching had developed in an ad hoc manner, lacked consistency, and coordination and was rarely formally assessed. The authors recommended an integrated approach to teaching palliative care beginning in the preclinical years to reinforce principles and practice across disciplines (Lloyd-Williams and MacLeod 2004). Cultural and institutional factors are common barriers to integrating palliative care into undergraduate education and include issues such as overcrowded curricula, lack of a local champion, and a healthcare system that prioritizes curative treatment over quality of life and the benefits of palliative care (Lloyd-Williams and Field 2002; Ramjan et al. 2010). In recent years, there has been a significant increase in the number of undergraduate programs offering palliative care education, especially in countries where government funding and policy initiatives have been provided to help prepare graduates meet future demand (Brajtman et al. 2007). The UK, Australia, USA, and Germany have seen particularly strong growth in this area, and there is a growing body of research reporting positive results from the evaluation of educational interventions, although there are few that measure the impact on patient care (Walker et al. 2016; Ramjan et al. 2010; Dickinson et al. 2008; Fitzpatrick et al. 2017).

In the UK, USA, Canada, and Germany, palliative care is a required component of undergraduate education, and there has been a recent proliferation of educational initiatives in these countries with legislation being a strong motivator

for educational development. However, even in these countries, the provision of palliative care education is variable, although this is more of a concern in countries where there are no competency requirements specifically related to palliative care. These issues are likely to undermine the quality of care and contribute to a shortage of specialist palliative care providers in the future (The Economist Intelligence Unit 2015).

Countries such as Australia and the USA have invested a great deal in developing national programs aimed at preparing the current and future workforce with essential knowledge and skills in the palliative care approach. In Australia, the National Palliative Care program, funded by the Commonwealth Department of Health and Aging, supports a range of national initiatives to improve access to and support the provision of high-quality palliative care. These programs include Palliative Care 4 Undergraduates (PCC4U) (http://www.pcc4u.org) which uses interactive web-based activities with accompanying resources and facilitator guides as well as workshops. In addition to this, the Programme of Experience in the Palliative Approach (PEPA) (https://pepaeducation.com) provides practicing healthcare professionals with opportunities for workplace training and workshops in palliative care. Both programs are widely available throughout Australia and provide a flexible and highly accessible means of delivery tailored to the needs of various disciplines. Other initiatives supported by the Australian government include CareSearch (https://www.caresearch.com.au) which is an online repository of palliative care information for patients, families, and healthcare professionals. CareSearch also offers online learning in the form of "End of Life Essentials," a series of six palliative care training modules for healthcare professionals working in the acute care setting. Similarly, St Christopher's Hospice in London, UK, provides a comprehensive suite of education packages, one of which is aimed at practicing healthcare professionals, known as QELCA (Quality End of Life Care for All). This program aims to empower health and social care professionals to provide a palliative care approach in all healthcare settings and includes a Train-the-Trainer program to equip teams who wish to lead the development of palliative care in their workplaces (http://www.stchristophers.org.uk/education/course/quality-end-of-life-care-for-all-qelca-train-the-trainers). Initiatives like this provide valuable resources to support continuing education and the provision of quality care at the end of life.

Care assistants who work in residential aged care facilities (RACF) are also important and often neglected; providers of palliative and end-of-life care given that the vast majority of residents in RACFs die there. Aged care facilities are becoming an increasingly common location for end-of-life care as the world's population ages and the prevalence of dementia increases. It is therefore essential that palliative care training for staff working in residential aged care facilities is a mandatory requirement for licensure, with special attention paid to addressing the learning needs of care assistants who provide the majority of hands-on care. Strong links must also be established with local hospices for ongoing liaison and support.

A good example of this model can be found in New Zealand where Hospice New Zealand, the peak body for hospices, has established the "Fundamentals of Palliative Care" course for care assistants employed in residential aged care facilities. This course is available nationwide and is provided by local hospices (MacLeod and Schumacher 2015). Research by Latta and Ross (2010) showed this course to be effective in preparing participants to care for residents who were dying and for validating and empowering care assistants in their work. The New Zealand Ministry of Health also provides funding for hospices to create palliative care liaison positions that work with and support staff working in residential aged care facilities to provide palliative care so residents can be cared for in their own environment, without unnecessary hospital admissions at the end of life.

In the USA, the American Association of Colleges of Nursing (AACM) developed the End of Life Nurse Education Consortium (ELNEC), a national initiative that was introduced in 2000 to improve the provision of palliative care throughout the USA. This course was developed with

support from the Robert Wood Johnson Foundation and uses a train the trainer approach to equip participants with the knowledge and skills required to teach undergraduate and postgraduate educators about palliative care so they can integrate it into their teaching. The ELNEC curriculum consists of eight learning modules that focus on the core competencies of palliative and end-of-life care which reflects the American Association of Colleges of Nursing's 2016 Competencies and Recommendations for Educating Undergraduate Nursing Students. This program has been widely disseminated across America (where it has been attended by 19,500 nurses and other healthcare professionals) and the world including 96 other countries where there is little or no provision of palliative care such as India, South America, and Eastern Europe. The ELNEC program has also been translated into several languages including Albanian, Czech, Romanian, Russian, Spanish, Hindi, Japanese, Korean, Chinese, and German and adapted to speciality areas such as geriatrics, pediatrics, and critical care ensuring an even wider reach (http://www.aacnnursing.org/ELNEC/About). While the ELNEC course has been proved to be effective in improving knowledge and skills (Glover et al. 2017), and is slowly being integrated into undergraduate nursing programs, the Institute of Medicine 2014 report: *Dying in America: Improving Quality and Honouring Individual Preferences near the End of Life* describes current nursing education as lacking adequate emphasis on palliative and end-of-life care.

There is no equivalent of ELNEC for undergraduate medical students in the USA so training varies widely between institutions and is described as being disjointed and sporadic (Horowitz et al. 2014). Palliative care is a required competency for nursing training in the USA, but the same cannot be said for medicine as the Liaison Committee on Medical Education (LCME) does not require medical schools to teach palliative care competencies, and it is not specifically mentioned in its standards. The Association of American Medical Colleges (AAMC) does however include some requirements that are directly related to palliative care, but this has not been translated into medical education in a consistent manner and varies widely between universities from as little as 2 h total teaching through to courses that require weeks of training and clinical experience (Horowitz et al. 2014; DeCoste-Lopez et al. 2015). While a 2014 survey of US medical schools reported 43 out of 51 deans describe palliative care education as being important (Horowitz et al. 2014), there appears to be a mismatch between the perceived importance and the actual delivery of palliative care education in undergraduate medical programs in the USA.

Canada has a longer association with palliative care education and introduced a standardized medical curriculum in 1993. However a 2001 survey by Oneshuk et al. (2004) reported wide variations in time allocated to palliative care, lack of curricula content, and limited availability of teaching staff and associated resources. Similarly, in nursing schools, teaching tends to be threaded throughout the curriculum, but the degree of emphasis is dependent on the level of commitment of teaching staff and the availability of clinical teachers with experience and expertise in this area (Brajtman et al. 2007).

There are many palliative care educational resources available for Canadian physicians such as Learning Essential Approaches to Palliative Care (LEAP) (http://pallium.ca/professional-development/leap-2/) and Ian Anderson Continuing Education Program in End-of-Life Care (https://www.cpd.utoronto.ca/endoflife/default.htm), but these have not necessarily translated into physician training (Downar 2018). Downar suggests that palliative care interventions are undermined by the hidden curriculum and suggests that interventions must be accompanied by continuing education and faculty development to create lasting change in physician behavior.

In the UK, the National Institute for Health and Clinical Excellence (NICE) provides national guidance, advice, and standards based on best evidence to assist in the planning and delivery of healthcare services, including issues related to palliative and end-of-life care. These guidelines have been incorporated into healthcare education to ensure the health workforce is adequately prepared to meet the needs of the population,

including those suffering from life-limiting conditions. A 2006 national survey of all 66 undergraduate nursing programs in the UK (response rate of 79%) reported that palliative care plays a significant role in undergraduate education with an average of 45 teaching hours devoted to this subject (Dickinson et al. 2008). This is a significant improvement on a 2002 study that reported an average of only 12.2 h of palliative care teaching in undergraduate nursing degree programs (Lloyd-Williams and Field 2002), which illustrates the development that has taken place over a relatively short period of time.

In medicine, these issues are addressed by the General Medical Council in "Tomorrow's Doctors" which outlines the outcomes and standards for medical education in the UK (General Medical Council 2009). The Association for Palliative Medicine in Great Britain and Ireland (2014) has since developed an undergraduate curriculum that is mapped to these outcomes and as such provides valuable guidance for medical student education. A recent study published in 2016 by Walker et al. (2016) that surveyed course organizers from all 30 medical schools in the UK reported that all courses provide mandatory teaching on "last days of life, death and bereavement" and offer an average of 36 h of palliative care teaching that is integrated into the curriculum with wide assessment. This can be followed up after graduation by participation in the "Quality End of Life Care for All" (QELCA) program at St Christopher's Hospice, London (Gillet and Bryan 2016). This accommodates practicing physicians experiencing hospice care through a 5-day clinical immersive practice much like the PEPA program in Australia.

In Europe, the European Association for Palliative Care (EAPC) has developed consensus guidelines on the core palliative care competencies for primary palliative care providers of all disciplines (Gamondi et al. 2013). These guidelines provide a useful framework for curriculum development, both in Europe and around the world.

In order to determine the extent of undergraduate palliative care education, an international collaboration of researchers conducted a comprehensive survey of European universities in the World Health Organization European Region with a response rate of 81%. The survey revealed palliative care is being taught in a substantial number of undergraduate medical schools, but there is wide variation between countries. For example, 28 countries (65%) include palliative care in the curriculum of at least one of its universities. In five countries (12%) including Lithuania, Poland, Latvia, Finland, and Spain, palliative care is taught in half of the country's medical schools, and in ten countries palliative care is taught in less than half of medical schools. In 13 countries (30%), palliative care is taught in all medical schools (UK, Israel, Norway, Belgium, France, Malta, Austria, Germany, Ireland, the Republic of Moldova, Hungary, Switzerland and Slovenia); 6 of these countries (those underlined) include palliative care education as a compulsory component of undergraduate training, while 14 mainly Eastern European countries do not include any palliative care teaching at all (Carrasco et al. 2015). Unsurprisingly, these countries rate in the lower half on the 2015 Quality of Death Index (with some not even featuring), which may be a reflection of a lack of government investment in palliative care policy and resources.

Important advances have taken place in Switzerland and Germany since palliative care education became a mandatory component of undergraduate education in 2013, with increases in palliative care content and academic positions to support development (Eychmuller et al. 2015; Weber et al. 2011). However a recent review of international undergraduate medical education cites Ilse et al. (published in German) describing the implementation of this teaching as being uneven and fragmented (Head et al. 2016) with only minimal requirements for nursing education in the legislation.

In Japan, there is increasing acknowledgment of the role of palliative care in healthcare delivery with a national study by Hirakawa et al. (2005) reporting 45% of medical schools and 68.9% of nursing schools that incorporate end-of-life care in their curricula. There is increased emphasis in palliative care in nursing curricula illustrated by 35.5 mean teaching hours which includes clinical learning opportunities and assessment, compared with 7.6 h in medicine.

There is, therefore, an increasing global recognition of the importance of incorporating palliative care into undergraduate curricula in medicine and nursing to prepare graduates to meet the current and predicted future need. The UK and Australia currently lead the world in terms of palliative care education and service delivery (Economist Intelligence Unit 2015) with a steady increase in the number of countries incorporating palliative care into their teaching to improve the provision of a primary palliative care approach in nonspecialist settings. Much of this work has been prompted by legislative requirements and government policy directives and supported by the work of professional bodies such as the European Association for Palliative Care and governing bodies within each country.

Despite increasing availability, palliative care continues to be underrepresented in many areas throughout the world where it competes for space in overcrowded curriculums and is often seen as a "soft subject" (i.e., nonessential). As a result, there is widespread variability and lack of consistency in content, organization, delivery, and curriculum time. Although evaluation studies report improvements in knowledge, skills, and attitudes, graduates continue to report feeling unprepared to provide end-of-life care with anxiety related to this part of their role being a common theme (Walker et al. 2016; Gillan et al. 2014). It is unclear whether this is due to the emotionally challenging nature of the work or because of deficiencies in their education, but it is likely to be a combination of the two. Either way, there are important implications for graduates' ability to care for people who are dying, which may compromise the quality of care and undermine graduates' self-efficacy at a crucial point in their professional development.

Despite the evidence that undergraduate and continuing education in palliative care has increased, the curative model is still predominantly considered the most relevant for medicine. In the jargon of the curative model, patients whose illness cannot be stopped or slowed are termed "untreatable." From a cure-oriented perspective, the care of such patients is still considered by some to be outside the purview of medicine. Medical students learn humanistic skills in their preclinical learning, but this can often be subtly undermined during their clinical attachments through a process of socialization whereby students become enculturated by the attitudes of their senior colleagues which may not be supportive of a palliative approach to patient care.

With that being said, it is important to acknowledge that undergraduate medical education is changing with an increasing emphasis on the importance of applying biomedical knowledge within a bio-psycho-social-spiritual model of care which is consistent with palliative care philosophy and responds to individual patient and family needs. This represents a significant shift in medical culture which has traditionally operated out of a biomedical approach that rewards technical skills over "softer skills" such as communication, which frequently involve emotionally draining encounters at the bedside, thus placing high value on curative interventions as opposed to palliative, whole-person, and family-centered interventions. These latter interventions often appear to encourage greater intimacy with the patient and family as we share in and support them through what is for many the most significant and challenging period in their lives. However, even in the palliative care literature, there is evidence of the danger of the intimacy that can often occur in these end-of-life situations that is associated with the emotional burden of accumulated grief. While intimacy often takes us by surprise and strengthens the therapeutic connection with patients and families, it is often accompanied by the fear that we may be overwhelmed by another's agony, suffering, chaos, and disintegration (Barnard 1995). It is essential therefore that interdisciplinary team members are well supported through comprehensive undergraduate and continuing education as well as opportunities for critical reflection and peer support.

5 Advanced Specialty Training in Palliative Medicine

The Joint Committee on Higher Medical Training in the UK first published a palliative medicine curriculum in 1998 that sets out standards

for trainees in palliative medicine in all areas including clinical, education, and research (JCHMT 1998).

In 2010 the Royal Australasian College of Physicians (RACP) published their curriculum for advanced training in palliative medicine (revised and updated in 2013). The aim of these curricula is "to ensure that specialists in palliative medicine have explored the optimum way to manage patients with active, progressive and far advanced disease for whom the prognosis is limited and the focus of care is on quality of life." The RACP program is built around work-based assessments and learning tools developed from the CanMEDS program developed by the Royal College of Physicians and Surgeons of Canada in the 1990s. Its main purpose was to "define the necessary competencies for all areas of medical practice and provide a comprehensive foundation for medical education and practice in Canada" (http://www.royalcollege.ca/rcsite/canmeds/canmeds-framework-e). Essentially this program for advanced training in palliative medicine identifies and describes the abilities physicians need to effectively meet the healthcare needs of people they serve. These abilities are grouped as Medical Expert, Communicator, Collaborator, Leader, Health Advocate, Scholar, and Professional. Prospective trainees must have completed RACP Basic Training or be a Fellow of a prescribed medical college. At the completion of the Advanced Training Program in Palliative Medicine, as defined by this curriculum, it is expected that a new Fellow will have developed the clinical skills and have acquired the theoretical knowledge for competent palliative medicine practice. It is expected that a new Fellow will be able to:

- Express expert knowledge of the pathophysiology, symptom
- Explain management, psychosocial, and spiritual issues related to life-limiting illness and imminent death
- Understand the experience of disease from the perspective of a patient and the meaning and consequences of illness to a patient and their family
- Make appropriate clinical decisions to provide medical care that is structured around the patients' and families' needs, their understanding and priorities, with the aim of maximizing QoL, relieving suffering, supporting the family, and normalizing their experiences
- Display particular expertise in the management of patients within the home, as well as the hospital and hospice
- Describe the natural history and role of disease-specific treatments in the management of advanced cancer and other progressive life-limiting illnesses
- Practice culturally responsible medicine with understanding of the personal, historical, contextual, legal, cultural, and social influences on both health workers and patients and families
- Provide expert advice as a consultant
- Establish therapeutic and supportive relationships with patients and their families based on understanding, trust, empathy, and confidentiality
- Confidently discuss end-of-life issues with patients and their families
- Sensitively explore patients' concerns across physical, psychological, social, cultural, and spiritual domains
- Communicate effectively with patients, their families, and other health professionals involved in the patients' care
- Manage his/her own time and resources effectively in order to balance patient care, professional development, managerial and administrative duties, learning needs, and personal life
- Work effectively and efficiently in a healthcare organization
- Manage human resource, financial, quality assurance, data management, and administrative aspects of his/her own practice or palliative care service
- Allocate finite healthcare and health education resources effectively (https://www.racp.edu.au/docs/default-source/default-document-library/download-the-advanced-training-in-palliative-medicine-curriculum-(1mb).pdf?sfvrsn=2)

Trainees need to undertake a learning needs analysis, partake in case-based discussions, write up case studies, and are advised to undergo communication skills training, brief clinical examinations, reflection, and research.

In the USA, requirements for aspects of palliative medicine training were first outlined in the mid-1990s, but by 2001 there were still relatively few residency or fellowship requirements to provide any palliative medicine training outside internal medicine, geriatrics, and neurology (Case et al. 2013). Hospital palliative medicine consult teams have increased in number over the last years, and this has encouraged the development of more palliative medicine education. Hospital palliative medicine is now recognized as a specialty, but there are still not enough palliative medicine specialists to meet the wide-ranging needs of the population.

Downar (2018) has provided a helpful overview of the resources for education, training, and mentoring for all physicians providing palliative care which he suggests can serve as a framework to improve palliative care as a whole in Canada.

6 Addressing the Learning Needs of Family Carers

Family carers have significant learning needs if they are to be able to care for their loved one at home. Without the considerable support, sacrifice, and willingness of families to provide care, many patients who would prefer to be at home might otherwise have to be cared for in hospital or a residential care facility. Such caring requires dedication, skill, and a certain amount of knowledge. However, the presence of effective education programs to provide relevant knowledge is fairly limited. One early example was undertaken with the support of the Project Death in America. Patients with advanced cancer and their families were invited to attend a 90-min education program that taught basic problem-solving principles using a cognitive-behavioral framework. The authors surmised that most education programs focused on delivering information rather than problem-solving skills and proposed that one-on-one teaching may provide more effective results (Bucher et al. 2001).

The team at the Centre for Palliative Care in Melbourne have been innovative in their approach to caregiver education. They have undertaken their own work and provided a helpful systematic review of psychosocial interventions for family carers of palliative care patients (Hudson et al. 2010). They noted that interventions included psycho-education, psychosocial support, carer coping, symptom management, sleep promotion, and family meetings. Only three studies in that review were randomized controlled trials which met the criteria for the highest-quality evidence. They conclude that paper by asking:

> *First, how can psychosocial interventions be designed to be effective given the typically short period of time available to intervene?*
>
> *Second, what is the most useful way to determine which family carers need significant psychosocial support?*
>
> *Third, how can health services meet the support needs of the entire family when many may only be resourced to support the primary family carer?*
>
> *And finally what are the priority interventions and methods of delivery that are required for development and testing in the family carer population?* (p. 4)

Answers to these questions are yet to appear consistently in the literature. That group's own intervention demonstrated that a group education program to prepare family caregivers for the role of supporting a dying relative at home was accessible, applicable, and effective. In particular they found a significant positive effect in preparedness for the caring role, caregiving competence, caregiving rewards, and having information needs met (Hudson et al. 2008).

There are clearly many other ways to help to educate carers. One initiative is an open website "The Palliative Care Bridge" www.palliativecarebridge.com that uses recorded materials from experts in the field. There are over 70 short video interviews and presentations on all aspects of palliative care including interviews with patients and family members.

Palliative Care Australia have developed a massive open online course (MOOC) on death, dying and palliative care that is open to anyone

aged 18–100 who has a computer. The 4-week course is presented by the online palliative care resource CareSearch and aims to increase death literacy in the community and engage people in conversations on the topic (http://palliativecare.org.au/new-course-on-death-dying-and-palliative-care).

Many hospices also run courses for family carers which include aspects of the dying process, communication, grief, and bereavement. Macmillan, the leading charity support at the end of life in the UK, runs face to face and online courses for carers of all experiences. A huge selection of resources are available at https://learnzone.org.uk/.

7 Educational Methods

Given the increasing demand for palliative care education, it is important there is a wide range of flexible and accessible educational modalities available to meet the learning needs of all, many of which have already been mentioned.

There is a great deal of variety in approaches to teaching and learning about palliative care from the traditional didactic lecture to simulation, eLearning, small group discussion, and interprofessional education. Ideally, the method should be that which is best suited to the audience and content being delivered. Objectives must be realistically achievable (given the timeframe and participants' level of learning), measurable, and clearly stated. They must also be aligned with prior learning and experience and tailored according to learning needs. Of course, theoretical learning must be partnered with opportunities for practical experience including critical reflection with supervision and feedback from expert clinicians. Undergraduate students should also have opportunities to observe skilled palliative care professionals in action, such as being involved in team discussions about care planning, witnessing high-stakes conversations (about breaking bad news, prognostication, transition to palliative care, and advance care planning), as well as opportunities to be directly involved in caring for people who are dying. These are some of the most valuable, influential and enduring learning experiences a student can have.

The European Association for Palliative Care recommends 10 core competencies that all health and social care professionals should achieve, regardless of the healthcare setting they work in. These competencies provide a useful framework for palliative care education, and while they were developed for a European audience, they are easily transferable to other countries. The White Paper on Palliative Care Education can be accessed through the EAPC website http://www.eapcnet.eu/Themes/Resources/Education/EAPCWhitePaperonEducation.aspx.

Similarly, other countries have specific guidelines and legislative requirements for palliative care education that curriculum developers need to be familiar with to ensure their educational programs align with national priorities.

Relf and Heath (2006) argue that effective teaching in palliative care needs to translate knowledge into behaviors that make a "positive difference to the people we work with, namely our colleagues, patients and all those who care for them." They identify several experiential techniques, as others have done, to provide opportunities for reflection, support, and raising awareness of what influences attitudes, assumptions, and the way we respond. They suggest the use of role-play with reflection and sculpting as useful educational methods to stimulate reflection and self-awareness.

Finally, distance education methods have been shown to be of use to informal caregivers in palliative care in Australia without relying on Internet access or having to travel to group sessions (Forbat et al. 2018). Others have demonstrated the usefulness of classroom-based education for enhancing health and social care professionals' skills for delivering end-of-life care (Pulsford et al. 2011). We now turn our attention to specific educational methods that require focused discussion.

7.1 Simulation

There is growing interest in the use of simulation-based learning experiences (SBLE) in the training

of health and social care professionals in order to prepare students to meet the needs of patients and families who require a palliative approach to care. While there is no substitute for real patient interaction, the unpredictable nature of the clinical setting means that student learning can be highly variable. Simulation is one way of providing consistent learning opportunities to ensure all students can practice core skills in a safe environment with supervision and feedback from experienced clinicians and educators.

Two recent reviews showed that learning activities involving the use of high fidelity mannequins, role-play, and/or simulated patients (actors) appear to be an effective way of enhancing student learning in palliative care, especially when blended with a second modality such as eLearning when used in preparation for the simulation. Skills such as patient assessment, communication (including spiritual and cultural issues), and interprofessional teamwork were all seen as being particularly amenable to simulation, all of which are essential skills in palliative care (Smith et al. 2018; Kirkpatrick et al. 2017; Ellman et al. 2012).

An attractive feature of simulation is that it facilitates critical reflection through the debriefing and feedback process, which allows students to learn from experience (without fear of harming the patient) while developing important clinical and communication skills. Evidence also suggests that palliative simulation activities can improve knowledge and confidence (Pesut and Grieg 2018). However, it is unclear how well learners are able to transfer these skills to the clinical setting with a recent meta-analysis by Selman et al. (2017) showing a smaller effect of communication skills training on interactions with real patients, compared to those demonstrated in a simulated interaction. Personalized feedback on recorded simulated patient interactions however was shown to be helpful in improving clinicians' ability to demonstrate empathy during real patient encounters (Selman et al. 2017).

While simulation holds a great deal of promise as an educational modality, there are important factors that need to be taken into consideration in order for a simulation activity to be successful. These include involving key stakeholders in the design, planning and delivery (especially in interprofessional simulations); clear, achievable, and measurable learning objectives; modality (i.e., high vs low fidelity, actors, role-play, blended methods); authenticity (i.e., as close to reality as possible); and careful debriefing which includes being mindful of safety issues if a student should become distressed by emotionally upsetting content (such as breaking bad news). It is also essential that learners have opportunities to transfer and consolidate the skills learned in a SBLE into the clinical setting through observation of expert clinicians in action and supervised interactions with real patients with personalized feedback from clinicians to improve performance.

In the context of today's high-pressure, high acuity healthcare settings, simulation offers flexible, safe, and consistent opportunities for students to learn and practice essential skills in palliative care.

7.2 Interprofessional Education (IPE)

One of the cornerstones of palliative care is interprofessional teamwork, which is essential in order to be able to respond effectively to the patient and family's physical, psychological, social, and spiritual needs. No one profession is skilled in all these areas, so team members must work collaboratively to meet patient and family needs.

The World Health Organization recommends interprofessional education as a necessary step toward preparing a collaborative practice-ready health workforce that is better prepared to respond to local health needs (WHO & Health Professions Network Nursing and Midwifery Office: Department of Human Resources for Health 2010). A common definition of interprofessional education is that which "occurs when two or more professions learn with, from and about each other to improve collaboration and the quality of care" (Barr 2002 p. 8). The assumption is that health professionals who learn together are more likely to be able to collaborate well in interprofessional teams.

In order to learn these skills, students need to have opportunities to learn with other health and

social care students during their undergraduate training, both in the learning and clinical settings, to prepare them for working in interprofessional teams in the future. Students' observations of effective interprofessional teamwork on clinical placements help students contextualize learning and avoid the risk of education out of context becoming "idealized," thus creating difficulties when it comes to putting into practice the knowledge, skills, and attitudes learned. Furthermore, a lack of interprofessional learning opportunities can lead to clinicians practicing in silos, thus creating rigid professional boundaries and power structures that militate against effective teamwork and the shared care that characterizes communities of practice as described by Étienne Wenger (1998). By this we mean a group of people who share a concern or a passion for something they do (e.g., healthcare) and learn how to do it better as they interact regularly. This reflects the fundamentally social nature of human learning. Hospice and palliative care units provide an ideal setting for learning these skills, especially in the advanced years of undergraduate training.

Formal interprofessional programs require considerable attention to process: letting go of personal and professional biases and assumptions, exploring and defining roles to diminish stereotyping and develop understanding of each other's strengths and abilities; and debriefing to examine system and individual responses. Much of interprofessional learning for palliative care will inevitably take place within small group settings. Small group work benefits from the usual considerations of the learning environment and brings with it additional requirements such as introductions, credentialing, agenda or objective-setting, agreement on ground rules, a modus operandi, and so forth. Whether learning in a theoretical way through cases or problems or reviewing clinical situations, there are certain considerations that can improve effectiveness for this sort of learning (Oandasan and Reeves 2005). For interactive learning to be effective, there is a need to maintain group balance, ensuring that disciplines are not likely to dominate by being overrepresented. The group size must be of an order that facilitates easy communication among the group. Finally, the group is most effective for learning where there is stability with little "turnover" and members can learn together for some time.

In outlining his views of a social theory of learning, Wenger (1998) argues that in order to learn effectively, together we must:

- Discover shared meaning, a way of talking about our abilities and our experiences that can be shared
- Practice a way of talking about our shared histories and social frameworks that mean we can understand each other
- Negotiate identity, a way of talking about how learning changes who we are

To this should perhaps be added that we must also have a willingness to learn and work together, have trust and confidence in each other's abilities, and have a mutual respect of each other's abilities and contributions. How we establish these attitudes and behaviors in the workplace is crucial. Students joining communities of practice that are already functioning more or less effectively (such as clinical teams) are seen to be "on the outside," inexpert, and inexperienced. It is important for their professional development that they are made to feel legitimate members of the team and included as much as possible in team activities. There is some risk for students in this process since they may unknowingly wander from one professional jurisdiction to another. Introductions, orientations, and role definitions all help, but the routine practice of the community is likely to be the greatest determinant of emergent professional identity. In an effectively functioning community of practice, the student is likely to witness negotiations, favors, deals, and trades between professionals conducted in the best interests of the patient – in essence, a team learning with, from, and about each other. These can be transforming experiences in the formation of professional identity and can be the subject of reflective activities. It is also important to recognize that the social dynamics of the community of practice potentially presents students with a variety of role models, a function of which the members may or may not be aware.

In a systematic review of the development of an evidence base for interdisciplinary learning, Cooper et al. (2001) identified many educational interventions from the literature which can be used for interdisciplinary learning. The prominent educational methods used were small group teaching, case studies (real or simulated), and experiential learning. Traditional didactic methods were also used in approximately one third of the interventions. The summary of the main findings of this review showed the largest effects of interdisciplinary learning were on students' knowledge and attitudes, skills, and beliefs and in particular on understanding of professional roles in team working, ideal then for learning in and about palliative care. The smallest effects were for a transfer of learning into students' experiential practice and an effect on students' learning environments.

Pippa Hall (2005) pointed out that physicians traditionally learn independently in a highly competitive academic environment. Nurses learn early in their career to work as a team, collectively working out problems and efficiently exchanging information. She also suggests that the physician-patient relationship tends to be authoritarian, whereas other professions such as social work and nursing have placed more value on patients' self-determination. This variance has led to tensions within interprofessional teams in palliative care where role "blurring" exists. There is the possibility with interprofessional learning of identifying where one role ends and another begins which is clearly an attractive option. Collaboration in the development of effective team work is fundamental, and Norsen et al. (1995) have identified six collaborative skills that are crucial for teamwork that should be addressed in any professional education program and still seem relevant after more than 20 years:

- Cooperation – acknowledging and respecting others' opinions and viewpoints
- Assertiveness – supporting one's own viewpoint with confidence
- Responsibility – accepting and sharing responsibilities and participating in group decision making and planning
- Communication
- Autonomy
- Coordination – efficient organization of group tasks and assignments.

Alternatively, if we identify competencies for palliative care practice in an interprofessional way, we can utilize a format like that is proposed by Hugh Barr (1998) in which "collaborative competencies" are outlined:

- Describe one's roles and responsibilities clearly to other professions
- Recognize and observe the constraints of one's role, responsibilities, and competence, yet perceive the needs of a wider framework
- Recognize and respect the roles, responsibilities, and competencies of other professions in relation to one's own
- Work with other professions to effect change and resolve conflict in the provision of care and treatment
- Work with others to assess, plan, provide, and review care for individual patients
- Tolerate differences, misunderstandings, and shortcomings of other professions
- Facilitate interprofessional case conferences, team meetings, etc.
- Enter into interdependent relationships with other professions

Palliative care is the product of a shared vision of care between the healthcare team, the patient, and their family. The care plan is informed by the patient narrative, which incorporates their values, goals, and priorities with care orientated toward realizing those values, goals, and priorities, including actions and activities that will be instrumental in helping them achieve those goals. The unique course of events and experiences taken by the dying person and their family combined with all the accompanying professional work (i.e., what the healthcare team does using their combined expertise) constitutes the trajectory of dying. In daily practice, there will be many tasks which, in total, constitute care with some degree of complementary overlap between professions. It is therefore essential that students have opportunities to learn how to work effectively as a team

member which is best achieved by learning with, from, and about each other.

Gadoud et al. (2018) have described the perceptions of nonmedical palliative care health professionals (nurses, social workers, and physiotherapists) involved in medical student education in palliative care. Essentially, the staff saw the benefits and value of the experience as providing a different perspective of palliative care delivery, offering a greater understanding of interdisciplinary teams and giving patients a feeling of importance and the opportunity to contribute to student learning. The authors of this study suggest that utilizing such staff "is a practical and rewarding way to achieve undergraduate medical education in both palliative and interprofessional care" (p. 5).

One of the taxing questions for palliative care educators is how and when to introduce the concepts and realities of interprofessional education. While it is clear that there are discipline-specific areas of learning, there is no doubt that in an area of healthcare that relies so heavily on interprofessional working, there is great merit in introducing these concepts at an early stage. To summarize, in the development of an interprofessional educational activity, we must ask:

- What are the goals we are trying to achieve in having students learn together?
- Based on these goals, when should we introduce the learning to students?
- What strategies should be used to accomplish these goals? (Oandasan and Reeves 2005).

7.3 Learning in the Clinical Setting

The clinical setting is critical for applying theoretical knowledge in practice, learning and consolidating new skills both technical and humanistic, learning to work effectively as a member of an interprofessional team, and learning how to care.

The affective quality of work (and learning) is high in the palliative care context as there is often considerable emotional work to do and support required to help patients and families process the losses that occur during illness and upon (and following) the person's death. Consequently, the emotions and values of both patients and professionals must be on the educational agenda. Case studies, recorded patient interviews, and role-plays with small group discussion are good vehicles for the exploration of these issues away from the immediate pressures and demands of the workplace. Briefings, debriefings, and case reviews can serve a similar purpose in the practice setting.

Role modeling is an important and often underestimated part of the informal curriculum that occurs in clinical settings. Observing expert clinicians communicating in difficult situations (such as breaking bad news, discussions about transition to palliative care, and advance care planning) can be a powerful and influential learning experience, especially when followed with discussion, that helps students expand their repertoire of verbal and nonverbal communication skills and provides a point of reference their future practice. Unfortunately, students are often excluded from these conversations out of a well-intentioned desire to protect the patient from unnecessary intrusion at a vulnerable time or the physician's own discomfort in being watched especially if they lack confidence in their ability in such situations. However, if the student has an existing relationship with the patient, it is important for them to have opportunities to observe these interactions (with the patient's consent) as well as opportunities to participate in the care of patients and families with palliative and end-of-life care needs in order to provide the necessary experience to increase their self-efficacy in palliative care.

Aside from formal teaching, much education in palliative care will take place in the clinical setting, and all clinical teachers need to be aware of the learning outcomes students are required to achieve. However, learning in the clinical setting can be messy and unpredictable, and there may be compromises and other negotiations that need to be made to achieve those outcomes which may require further educational work outside the care setting. Value can be added to work experiences through systematic processes of critical reflection

such as using portfolios, logbooks, journals, and/or thought-provoking episode reports to facilitate post-encounter processing and analysis. A helpful example of this might be the Professional Development and Recognition Programme (PDRP) espoused by nursing in New Zealand. The PDRP framework and criteria have been developed cooperatively by District Health Boards and the New Zealand Nurses Organisation to advance professional development in nursing, to support nurses in demonstrating competency to the Nursing Council of New Zealand (2018), and to fulfill obligations negotiated under the nurses' employment agreements. These programs aim to promote and reward nursing expertise and recognize the contribution of nurses to quality patient health outcomes (http://www.nursingcouncil.org.nz/Nurses/PDRPs).

Similar examples of self-reflection have been described. Brady et al. (2002) used narratives to track a group of house staff through 3 years of training to give the authors an understanding of the "interplay among residents' interactions with patients, their own personal issues and their struggles during several discrete stages of their professional development." One goal of the exercise was to encourage the trainees to become self-reflective. The authors felt that residents progressed through a period of "expressing ideal images of themselves as physicians through a bleak, discouraging stage of development and finally entered a stage where they could feel confirmed as professionals by their relationships with patients." By adopting this method, the teachers encouraged deeper and clearer thinking about the young doctors' roles and therefore help them to realize that things they learn about themselves will influence their practice as physicians. Wear (2002) used students' narratives on end-of-life care to illustrate students' worry and concern about end-of-life care and their perceived lack of preparation for such care. The students didn't feel well prepared or supported as they cared for their first dying patients, which continues to be a common theme in the international literature. They did however identify their desire for more support and role modeling from residents and attending physicians.

8 Summary

Increasing demand for palliative care, driven by an aging population and an increasing prevalence of chronic, life-limiting conditions, makes palliative care education an essential requirement for all health and social care professionals in order to prepare them to meet the needs of the world's population into the future. Training in professional programs must begin at undergraduate level and extend into continuing education with increased availability of advanced specialty training to combat the predicted future shortage of palliative care specialists.

The changing emphasis toward more community-oriented care indicates a need for more education and training in these settings to enable people to remain in their own homes and communities for as long as possible and to die there if that is their wish. This includes meeting the educational needs of family carers and health and social care professionals employed in community settings, including staff employed in residential aged care facilities.

This chapter has discussed current issues related to palliative care education and the strategies that can be used to deliver high-quality palliative care for all, at the heart of which is the relief of suffering in all its forms through the power of education.

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Part IV

Organization of Palliative Care in Different Settings

Home Care, Primary Care

50

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Contents

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_48

Abstract

Care at the end of life has developed into a sophisticated specialty, historically modeled around the needs of incurable cancer in terms of complex, rapidly developing symptomatology and psychopathology in a predictable time frame. It is ill-equipped to manage people dying of other conditions, and the aging of the population will see the rise of multimorbidity, frailty, dementia, and organ failure as predominant causes of disability and death. The existing specialized, hospital-focused, and subspecialized health system that currently manages very ill people will not be able to cope with the complexity, multimorbidity, and unpredictability that characterize the future. Generalists, particularly community-based services, will inevitably have a very significant role to play.

This chapter examines the role of primary care, specifically general practice, in managing end-of-life care. It describes the similarities between the aims and objectives of general practice and palliative care, the scope of generalist end-of-life care, the past performance of general practice at the end of life, and models of care that can enhance both GP performance and integration between specialists and generalists. It concludes with initiatives that will facilitate national policy development to promote effective end-of-life care.

1 Introduction

The world has made spectacular advances in overcoming illnesses as diverse as cancer and sepsis. As a result, the average survival rate has increased dramatically, and the improvements in quality of life for most of those years have been impressive. Most of us can be confident that we will be living well into our 80s. While we celebrate "conquering cancer" (and other diseases), what is not discussed much at all is that there is a limit to the length of time we will live. The vast majority of people will die between the ages of 70 and 90 and virtually are all dead by about 100 years of age (World Health Organization 2015). Medical advances have simply delayed the inevitable.

As the population ages rapidly, so the absolute number of deaths per annum will rise. The absolute numbers who will die has to increase faster than the rate at which we are aging. Etkind et al. estimate that the number of people dying per annum in the UK will rise by 25.4% as a result of a higher proportion of older people (from 17.7% $\geq$ 65 in 2014 to 24.2% in 2040) (Etkind et al. 2017). Australian predictions suggest that the picture will continue to escalate beyond 2040. By 2016, the number of deaths was predicted to rise by over 250% from 2011 to 2061 (Australian Bureau of Statistics 2016) (Fig. 1). Moreover, the number whose dying can be anticipated and who will probably benefit from palliative care will escalate from approximately 75% in 2014 to up to 87% in 2040 (Etkind et al. 2017). The need for skilled end-of-life care will escalate.

In addition, the nature of the causes of death is changing. Gill et al. analyzed the cause of death of previously well 70-year-old people and found that the greatest cause of death was frailty (28%), followed by any organ failure (21%), cancer (19%), and dementia (14%) (Gill et al. 2010). Seventy-nine percent of this cohort had a predictable course to death, with the majority of people dying after a prolonged period of disability and ill health. Frailty, the most common cause, is caused by an accumulation of age-related illnesses, impacting on bodies with less capacity to maintain homeostasis. Older people will be taking more medicines than before, with the accompanying risks of expected and unexpected adverse events and drug interactions.

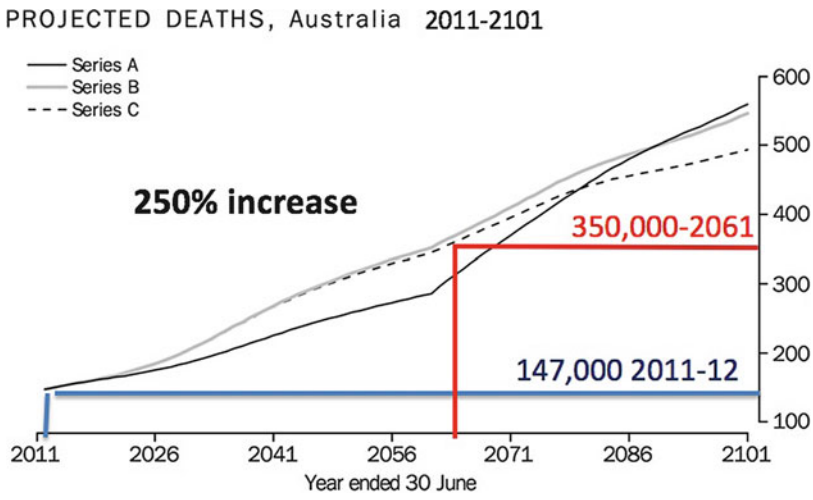

Fig. 1 Annual deaths from 2011 to 2101 in Australia

2 Society's Response: Palliative Care

Society's response to dying has changed dramatically since Cicely Saunders developed a systematic and deliberate response to the problems of distressing deaths from terminal cancer. The sustained study of pain and symptom management and a complete change in approach to death from a perceived medical failure to an expected part of the human experience have had profound effects on modern health care.

Better understanding of pain management and the development the specialized institutions to manage the end of life were the initial response. Better understanding of the management of other symptoms, the psychology of dying, vastly improved communication skills, and better organization of care have put very high quality of care in reach of most people with cancer in developed countries. Indeed, the proportion of people dying of cancer who access palliative care is around 68 percent (Rosenwax and McNamara 2006). Specialist palliative care has largely aligned with cancer care. Palliative care services are often co-located with oncology departments. There may be beds allocated to palliative care services, or the service may be a consultative service to other clinical units.

This model has served these patients well, particularly with timely referral. It is not perfect, particularly when patients are referred too late to have a demonstrable impact on the patient and family's well-being. There are two main reasons the majority of palliative care services manage cancer. The first is historical. The dramatic and tragic course of cancer for many patients makes improvement of the end of life an obvious backdrop for this sort of care. Secondly, with relatively predictable time courses and relatively predictable symptoms, it has been relatively easy to design service delivery to suit end-of-life cancer care.

However, the proportion of people without cancer who die without accessing specialist palliative care is disturbingly high (Rosenwax and McNamara 2006), in spite of the symptom burden of conditions like advanced heart failure being the equivalent of that of advanced lung cancer (Murray et al. 2002). There are several problems in providing specialist palliative care to this group. First, the illness trajectory of these conditions is variable (Fig. 2). A typical organ failure trajectory has multiple relapses and remissions, and the timing of these is unpredictable. Secondly, a person with organ failure may have a prognosis of years before death. The same applies to the person with advanced multimorbidity. They often have substantial care needs relating to mounting disability, but it might take years to recognize that the person is approaching death. Many will have dementia, which in the latter stages limits the ability to undertake more than

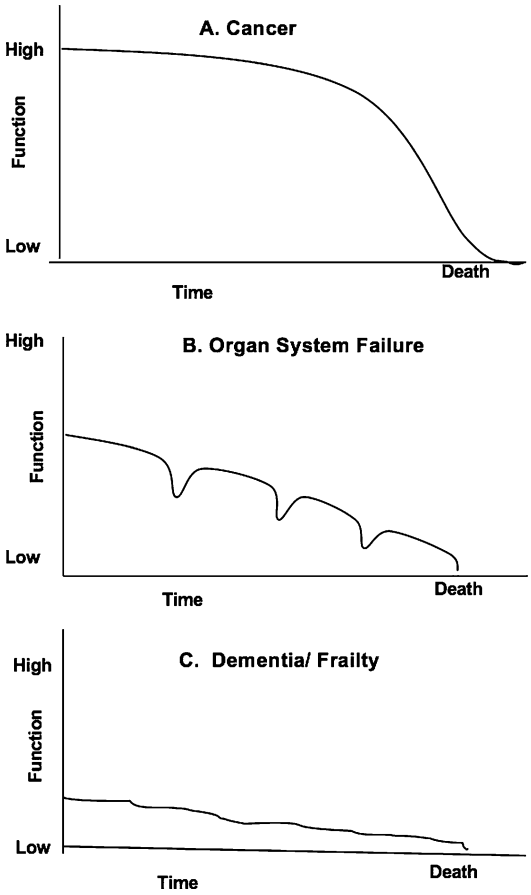

Fig. 2 Trajectories of illness at the end of life

the most basic of activities of daily living. In addition, people with dementia also suffer substantial symptom burden over and above the burden of the underlying condition. For example, approximately half of all people with advanced dementia are reported to suffer pain to some degree (van Kooten et al. 2016).

The end-of-life care model designed for the intense, accelerating need for care seen in cancer palliative patient is not going to work in most people with nonmalignant disease approaching end of life. Currently, about 80% of the patients of specialist palliative care units have a primary diagnosis of cancer (Australian Institute of Health and Welfare 2014). Who looks after the non-cancer deaths? Certainly not specialist palliative care – they are being stretched with the current illness mix. The number of referrals to Australian specialist palliative care services grew by 52% in the decade from 2002 to 2012 (Australian Institute of Health and Welfare 2014), and the services have little ability to take more on. More of the same is not going to work, and urgent attention needs to be paid to alternative models of care.

This chapter aims to describe the place of primary care in the care of people at the end of life, with a particular emphasis on primary care. It examines how ideal primary palliative care could work and the evidence in support of integrating primary care into the management of complex end-of-life conditions. In addition, it demonstrates the performance of general practice as reflected by a systematic review of the literature undertaken to 2014. Finally, it documents some of the major policy initiatives that seek to embed primary palliative care into routine end-of-life care.

3 General Practice, Primary Care and Palliative Care

There are major similarities between the definitions of general practice and of palliative care (Box 1). Both emphasize the importance of treating the whole person. Both emphasize the importance of high-quality assessment and management of people's problems. In addition, family practice emphasizes health promotion and prevention and understanding the context in which the patients live work. End-of-life care is a natural fit for primary care.

Box 1 Definitions of Palliative Care and General Practice

WHO Definition of Palliative Care

Palliative care is an approach that improves the quality of life of patients (adults and children) and their families who are facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and correct assessment and treatment of pain, and other

(*continued*)

Box 1 (continued)
problems, whether physical, psychosocial, or spiritual (World Health Organization 2004).

European Definition of General/ Family Practitioner

General practitioners/family doctors are specialist physicians trained in the principles of the discipline. They are personal doctors, primarily responsible for the provision of comprehensive and continuing care to every individual seeking medical care irrespective of age, sex, and illness. They care for individuals in the context of their family, their community, and their culture, always respecting the autonomy of their patients. They recognize they will also have a professional responsibility to their community. In negotiating management plans with their patients, they integrate physical, psychological, social, cultural, and existential factors, utilizing the knowledge and trust engendered by repeated contacts. General practitioners/family physicians exercise their professional role by promoting health, preventing disease, and providing cure, care, or palliation. This is done either directly or through the services of others according to health needs and the resources available within the community they serve, assisting patients where necessary in accessing these services. They must take the responsibility for developing and maintaining their skills, personal balance, and values as a basis for effective and safe patient care (WONCA Europe 2011).

In fact, as experts in multimorbid care, general practice is where most of end-of-life care should and probably already does take place. It is not clear whether GPs understand that they are already providing end-of-life care as they manage multimorbid and frail older people. There are different perceptions of what palliative care and end-of-life care actually comprise. The classic picture of palliative care involves intense care at the end of life: managing uncontrolled symptoms, rapidly changing and accumulating symptom burden, patient fears, and relatives who are frightened and distressed. And that is what a lot of end-of-life care is like. However, there is another form of end-of-life care which ideally takes place much earlier – months from death is ideal. Here there is a recognition of the inevitability of dying at some stage in the future. Together with the patient, future patient wishes are articulated. Clinicians anticipate future medical and situational problems and start to put into place strategies to manage these when they arise. These are both legitimate forms of end-of-life care but very different (Fig. 3).

4 Multidimensional Care

Murray et al. have gone further to describe the nature of palliative care, calling it a four-dimensional activity. These dimensions are physical, psychological, social, and spiritual dimensions of care (Murray et al. 2007). This framework is very useful in identifying and planning treatment. Different versions of this work have been done. For example, Eychmüller and colleagues (Eychmeuller 2012) have also undertaken work to identify the essential elements of palliative care, developing the SENS structure of palliative care planning and treatment: ***S****ymptoms* both current and anticipated; ***E****nd-of-life decisions* that have to be made; the ***N****etwork of care* required around the patient; and ***S****upport for the family* required to manage the situation. They go on to define the goals of comprehensive care: the so-called 4-S goals, improving ***Self-help*** capacities; promoting ***Self-determination***; ensuring ***Safety***; and assuring ***Support*** for the family.

5 Consumer Expectations of the Role of GPs and Primary Care at the End of Life

A systematic review by Johnson et al. (under review) identified the expectations of patients and their immediate carers of the role of GPs and primary care health professionals at the end of life.

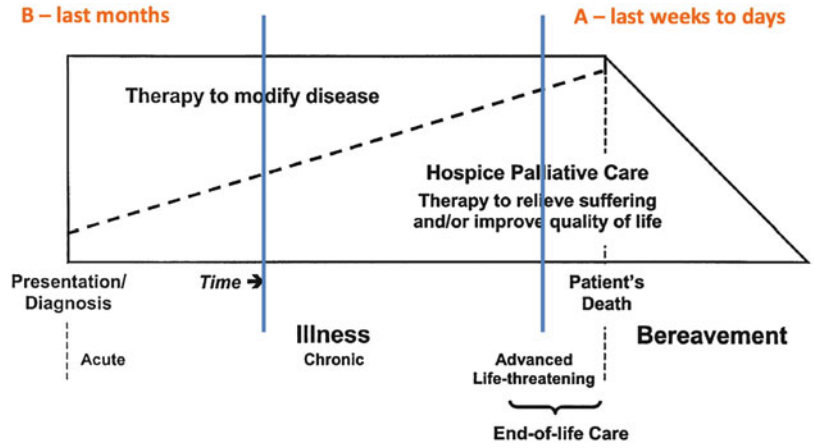

Fig. 3 Different aspects of palliative care dependent on time from death

Continuity of care was considered an important aspect of care (Borgsteede et al. 2006; Neergaard et al. 2008). Different elements were identified in the literature:

1) *Relational continuity of GP care*. Patients and their immediate carers prefer that care is provided by the same known GP (with backup from the same clinic when necessary), rather than different GPs (Borgsteede et al. 2006). Further, patients also preferred to continue their relationship with the GP across different care settings, thus requiring ongoing and close cooperation between the patient's GP and their specialists during the final illness. This relationship should ideally persist with the next of kin, even after the death of the patient.

2) *Informational consistency*. The patient's primary care providers should be the repository of the patients' clinical information. This information should be shared across all health providers to promote consistent care and reduce the need for patients to continually retell their story (Neergaard et al. 2008). Effective means of information sharing is an increasing theme for health care in general. Having a shared clinical record is already a reality in some jurisdictions (e.g., Spain, UK) but not others. Sharing information between specialists and carers is eventually being developed in other places (e.g., Australia). Until that is universal, some means of information sharing should be devised, and primary care practitioners are in a good position to enable that to happen.

3) *Consistency of information provision*. The role of caring is highly stressful, and most carers do not have a health-care background. They are being asked to care for the most unwell people and need good information to do this job. Minor differences in the information provided create anxiety and distress. Consistency of information provision minimizes this problem (Boyd et al. 2004). GPs can be the providers of information or the interpreters of information from others to allay concerns and ensure high-quality care provision.

Interprofessional communication. Patients and carers believe that high-quality interprofessional communication regarding diagnosis, treatment, and prognosis facilitates good end-of-life care (Borgsteede et al. 2006). While patients developed strong rapport and relationships with health professionals in the acute care setting (Aabom and Pfeiffer 2009), they needed to see overt collaboration between those health professionals and other agencies involved in palliative care provision and their GP to feel confident that all health professionals were working together (Neergaard et al. 2008). The GP could be a key carer if the GP-patient relationship was established and effective. Some patients suggested that GPs should be proactive in engaging with health professionals such as oncologists and palliative care services and that oncologists should inform patients of the important role of GPs in end-of-life care (Borgsteede et al. 2006; Neergaard et al. 2008).

Patients believe they benefit from a strong therapeutic relationship with their GP (Slort et al. 2011). Consistently seeing the same GP contributed to a greater knowledge of the personal needs and preferences of the individual, increasing trust and mutual understanding (Michiels et al. 2007). The GP in such a therapeutic relationship would take time to be engaged and "listen carefully," be able to deal with strong emotions, and be able to assist patients with advance care planning to improve patient, carer, and family outcomes (Slort et al. 2011).

Patients observed that they were often the subjects of a health professional-led approach to care, rather than a partnership between health professionals, the patient, and any relevant carers and family members (Boyd et al. 2004). They considered such a partnership a more effective approach, which would empower patients and their carers and facilitate patient-centered care. The limited palliative care experience of some GPs was perceived by some patients and carers to impact on their ability to provide more than basic psychosocial and carer support (Farber et al. 2003).

A ***GP's communication skills*** were particularly valued by both patients and carers (Borgsteede et al. 2006; Neergaard et al. 2008; Grande et al. 2004). Attributes such as trustworthiness, respect, kindness, caring, sympathy, honesty, and sensitivity fostered constructive and collaborative relationships between GPs, patients, and carers (Grande et al. 2004). Patients preferred GPs to be open and initiate discussions about end of life (Slort et al. 2011).

Ready access to and availability of GPs and other health professionals were considered fundamental to good end-of-life care (Borgsteede et al. 2006; Neergaard et al. 2008). Patients needed to be able to see their GP without protracted waiting times for appointments or having to wait for long periods on the day of appointments (Borgsteede et al. 2006). As a patient deteriorated, having a GP who was available out of hours and who conducted home visits was essential if the patient wished to remain at home (Borgsteede et al. 2006; Neergaard et al. 2008; Slort et al. 2011). A GP's lack of time was a barrier to continuity of care.

Patients expect GPs to be competent at diagnosing problems and in the management of their symptoms (Borgsteede et al. 2006), but this was not always the case (Grande et al. 2004). They wanted GPs to be well informed about their condition, how to manage symptoms, and to be aware of the side effects of treatment (Borgsteede et al. 2006; Slort et al. 2011). Patients wanted information about symptoms and their management to be shared with them (Grande et al. 2004).

Patients and carers expect GPs to facilitate or enlist help from other agencies to enhance EOL care. In particular, shared care between GPs, community services, and specialist services was appreciated by them, including engagement with palliative care services when required (Neergaard et al. 2008). Community support services can facilitate access to equipment and supplies.

While some patients and carers identified the importance of the psychological, social, and spiritual support which could be provided by GPs (Grande et al. 2004), others had not considered that they might use the GP for non-biomedical or nontreatment-related issues. They did not want to inconvenience or disturb a busy GP for what they considered "minor matters," despite increasing psychosocial concerns as the disease progressed. Some clinicians described their patient care largely in terms of treating the disease.

6 What Does End of Life Look like in the Community?

End-of-life care in primary care comprises escalating need for care starting months from death and some intense care at the end of life. There are three essential elements to this "early palliative care." First, in order for deliberate planning and management to take place, there has to be a conscious recognition that the end of life is approaching. When that decision is made, then some form of planning should take place. Finally, the health team needs to be ready to enact the plan when the time comes.

7 Essential Steps in Primary Palliative Care

7.1 Identifying Approaching End of Life

Identifying people approaching the end of life seems such a simple proposition, and yet it is not often deliberately done. The identification of patients for palliative care tends to rely on practitioners' subjective judgment (intuition and knowledge), rather than established guidelines (Harrison et al. 2012). Cancer patients had the greatest likelihood of being identified as being in need of palliative care. Patients with non-malignant but advanced and progressive illnesses were less likely to be formally identified for palliative care prior to death (Harrison et al. 2012). This may be because of a perception that palliative care is only the care at the end of life.

Our group has done recent work (under review) that shows that GPs' recognition of approaching end of life is tacit, and they will not often raise it with patients de novo, unless the patient raises the possibility first. If patients raise it, then proceeding to appropriate planning is relatively smooth. If they do not, then the GP is loathe to raise the possibility of impending death. However, the GPs reported that they did subtly, perhaps consciously, shift their care toward comfort care.

Burridge et al. (Burridge et al. 2011) describe "consultation etiquette" – where the patient is too polite to "bother the doctor" with their problems and doctor is too polite to raise issues like this one with the patient. Thus consideration of very important issues like this one is deferred and perhaps never addressed.

7.1.1 Attempts at Systematic Identification of Patients Nearing the End of Life in Primary Care

There have been concerted attempts to systematize the identification of patients approaching the end of life. Keri Thomas of England initiated this movement and developed a sophisticated process of identification through screening of GP patient lists, planning care, and enacting the plan – the so-called Gold Standards Framework (Thomas 2007). There have also been other tools or checklists to assist in the identification of people approaching the end of life. A systematic review has identified four main identification tools and assesses their practicality in the practice setting (Maas et al. 2013). What is clear is that any systematic identification process has to be compatible with the health systems in which they operate. The tools available very clearly illustrate this. Gomez-Batiste in Catalonia, Spain, developed a tool (NECPAL) that could interrogate electronic records and required smaller amounts of input from clinicians (Gomez-Batiste et al. 2013). Spain has a single electronic record that follows the patient through the entire health system. Thomas' Prognostic Indicator Guide (PIG) (Thomas 2011) works in the context of UK's system of capitation payments and rewards for meeting public health targets. This enables practice staff to spend time searching patient records for people suitable for a Palliative Care register and be rewarded for doing so. This will not work in a fee-for-service environment like the Netherlands or Australia, where practitioners only get paid for seeing patients.

Research into the implementation of screening tools has taught several lessons. In the Netherlands, a tool was developed that identified people with advanced cancer and end-stage lung and heart failure, but not those with non-specific frailty or multimorbidity (Thoonsen et al. 2015). The project trained GPs in its use – a good strategy in a fee-for-service environment. However, in an RCT, there was no difference in patient identification when all GPs who were randomized to training in the tool were considered, as half the intervention group did not use it (Thoonsen et al. 2015). However, there were significant improvements in patient identification and multifaceted care when analyzing those GPs who did use the tool (Thoonsen et al. 2015). The Supportive and Palliative Indicator Tool (SPICT) has been the one most used internationally (Highet et al. 2014). It is short (one page) and more inclusive than exclusive of patients through the use of broad categories of disability. It is also constantly being revised and upgraded through web page

(www.spict.org), inviting commentary and registration of its use. It has been translated into several languages as well.

A literature review of the impact of the Gold Standards Framework (Shaw et al. 2010) showed that, in spite of financial incentives to maintain palliative care registers, many people who did die did not appear on the register, as it contained predominantly people with advanced cancer. Why this was the case is yet to be fully determined.

While the concept of screening patient lists is very logical on paper, it appears that converting the idea into practice is another issue. We learn from this literature that GPs recognize deterioration to death with cancer more easily than for end-stage nonmalignant disease. We also learn that relying on GPs to use a tool offered to them is no guarantee of use, even if use does achieve the desired result.

Our group wondered whether there was benefit in using screening tools at all and tested the ability of screening tools to predict death against GP intuition (Mitchell et al. 2018a). We showed that screening tools was more effective than intuition in predicting those who did die but only among those patients that a GP considered were at risk of death. There was no difference between the groups in identifying people who died when whole practice lists of patients over 70 were screened. There was also a very high false-positive rate of identification of risk of death with both techniques. We showed that deliberately screening for likely death was not a useful means of identifying the cohort of people with end-of-life needs, and recognition of escalating needs was a better approach to explore.

Taking identification out of the hands of GPs and making screening an automatic procedure, for example, through electronic records surveillance, may have promise (Mason et al. 2015). The problem will be to have a screening process to identify people at risk, but with appropriately modest false-positive rates. A positive test demands a response, and a high false-positive test will place an unreasonable burden on practitioners if developing a comprehensive care plan is the response. Either a graded response proportional to the level of risk is developed, or a less sensitive and more specific set of search criteria are generated.

Zheng et al. did elegant work in Scottish general practices to see if the problem of end-of-life recognition was the term "palliative" (Zheng et al. 2013). They showed that people with nonmalignant diseases – organ failure and frailty/multimorbidity/dementia – were hardly ever placed on the practice palliative care register as at risk of dying compared with cancer, where three-quarters of cancer patients were identified on the register and in a timely manner. By changing the title of the register to a "supportive needs register," recognition of people who died from nonmalignant was 40% at the time of death, and much earlier recognition occurred.

One issue is that dying in primary care is a low prevalence event in primary care. As the population ages, patient deaths will become more prevalent. However, while patient death will never be a routine event, the incidence of frail and multimorbid patients will rise, all of whom will die. At what point should a doctor "change gears"? Should it be a sudden transition, or a gradual escalation of response to need? The answers to these questions are not yet clear.

In summary, identification of the patient is the essential first step to proactive end-of-life care. While appearing logical, it is in fact highly complex to enact it systematically in the community.

7.2 Planning Care

Once a person is identified as requiring palliative care, ideally some sort of plan needs to be generated. This again is not as easy as it sounds. There are two elements to proactive care planning – advance care planning and clinical care planning (Fig. 4).

7.2.1 Advance Care Planning

Much effort has been made to facilitate advance care decision-making. The rationale is that medical care needs to reflect the individual's goals and aspirations for the remainder of their life, along with preferences for the type of health care they want to have. This is very important in hospital practice, so that care which can be very expensive and which may not produce demonstrable

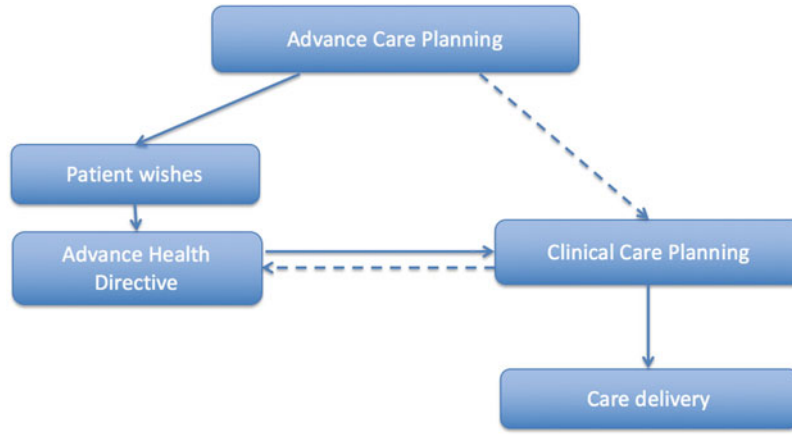

Fig. 4 A concept map of care planning for the end of life (Mitchell. 2014a)

benefits is only offered to those who really want it. The second element of advance care planning is to appoint substitute decision-makers in the event that the person cannot articulate decisions for themselves. These people are usually, but not always, next of kin.

7.2.2 Clinical Care Planning

A second form of care planning is also highly desirable but less considered. This is clinical care planning. Most people with serious illness have predictable complications. For example, a person who has severe heart failure will almost certainly wake up in the middle of the night breathless at some point in the future. What can be done to prevent that? What actions can minimize the breathlessness and facilitate the patient settling without an emergency admission to hospital when it does happen? It should be possible to anticipate these issues and prepare plans that can be enacted when the anticipated problems arise.

7.2.3 Integrating Specialist and Generalist Care

Being ill with multiple conditions can be problematic. Hillman describes a health system where the consequences of lack of integration include a lack of clear decision-making, deferral of critical decisions these often being made by intensive care specialists by default (Hillman and Cardona-Morrell 2015). Gawande describes multiple personal experiences of a loss of focus on the whole person, with decisions being made for reasons far removed from what the patient wants or will provide long-term benefit (Gawande 2014).

General practitioners manage multimorbidity as a matter of course. They are also usually very aware of the personality and social circumstances of the individual, which becomes important in anticipating the needs of people at the end of life.

Management of patients with multimorbid problems is not well coordinated between GP and the specialist team(s). A systematic review of integration programs that deliberately integrated general practitioners with specialists found only 14 such studies (Mitchell et al. 2015). By contrast, there are dozens of studies testing integration in a range of specialist settings. Here integration means integration of different specialist treatment modalities. Actual interventions aimed at bringing medical specialities together are unusual. For example, a Cochrane review of integration in COPD care involved 26 studies, only 2 of which aimed to improve interprofessional integration (Kruis et al. 2013).

Bringing together the contextual knowledge of GPs and the content knowledge of specialists should be of benefit to patients facing the end of life. A number of interventions supporting this form of care have been tested.

The one with the strongest evidence base is case conferences between specialists and GPs.

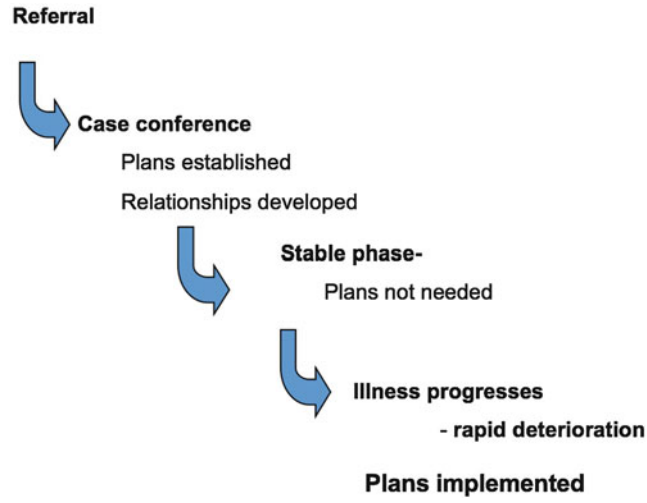

Fig. 5 Mechanism of action of GP specialist case conferences at the end of life

The rationale is that GPs know the context of the patient and their family, while specialist teams have the content expertise. The combination of these two things should be effective in improving patient outcomes. Australian general practice is funded through a blending of fee-for-service and outcomes based funding. In recognition of the importance of integrating GPs into the care of complex and chronic conditions, government rebates for participating in case conferences with other health professionals are available. Both trials used this opportunity to test the above hypothesis. Abernethy et al.'s study (the world's largest randomized controlled trial in palliative care) showed 30% reductions in admissions to hospitals and a mean 10% improvement in maintenance of functional capacity from diagnosis to death (Abernethy et al. 2013). Mitchell et al. showed improvements in the patient's quality of life in the last month of life (Mitchell et al. 2008b).

The assumed mechanism of action for this improvement was that the case conference took place and a joint plan of action was negotiated and the palliative care team members and the GP became acquainted with each other, creating communication channels. This plan was often not enacted immediately because there was often a latent period when the patient was stable. However, when deterioration did occur, the latent communication channels were activated, plans were in place and enacted promptly, and the patient's outcomes were better than those of normal care (Fig. 5).

It appears that a key element of successful GP specialist integration is buy-in from the GPs. Active negotiation of the plan between specialists and GPs appears to work better than passive receipt by a GP of a plan formulated by the specialists – someone else's plan (Mitchell et al. 2008a). Thus the major difference between the program impact was that the GP was an integral part of the planning process – he or she had buy-in – whereas in the geriatrics trial, the primary care practitioner was a passive recipient of someone else's care plan.

7.3 Implementing Care

Once patient and carer needs are identified and care planned, the plan has to be implemented. Recent work (under review) indicates that the GPs' understanding of the patient's willingness to accept their nearness to death determines how overtly a plan to implement end-of-life care is articulated. If the patient can articulate an awareness and acceptance of impending death, then the GP will discuss end-of-life care overtly. If not, then GPs instinctively and subtly changes care goals to include issues of importance at the end of life.

8 What Are the Outcomes for Primary Care-Delivered Palliative Care?

The following sections examine how well GPs perform palliative care from different perspectives. They arise from the series of systematic reviews mentioned in the acknowledgments at the commencement of the chapter.

8.1 Symptoms (Mitchell et al. 2018)

8.1.1 GP-Identified Symptoms

General practitioners (GPs) found symptoms associated with the terminal phase as the most distressing for the patient (Mitchell and Seamark 2016). Of those patients who were cared for at home in the terminal phase of their disease, the main symptom was fatigue, which was a documented symptom in almost all patients (Leemans et al. 2012). Other common symptoms included anorexia, drowsiness, pain, dyspnea, and psychological distress. Pain was perceived as causing less suffering than these in the terminal phase (Mitchell and Seamark 2016).

8.1.2 Did GPs Respond Adequately to Patient Symptoms?

Primary health-care professionals were well placed to recognize symptom issues in palliative care patients. A study comparing agreement on symptom assessments between patients at home with those of nurses and GPs demonstrated high levels of symptom identification (Ewing et al. 2006). Gastrointestinal problems such as nausea, vomiting, and constipation were recognized by GPs more than by the patients themselves. Nonmedical health professionals were more likely to note psychological issues and bestow greater significance to them than patients did themselves. Pain scores were comparable between all groups throughout.

In general, GPs expressed confidence responding to the symptoms identified by their palliative patients (Leemans et al. 2012; Blazekovic-Milakovic et al. 2006; Kuin et al. 2004; Canto et al. 2000). They felt most comfortable in responding to pain. They were least comfortable managing dyspnea, followed by fatigue. However, a study in Spain identified that the majority of GPs felt confident managing pain, dyspnea, and epilepsy by themselves (Canto et al. 2000).

General Psychological Care General practitioners perceived emotional support as being one of the most important aspects of palliative and terminal care they managed (Blazekovic-Milakovic et al. 2006; Ledeboer et al. 2006). They used supportive conversations, assistance with administration procedures, coordination of care, and management of carer and family distress to address patient distress (Canto et al. 2000; Demagny et al. 2009). While GPs felt they were predominantly comfortable providing this care, there were a number of challenges. GPs were often troubled by conversations about death and spirituality (Kelly et al. 2008). In one study, only half of GPs had involved patients in conversations regarding dying, viewing patient stoicism, and the presence of other family members as common barriers. Spirituality was seen as a difficult subject, often viewed by GPs as involving only religious beliefs, and thus rarely discussed. A common theme throughout all such studies was a lack of formal education and experience in this area, with GP eager to participate in further training (Canto et al. 2000).

8.1.3 Effectiveness of GP Symptom Control

(a) ***Pain***. While most general practitioners had adequate knowledge of general pain management, deficits in some GPs' knowledge of treating cancer pain may have resulted in ongoing pain at the end of life (Anquinet et al. 2011). They were also challenged by managing comorbid symptoms, such as neurological symptoms in patients with high-grade gliomas (Sizoo et al. 2010).

There was insufficient evidence available to assess whether GP management provided adequate relief: assessment of suffering, effective cancer pain management (Gott et al. 2010), patients' roles in end-of-life care and advance

care planning, artificial nutrition and hydration, and the understanding of sedation versus euthanasia in relation to pain management (Anquinet et al. 2011).

(b) ***Breathlessness***. GPs were reluctant to prescribe opioids for breathlessness associated with severe COPD, even though they were aware of their proven benefit (Gott et al. 2010; Young et al. 2012). The main reasons for their hesitancy were the lack of education or knowledge of guidelines (Young et al. 2012), perceived scarce evidence supporting expert groups' recommendations for the long-term use of opioids for breathlessness (Young et al. 2012), and the fear of censure (Gott et al. 2010; Young et al. 2012). Some GPs would rather hospitalize patients than prescribe opioids for breathlessness (Gott et al. 2010).

8.1.4 Gastrointestinal Symptoms

One community-based audit showed that 30 of 88 patients were prescribed laxatives (Mitchell and Seamark 2016). Of these 11 were co-prescribed with opioids and 19 for non-opioid-related constipation. Thirty-six patients of the 88 patients had nausea. Most were treated with a single antiemetic, or two antiemetics tried sequentially, while only two had a combination of two antiemetics. In one study, gastrointestinal symptoms were reported as the most frequent symptoms identified by GPs (Borgsteede et al. 2007a). GPs identified nausea and vomiting as more prevalent and more severe than patients reported it, but under-recognized constipation as a problem (Ewing et al. 2006). In a 2002 survey of GPs prescribing an opioid, reported 57.6% would prescribe an antiemetic, only 33% a laxative (Oxenham et al. 2003; Borgsteede et al. 2009), and 20.7% both in the first few days (Barclay et al. 2002).

8.1.5 Depression

GPs experienced difficulties diagnosing and managing depression within the palliative care setting (Warmenhoven et al. 2012). GPs reported relying on clinical judgment, patient context, and the long-standing patient-doctor relationship to identify depression in palliative care patients, rather than making criterion-based diagnoses. The treatment of depression in palliative care was mainly supportive and non-specific, with antidepressants seldom prescribed.

8.1.6 Palliative Sedation

Palliative sedation is a recent phenomenon, performed when standard treatment is not able to control troubling symptoms. By sedating the patient to the point of unconsciousness, it removes awareness of the symptom and alleviates patient distress. The practice is only infrequently required (Donker et al. 2013) and should always be administered after close consultation with the patient and family. Continuous deep sedation until death does not always guarantee the dying process was free from symptoms (Anquinet et al. 2013). There was disagreement among practitioners about which symptoms actually necessitate palliative sedation (Sercu et al. 2014), as well as the potentially life-shortening intentions of sedation (Sercu et al. 2014). Reassuringly, a systematic review has showed palliative sedation does not shorten life expectancy (Beller et al. 2015).

A minority of GPs reported feeling pressure from patients, relatives, or colleagues to commence continuous sedation. This pressure was felt more strongly when patients experienced psychological symptoms (compared to physical symptoms) and when patients had greater estimated life expectancies (Blanker et al. 2012). Such pressure led to GPs seeking advice with respect to therapeutic options and/or specific information (Blanker et al. 2012; van Heest et al. 2009).

8.1.7 Barriers to Good Symptom Control

The need for more formal training in palliative care for GPs at both under- and postgraduate level was well documented (Farber et al. 2004; Hong et al. 2010; Walsh and Regan 2001; Groot et al. 2005). There was a particular need for education in the use of opioids (Hirooka et al. 2014; Gardiner et al. 2012; Todd et al. 2013; Salvato et al. 2003; Higginson and Gao 2012; Hawley et al. 2013) and referral for palliative radiotherapy (Vulto et al. 2009; Olson et al. 2012; Samant et al. 2006).

Another barrier identified by GPs was a lack of access to inpatient beds and home services support – often perceived as the result of bureaucracy – causing delay of essential symptom management or necessitating the patient to travel to hospital for simple procedures that could have been delivered in the home (Walsh and Regan 2001; Groot et al. 2007).

GP confidence in some settings providing palliative care was perceived as being low but increased with experience (Hirooka et al. 2014). The more frequently a GP performed palliative care activities, the more competent they felt (Farber et al. 2004; Gorlen et al. 2012). A death within a GP's population is a low prevalence event, which can exacerbates the GP's sense of inadequacy. However, those physicians who were more interested in palliative care did perform palliative care activities more frequently (Farber et al. 2004).

9 GP Understanding and Use of Opioid Therapy in Pain and Dyspnea Management

GPs were usually familiar with the management of common pain problems, the WHO guidelines on analgesics, and the use of oral opioids (Oxenham et al. 2003; Barclay et al. 2002). However, some gaps were identified: omission of rapid-release opioid use for breakthrough pain (Oxenham et al. 2003; Barclay et al. 2002), not prescribing laxatives and antiemetics when giving opioids (Oxenham et al. 2003; Barclay et al. 2002; Borgsteede et al. 2007b), and difficulty in converting oral opioids to subcutaneous forms (Oxenham et al. 2003; Barclay et al. 2002; Linklater 2008).

Older GPs (Young et al. 2012; Ben Diane et al. 2005), GPs with more experience in the treatment of terminally ill patients (Ben Diane et al. 2005), and those trained in palliative care and pain management (Ben Diane et al. 2005; Mas et al. 2010) were more likely to prescribe strong opioids. They were more comfortable prescribing opioids for cancer patients (Young et al. 2012; Borgsteede et al. 2007b) compared with other conditions and more particularly in the terminal phase (Harrison et al. 2012). Patient factors positively associated with GP opioid prescription included younger age (Harrison et al. 2012; Hirakawa et al. 2007) higher pain levels (higher pain associated with more opioid prescriptions) (Mas et al. 2010), repeated requests for pain medication (Mas et al. 2010), and the presence of relatives caring for the patient.

9.1 Advance Health Directives

9.1.1 Uncertainty about the Timing of ACP

Advance care planning (ACP) is done ad hoc in the terminal phase, is sometimes discussed but not documented, or is not done at all (Evans et al. 2013; Meeussen et al. 2011; Snyder et al. 2013; Vandervoort et al. 2012). Difficulties associated with the unpredictability of the end-of-life trajectory and the absence of a clear beginning of the final stages of non-cancer patient deaths created uncertainty among clinicians about when such a discussion should be initiated (Meeussen et al. 2011; De Vleminck et al. 2014; Evans et al. 2014). Consequently, for non-cancer patients, ACP often occurs in the last week of life (Meeussen et al. 2011; Snyder et al. 2013) despite patients' preference to have a discussion with their GP earlier (Robinson et al. 2012). Discharge from hospital was a common trigger for initiating ACP (Meeussen et al. 2011; Boyd et al. 2010). ACP is more likely to be completed if the patient was in hospital as opposed to the community, as the hospital-treating doctors were more likely to recognize changing clinical status (Boyd et al. 2010).

Several ***factors that influenced the completion of ACP by GPs*** were identified. In terms of provider characteristics, an advance care plan was more likely to be completed if the GP was older and had more clinical experience (Snyder et al. 2013); if the GP was comfortable discussing ACP (Farber et al. 2004; Snyder et al. 2013; Evans et al. 2014); if they had appropriate education and training in ACP (De Vleminck et al. 2014; Robinson et al. 2012; Boyd et al. 2010; Cartwright et al. 2014; Rhee et al. 2013); and if the GP was involved and trained in palliative care (Farber

et al. 2004). There were also issues with the quality of ACP, as studies showed that where end-of-life discussions took place, not all holistic aspects were addressed such as spiritual and existential concerns, social issues, and cultural differences (Farber et al. 2004; Snyder et al. 2013; Evans et al. 2014). Lack of time was also described as a barrier to ACP (Brown 2002).

Patient characteristics and patient interest in ACP also influenced the GP's involvement. If patients lacked awareness of their diagnosis and prognosis or did not initiate such a discussion, ACP was often not raised by the GP (De Vleminck et al. 2014). GPs also found it difficult to introduce ACP to patients who are not already interested or informed about it (Brown 2002). Older patients with non-cancer diseases often had less detailed ACP discussions (Evans et al. 2014). Despite these influences, patients want to discuss ACP with their GP but at a much earlier phase (Robinson et al. 2012).

Other factors that influenced completion or implementation of ACP were identified as concerns about the legal standing (Rhee et al. 2013; Robinson et al. 2013) and currency of ACP documents (Bull and Mash 2012), confusion around the terminologies and systems particularly with substitute decision-making (Cartwright et al. 2014), uncertainty around validity of ACP forms given there are multiple available (Robinson et al. 2013), concerns about making binding decisions about the future given the uncertainties of disease trajectories, and lack of awareness that ACP can be modified (Boyd et al. 2010; Rhee et al. 2013; Robinson et al. 2013).

In addition, organizational and care setting factors were found to influence the completion of an advance care plan. Incorporating ACP as part of standard care and having organizational protocols and systems for ACP, especially in residential care facilities, were found to be important in increasing the use of advance care plans (De Vleminck et al. 2014; Mitchell et al. 2011). ACP was also more likely to be considered in the context of end-of-life care and in the provision of palliative care (Evans et al. 2014; Boyd et al. 2010).

10 Determinants of whether the Completed Advance Care Plans or Directives Are Implemented

These included advance care plan factors such as its availability, currency, and legality of the forms (Rhee et al. 2013; Robinson et al. 2013; Bull and Mash 2012), timing of ACP (Meeussen et al. 2011), patient illness factors (e.g., quality of life of patient, level of functionality, and prognostication), organization and care setting factors (e.g., prioritizing life-sustaining treatments, policies, and protocols to support use of advance care plans), awareness, and attitudes of health professionals and family to ACP (e.g., families' understanding of the disease progression, GPs' desire to avoid family dissent) (Rhee et al. 2013).

10.1 Caring for Carers

Ninety percent of patient care in the final year of life occurs at home (Hinton 1994), with many patients moving to an inpatient setting in the final days of life. Hence, much of the burden of caregiving is managed in the community, with the greatest burden falling on primary caregivers (Aoun 2004). Care may be equivalent to a full-time job, with 20% of caregivers providing full-time or constant care (Aoun 2004).

Caring for a patient with end-of-life needs carries a number of implications. It is often provided by people who are themselves elderly and/or ill, and caregiving may exacerbate the illness burden. Caregivers of patients receiving PC have lower quality of life (QoL-impairment in physical functioning, general health, and vitality) and worse overall physical health than caregivers of patients receiving curative or active treatment (Weitzner et al. 1999). As patients deteriorate physically, caregiver QoL worsens, suggesting a greater need for support at this time (Grunfeld et al. 2004). Furthermore, while many caregivers feel positively about caregiving and derive deep satisfaction in this role, caregivers may also experience a number of physical and psychosocial issues, including reduced social contact, significant financial burden, sadness, anger, or

resentment which may increase the risk of psychiatric morbidity and complicated grief (Aoun et al. 2014). Additionally, caregivers report a number of unmet needs across a variety of areas, including information, communication, and support from services (Aoun et al. 2005). Family members whose own needs are not identified and addressed early have greater needs and less trust and confidence in the health-care system and cope more poorly in the later stages than families who have been informed and supported throughout the course of the illness (Kristjanson and White 2002).

However, despite the shift to include family members and primary caregivers as active participants in PC (Sepulveda et al. 2002), it is still common that the primary focus of the caregiver and of health professionals is on the needs and comfort of the patient, meaning that caregiver needs and distress may be considered secondary to the patient's and may be (Butler et al. 2005). For example, in 2003/2004, the patient was the client in 98.3% of referrals to Home and Community Care services, yet caregivers are a target group of that program. It has also been suggested that caregivers may be reluctant to raise their own needs with their health-care provider, as they do not wish to put their own issues before the patient's or bother the health-care professional (Hudson et al. 2004). On the other hand, health-care professionals are often working under tight time restraints, with the average Australian general practice consultation in lasting only 14.9 minutes (Britt et al. 2016), making it difficult to assess both the patient and caregivers needs in one appointment. Countering this short-time period is the fact that GPs frequently see patients several times to resolve a complex problem.

11 Does Primary Care Involvement Impact on the End-of-Life Outcomes?

Although international literature highlights GPs' variable levels of knowledge about PC and symptom control (Barclay et al. 2003) and their lower perceived levels of competence in these areas compared to specialist PC services, GPs are in an optimal position to evaluate and assess the needs of caregivers. GPs are usually the first point of contact for patients and their caregivers and generally have an established relationship with the patients with palliative care needs as well as having an important contextual knowledge of the family and of the illness. Canadian research indicates that palliative care patients with a regular GP are less likely to seek care from emergency departments (Burge et al. 2003a) and are less likely to die in hospital (Burge et al. 2003b).

Whether the effort of involving the patient in end-of-life care ultimately depends on whether patient and carers are better off with GP involvement. What is the evidence that patients and carers do better with the involvement of their GP, compared with those who have little or no GP involvement?

11.1 Integrated Primary-Secondary Care

We have already presented the controlled trial evidence of the impact of case conferences between GPs and specialist palliative teams managing mainly cancer patients (Abernethy et al. 2013; Mitchell et al. 2008b). An RCT of facilitated family meetings at which GPs were invited to attend for terminal dementia patients in aged care homes showed no group effect on quality of life but improvements in pharmacological and non-pharmacological management of symptoms (Agar et al. 2017).

There is lower level evidence in favor of integrated care specialists and GPs caring for people at the end of life for nonmalignant end-of-life disease as well. Case conferences in end-stage heart failure showed impressive reductions in hospitalization, emergency visits, emergency visits not requiring admission (Mitchell et al. 2014b), and costs (Hollingworth et al. 2016). A uniform pain control pathway reduced palliative patient's pain in rural settings (Tateno and Ishikawa 2012), while half of head and neck cancer patients whose GP used a telephone advice service died at home,

but half also had some level of uncontrolled symptoms (Ledeboer et al. 2006).

It is important to observe that these initiatives were all initiated by specialist services and reached out to general practitioners. It is clear that the primary care and specialist care work in very different ways. GPs tend to react to problems, and their systems are often designed around reaction. By contrast, specialist services are organizations and are more used to working with multidisciplinary teams. They are in a far better situation to initiate collaborative models of care. Active collaboration between them improves outcomes but requires considerable effort to embed such initiatives. Stakeholders need to feel that the outcomes are worth the time and effort.

11.2 Advance Care Planning

There is some evidence that where an advance care plan is in place and implemented, patient preferences and wishes are more likely to be followed (Evans et al. 2013). Other patient outcomes of ACP include anticipated symptoms being identified earlier, greater control with symptom management, (Auerbach and Pantilat 2004) greater patient satisfaction with the GP, (Tierney et al. 2001) and increased support, contact, and visits by GPs in the last week of life (Evans et al. 2013; Meeussen et al. 2011). Moreover, when an advance care plan is completed, patients are more likely to die in their preferred place of death (Vandervoort et al. 2012).

11.3 Caring for Carers

There is one study of GP identification and management of the needs of carers of advanced cancer patients. Using a self-completed needs checklist to identify carer problems, the GP and carer addressed these issues in a carer-focused consultation. This found improvements in outcomes for carers who were anxious or depressed at baseline and who were caring for more ill people and enabled the identification of more needs than the normal care control group (Mitchell et al. 2013).

11.4 Place of Death

There is a significant association between home visits by GPs to patients with advanced cancer with the possibility of dying at home and not hospital (e.g., Burge et al. 2003b; Neergaard et al. 2009). Similar findings on the likelihood of home death were also found for home visits by community nurses to cancer patients (Neergaard et al. 2009).

12 Policy Initiatives

End-of-life care policy has largely focused on specialist palliative care and its role at the very end of life. By and large cancer care is its focus, and the principles and processes of specialist services are well established. Only now is it becoming clear that a far bigger issue is developing – the population is aging, most will die of diseases other than cancer, and the current way of caring for patients is simply not viable to manage massively increased numbers of frail, multimorbid people. In 2014, the World Health Organization passed a resolution declaring end-of-life care of fundamental importance (World Health Organization 2014), thus committing member countries to improving end-of-life care. A core part of this declaration was the central role primary care had to play in providing end-of-life care. Work done by Murray and colleagues through the European Association of Palliative Care Primary Care working group had underpinned that initiative. They developed a set of guidelines based on Stjernsward's work, to allow nations or regions to analyze their end-of-life policy in terms of four high level principles, policy settings, drug availability, education, and implementation (Stjernsward et al. 2007) (Fig. 6), and created a means of evaluating national health systems to show the extent of involvement of primary care in end-of-life care. They evaluated 29 European countries' responses to show a range of facilitators and barriers to primary care end-of-life care (Murray et al. 2015) (Table 1). From that work, national policy to address these issues can arise. The Toolkit has been translated into several languages.

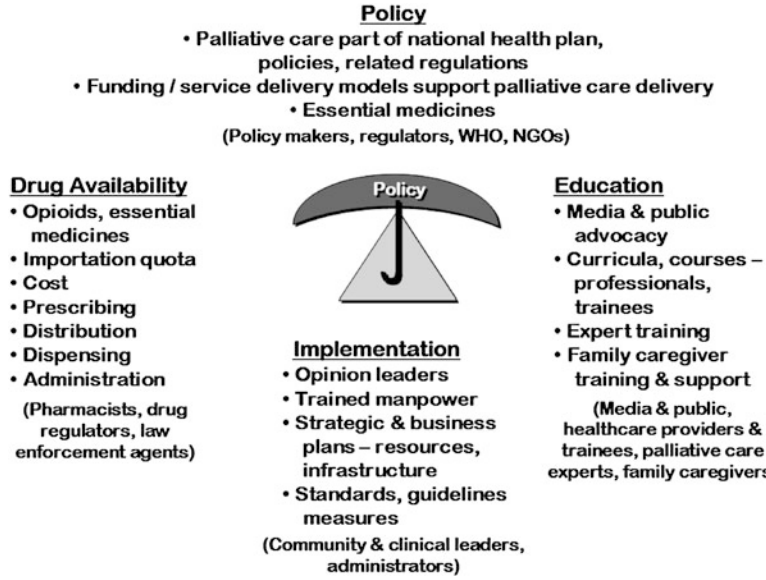

Fig. 6 Policy framework for developing palliative care services (Stjernsward et al. 2007)

Table 1 Barriers and opportunities to facilitate primary care involvement in end-of-life care provision (Murray et al. 2015)

Barriers	Opportunities
Lack of knowledge and skills among GPs and nurses	Training opportunities available in some countries
Financial systems not permitting reimbursements for palliative care	Examples of established primary care infrastructure
Issues hindering opiate prescribing	New national strategies supporting palliative care
Lack of professional or specialist support	Developing clinical networks in many countries
Poor identification of patients requiring palliative care	All patients have access to primary care
Limited public understanding and stigmatization of and palliative care	Increasing political support

Another international initiative has been led by Murray and Mitchell as co-Chairs – the International Primary Palliative Care Collaborative. This group was established in 2005 and has over 300 members from around the world. Its remit is to promote primary palliative care across the world through research, teaching, and local policy development. It has played an important part in developing the considerable momentum that has been evident in the last few years. Excellent work is currently happening in countries across the globe, bringing the critical role of primary care at the end of life to the attention of national governments.

13 Conclusion

Primary care and palliative care share a close affinity through an emphasis on the management of the whole person. In the age of specialist palliative care, a narrow view of end-of-life care has emerged which focuses on the last few weeks of life and largely relating to cancer and some particularly difficult degenerative diseases. The rapid aging of the population will lead to swelling numbers of deaths, with the major contributors being frailty, multimorbidity, organ failure, and dementia. These diseases, with their slowly accumulating needs and unpredictable illness course, are much more difficult to plan for, and a completely new approach to end-of-life care is warranted.

Further, the multidimensional nature of whole person care needs to be acknowledged and care arranged to meet these diverse needs.

Primary care has to take a major role in this. Complex medical problems will demand better

integration of care between patients, carers, primary care practitioners, and specialists. This will be a difficult transition for health systems built on disease and system-focused, subspecialist care, but one that has to commence now.

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Palliative Care in Residential Settings 51

Jo Hockley

Contents

Abstract

Many residential care settings for older people have been established on a culture of rehabilitation. However, this is changing. In many Western countries, recent policy is encouraging frail older people to stay longer in their own homes before going into 24-h care. As a result, on admission to these settings, older people are often considerably more dependent and frail than 10 years ago.

The palliative care needs of frail older people with multiple comorbidities admitted to residential care settings are significant. Palliative care is core to their work; such settings are now being compared to the former hospices that founded the hospice movement some 50 years ago. Hospices have an important role to play in reaching out to staff in

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_49

residential care settings and the frail older people they care for in order to support and enhance a palliative care approach.

This chapter describes some of the differences between palliative care for people with advanced cancer (often dying in mid-life) and those dying as a frail older person at the end of their lives with multiple comorbidities. It highlights a number of different quality improvement initiatives through which staff in residential care settings can be supported to adopt a greater palliative care approach.

Currently, nearly a quarter of the population in the UK, in Canada, and the USA die in care homes. In other countries, such as The Netherlands and Norway where there is greater on-site healthcare provision including physicians, it is nearer 50% of the country's population.

1 Introduction

This chapter aims to bring: greater awareness to the important place that residential care settings increasingly play in the care of frail older people at the end of life; highlight differences between the populations in these facilities compared to that of hospices; suggest opportunities and initiatives where a palliative care approach might be enhanced; and, finally, use narratives to bring alive important aspects.

For many years, residential care settings have been seen as places for rehabilitation where older people were admitted for companionship and to maintain independence for as long as possible. So much so that, in the UK prior to 2000, while a few frail older people died in the care home they were living in, most residents were admitted to the local hospital to die. Increasingly, however, countries across the world are concerned about how to meet the cost of institutional elderly care and are encouraging the provision of more care for older people in their own homes. Consequently, on admission to a place providing 24-h care, older people are now considerably frailer.

The result of such a policy has meant that there is not only greater frailty in people living in their own homes, which in itself needs to be proactively managed, but the majority of residents living/dying in residential care settings now have advanced, progressive, incurable diseases (IAHPC 2017) – ranging from Parkinson's disease and stroke to a number of different dementias. Gone are the places where the majority of residents would survive more than 3 or 4 years. The average length of stay in UK care homes is now 15 months with the majority of people dying within a year of admission to a care home with on-site nurses (Kinley et al. 2014a). Currently, nearly a quarter of the population in the UK, Canada, and the USA die in care homes; in other countries (i.e., The Netherlands and Norway) where there is greater on-site healthcare provision including physicians, it is nearer 50% of the population.

Staff working in residential care settings are being encouraged to develop their palliative care skills; however, palliative care is still not part of statutory training for residential care settings in many countries. This rise in both the complexity and number of comorbidities of frail older people requiring 24-h care at a later stage demands a higher level of skill and communication within facilities especially facilities where there is no on-site nursing (Handley et al. 2014).

Different terms associated with residential settings globally are now outlined before considering the following: the population of those who live and work in these settings; geriatrics and palliative care and the differing dying trajectories of frail older people; different models and initiatives to enhance palliative care in these settings; components of successful implementation of initiatives and their sustainability; and, innovations for the future.

2 Residential Care Settings Giving 24-H Care to Frail Older People

Froggatt and colleagues undertook a comprehensive mapping and classification of European care homes (with and without nursing) and their palliative care provision collecting data from 29 European countries (Froggatt et al. 2017a).

Their aim was to develop a typology of palliative care activity with respect to the implementation of various palliative care initiatives. They identified three types of facility: Type 1 ("on-site" physicians and nurses and care assistants), Type 2 ("on-site" nurses and care assistants but "off-site" physicians), and Type 3 ("on-site" care assistants with "off-site" physicians and nurses) (Froggatt et al. 2017b). Although the distinction over the years between Type 2 and Type 3 care homes with the regard to the professionals working there remains much the same, the distinction between the people living in these types of facilities is diminishing as the general residential setting population becomes distinctly frailer. Many countries worldwide are now merging the distinction between "low" and "high" care or "residential" and "nursing" care in institutions.

There are different terms used to describe the 24-h residential care given to frail older people and often more than one in the same country (see Table 1). For the purpose of this chapter, residential care settings for people requiring 24-h care will be called "long-term care facilities" (LTCFs) unless talking specifically about a certain country when the name relevant to that country will be used.

Every country has different ways of funding the 24-h care of frail older people. However, there are three broad categories of facilities: independent private ("for profit"), independent charitable foundations ("not for profit"), and government (health/local authority) in most countries. How care is funded for frail older people is gaining increasing attention by researchers and politicians in light of the aging population.

Globally, the development of palliative care services in residential care settings has, in the main, been less well developed than in other settings such as hospitals or hospices with their home care teams. An exception is The Netherlands. Here, in the 1980s, following a 5-year research project at Antonius IJsselmonde, Rotterdam (a 230-bedded nursing home), specific palliative care wards were created in large nursing home organizations in recognition of the needs of frail older people at the end of life (Baar 1999; Baar and van der Kloot Meijburg 2002).

In contrast, in the UK, where palliative care was first developed through hospices and their home care teams, it was not until the turn of the twenty-first century that palliative care services reached out to care homes. Many long-stay geriatric wards were closed down in 1990s, and the money was given to social care who then paid independent care homes to care for older people. While the social care needs of frail older people were considerably advanced, because care homes were now placed outside the NHS, they became isolated from palliative care developments occurring in the NHS and more difficult to reach.

3 The LTCF Population

3.1 Residents and Their Families

Those over 85 years are the fastest growing segment of the population in many western countries. In the UK, this group is projected to more than double by 2039 and is associated with increasing incidence of dementia (ONS 2014). In the UK, those requiring 24-h care in 2030 are projected to increase by 82% with an increasing demand from 400,000 to 630,000 care home places (Jagger et al. 2011).

As has already been mentioned, the LTCF population globally are increasingly frail with multiple comorbidities. In the UK, as many as 80% of residents in care homes have dementia or severe cognitive impairments (Alzheimers Society 2013). It is well documented that people with advanced dementia living in LTCFs can experience "social death" where they are passive recipients or objects of care being robbed of a meaningful interaction in the last months/years of life (Watson 2016). Holistic care and the importance of recognizing that the mind is not separate from the body but intricately made up of mind, body, and soul cannot be over emphasized especially in relation to someone with advanced dementia.

A white paper on the palliative care needs for people with dementia (van der Steen et al. 2014) details complete consensus from experts across 23 European countries in relation to the following:

Table 1 Type of 24-h residential care facility according to country

Country	Name given to facility	Staff employed in facilities	How funded
Australia (type 2 and 3)	Aged Care Facilities (ACFs)	RNs: Registered nurses ENs: Enrolled nurses PCAs: Personal care attendants AHPs: Allied health professionals	Health and social care Privately funded
USA (type 1 and 2)	Skilled Nursing Facilities (SNFs) or Long-term care facilities (LTCFs) or Continuing Care Retirement Communities (CCRCs)	RNs: Registered nurses LVNs: Licensed vocational nurses CNAs: Certified nurse aides CMAs: Certified medication aides APRNs: Advanced practice registered nurses	Medicare Medicaid Private insurance
Canada (type 2 and 3)	Long-term residential care facilities (LTC) or Nursing homes or Homes for the aged	RNs: Registered nurses LPNs: Licensed practical nurses or registered qualified nursing assistants PSW: Personal support worker Type 2 will have the above + physiotherapists + occupational therapists	Variation across the country – currently debating a universal public insurance scheme for long-term care (Grignon and Bernier 2012)
Europe (type 1, 2 and 3) Norway, Finland, Italy, and the Netherlands have elderly care physicians in their nursing homes	Long-term care facilities (LTCFs) or Nursing homes (NHs) or Care homes and care homes with on-site nurses (CHs; CHs-N)	RNs: Registered nurses NAs: Nursing assistants SCW: Social care workers	Different funding models across the different countries – mixture between "health and social care" funding, insurance, privately funded. Care of older people in the Netherlands, for example, is nearly completely covered by a national health insurance plan

Type 1: "On-site" nurses + care assistants + elderly care physicians
Type 2: "On-site" nurses + care assistants; "off-site" physician/s
Type 3: "On-site" care assistants only; "off-site" nurse/s + physician/s
Froggatt et al. (2017b)

- Person-centered care, communication, and shared decision-making
- Optimal treatment of symptoms and providing comfort
- Setting care goals and advance planning
- Continuity of care
- Psychosocial and spiritual support
- Family care and involvement
- Education of the healthcare team
- Societal and ethical issues

The domains provide a framework to guide important aspects of LTCF palliative care development in clinical practice, policy, and research.

3.2 Management and Staffing

Leadership of LTCFs is one of the single most important aspects for high-quality care for frail older people and its continuity in such settings. If staff are valued and supported by management in helping them progress and develop, then this generally cascades down into good care of residents and families. When one sees defensive care and/or poor communication especially in relation to palliative and end-of-life care, then this is often a result of poor leadership and poor role models where staff do not feel supported.

There is a wide variation between countries and even within different LTCF organizations in the same country in relation to staff development. The majority of staff have little healthcare training. Many young people choose to work in these facilities because they want to help frail older people; they come to help dress, feed, and chat to older people. Unfortunately, they are often not prepared with the demands of the work and the fact that many frail older people, who they have got to know very well over the months/year, will die in the LTCF.

In the UK, the majority of formal carers will be encouraged to have some vocational training −50% of staff in a care home should have Level 2 NVQ/SVQ (National/Scottish Vocational Qualification). Such a qualification is based around personal care, moving and handling, nutrition, oral care, etc. for frail older people but does not often include knowledge about different comorbidities and how to communicate about life/death issues. However, despite this, LTC staff are not unskilled. Often they have considerable insight into situations but are not given the opportunity or support to voice their opinions.

In most countries, there are little or no nurses working in LTCFs and no on-site medical support with some exceptions like The Netherlands and Norway. In the UK, only a quarter of care homes have on-site nurses. Where there are nurses, the ratio is in the region of 1 nurse to 30 residents with the rest of the staff being formal care workers. With increasing pressure on workloads and the "risk" that some LTCF staff feel when not having the knowledge and competencies in the care they are being increasingly asked to give, it is not surprising there is a high turnover of staff. In the UK, this has now reached worryingly high proportions. It could be argued that because of the lack of distinction is diminishing between older people residing in the different LTCF/care home settings and because managers are being encouraged not to transfer frail older people in the last months of life, that all LTCFs/care homes should provide "high" care and employ nurses and even care home doctors.

4 Geriatrics and Palliative Care

In 2017, both geriatric and palliative care specialists celebrate important milestones in their development as a speciality – geriatrics celebrate 70 years and palliative care celebrate 50 years. Dame Cicely gained huge insights from well-known physicians in the care of older people to underpin the hospice movement. It was Professor Worcester's seminal work, The Care of the Aged, the Dying and the Dead (1935), which had prominence both in Dame Cicely's writing and on her bookshelf.

In 1989, at the First International Conference on Palliative Care of the Elderly, Balfour Mount (1989, p. 7) also drew interesting analogies between geriatric practice and palliative care:

> Both make the whole person and his or her family the focus of care, while seeking to enhance quality of life and maintain the dignity and autonomy of the individual. Judicious use of investigations are advocated and both eschew unwarranted treatment while providing symptom control and relief of suffering. Both are necessarily multi-disciplinary and both are areas which prompt phobic reactions from society at large. . ..

However, despite the similarities drawn above, there are also differences not only between the settings but also within the care practices (see Table 2).

Respecting the choices of frail older people toward the end of life is extremely important. In 2012, a global initiative called "choosing wisely" was set up to help clinicians and patients engage in conversations about unnecessary tests/treatments and make wise and effective care choices. This initiative now involves professionals from

Table 2 Differences between cancer palliative care and end-of-life care in the elderly dying (Hockley 2002). (Reproduced with kind permission from Open University Press, Buckingham MK18 1XW)

Cancer palliative care	End-of-life care in the elderly dying
Focus in one disease process	Multiple disease processes
Emphasis on dying in mid-age or younger when life is generally seen as being "cut short"	Natural ending of life often understood by both the resident and those caring within the context of care homes
Clearer concept of "prognosis" so terminal care can be planned	Less predictable dying trajectory following a more dependent, lengthier disease process
Professional holistic relationship between patient and staff	Often a much closer/emotional relationship between resident and care home staff as resident becomes "part of the family" and may have lived in the care home months/year
More support from family/friends	Less support from family/friends – often care home staff and other residents seen as family
Both patient and family often want life extended	Elderly, frail people in nursing homes frequently speak about dying and that it would be nice "to go to bed one night and not wake up"
Morphine and other medication frequently used to control symptoms	Pain requiring strong opioids less common
Multidisciplinary model of care	Nurses and care workers having the greatest input of care
Patients more often cognitively intact	Greater percentage of residents in nursing homes are cognitively impaired

across 20 countries. As a result of this initiative, the Long-term Care Medical Directors Association of Canada have come up with six recommendations (see Table 3) that are all evidence-based with their relevant resources (https://choosingwiselycanada.org/long-term-care/). Such recommendations emphasize the importance of palliative care and geriatricians working together for the best care of frail older people.

Table 3 Recommendations from choosing wisely (Jones 2017)

1.	*Don't send the frail resident of a nursing home to the hospital unless their urgent comfort and medical needs cannot be met in their care home.* Transfers to hospital for assessment and treatment of a change in condition have become customary; however, they are of uncertain benefit and may result in increased morbidity
2.	*Don't use antipsychotics as a first choice to treat behavioral and psychological symptoms of dementia.* People with dementia can sometimes be disruptive, behave aggressively, and resist personal care. There is often a reason for this behavior, and identifying and addressing the causes can make drug treatment unnecessary
3.	*Don't do a urine dip or urine culture unless there are clear signs and symptoms of a urinary tract infection (UTI).* Unless there are UTI symptoms, such as urinary discomfort, abdominal/back pain, frequency, urgency, or fever, testing should not be done. Testing often shows bacteria in the urine, with as many as 50% of those tested showing bacteria present in the absence of localizing symptoms to the genitourinary tract
4.	*Don't insert a feeding tube in individuals with advanced dementia. Instead, assist the resident to eat.* Inserting a feeding tube does not prolong or improve quality of life in patients with advanced dementia. If the resident has been declining in health with recurrent and progressive illnesses, they may be nearing the end of their life and will not benefit from feeding tube placement
5.	*Don't continue or add long-term medications unless there is an appropriate indication and a reasonable expectation of benefit in the individual patient.* Long-term medications should be discontinued if they are no longer needed (e.g., heartburn drugs, antihypertensives), as they can reduce the resident's quality of life while having little value for a frail elder with limited life expectancy
6.	*Don't order screening or routine chronic disease testing just because a blood draw is being done.* Unless treatment can be given that would add to quality of life, don't do these tests. What is considered routine testing may lead to harmful overtreatment in frail residents nearing the end of their life

4.1 Different Dying Trajectory

When reaching out to LTCFs with quality improvement initiatives or supporting end-of-life care, it is important not to impose the more familiar model of palliative care developed for

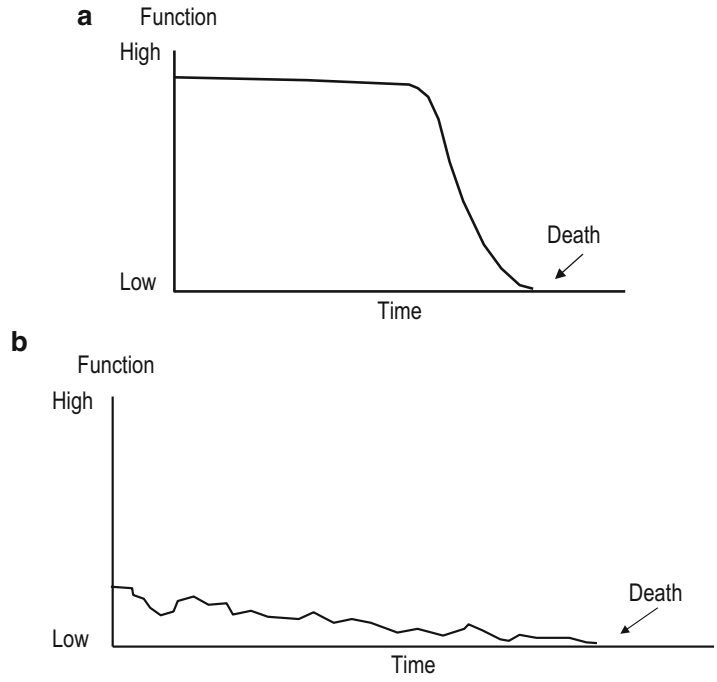

Fig. 1 (**a**) Different dying trajectories – cancer (Lynn and Adamson 2003). (**b**) Dwindling trajectory of frail older people – especially those with advanced dementia (Lynn and Adamson 2003)

people with advanced cancer. There is a difference between palliative care that has been developed for people with advanced cancer, typically from within specialist palliative care and the hospice movement, and palliative care for frail older people dying at the end of life from multiple comorbidities.

The dwindling dying trajectory, so well described by Lynn and Adamson (2003), is very different from the well-known, fairly predictable cancer trajectory – see Fig. 1a, b.

The phrase "bounce back" is an unknown phenomenon when caring for people dying in a hospice or a hospital and is uniquely tied to the dwindling trajectory of frail older people. A frail older person is seen to deteriorate, their medication is reviewed and discontinued, a greater attention to fluid intake is taken, and as a result the person "bounces back."

The danger of imposing a specialist palliative care model in the last days of life, where often opiates and hyoscine are used routinely, onto a frail older person who is dying with advanced dementia is vividly highlighted in the following case study (see Case Study A).

Case Study A: Mrs. A: 89 Years: Advanced Dementia (2012)

The Care Home Project Team at St Christopher's Hospice, London, (https://www.stchristophers.org.uk/education/training-and-research/care-homes/) was involved in development and training in a local care home without on-site nurses. The care home manager had contacted the local community palliative care team to come and review Mrs. A with advanced dementia who was dying. Mrs. A was in her late 80s and had been in the care home for a number of years; with her advancing dementia, she was pleasantly confused. However, she was now very frail and not drinking and clearly had days/week to live.

The community palliative care team were used to putting up syringe drivers when a person at home or in a care home without on-site nurses was dying. Because Mrs. A was slightly agitated, they decided

(*continued*)

to put up a syringe driver with a small dose of diamorphine 10 mg and Buscopan 20 mg/24 h. Within 3 days, Mrs. A had changed from her pleasant confusion to being increasingly agitated, shouting out, and unmanageable.

The Care Home Project Team were contacted and advised the immediate discontinuation of the syringe driver – the opiates had clearly accumulated because of Mrs. A's "old kidneys," and appropriate dehydration at the end-of-life. She was clearly dying but had no pain. It took the administration of s/c fluids and phenobarbitone to help reduce Mrs. A's distress, and she died peacefully 3 days later.

her thoughts – she had worked in the care home sector for many years and had had some training in palliative care. She queried why opiates were being considered when Miss B had no pain. She also queried the use of Buscopan as it would only increase the dryness in Miss B's already dry mouth and suggested: "What about giving a small dose of diazepam rectally to calm her?" Immediately the importance of what the staff nurse was saying was recognized. Following the rectal diazepam, Miss B was still able to take sips of fluid – the care assistants took it in turns to sit with her reading some favorite poetry. Miss B died 12 h later – peacefully and comfortable.

A different scenario (see Case Study B) highlights the benefits of "working alongside" staff in LTCFs – listening to what they would normally do, being open to learn from them in relation to the last day/s of life, and not imposing a specialist palliative care knowledge.

Case Study B: Miss B: 91 Years: Advanced Dementia (2004)

During research into death and dying in care homes with on-site nurses, staff were being supported to implement the "integrated care plan for the last days of life" (Hockley et al. 2005). Miss B, who had worked for many years as pharmacist, was now dying. She had been a "feisty" lady and had lived in the care home several years. If she didn't like your approach when you were helping her with her medication, you were in danger of the tablets being thrown back in your face. However, she now was very frail, reasonably calm, and just able to sip the fluids offered to her. The staff nurse asked for advice, and a typical response from a nurse specialist in palliative care was given: s/c diamorphine 2.5 mg and s/c Buscopan 10 mg. Importantly, the staff nurse offered

As can be seen from Case Study B, the dying process of frail older people is often a natural process requiring little extra medication. William Osler (1849–1919) is well known for saying "pneumonia is the old man's friend," and although written over 150 years ago before the invention of antibiotics, it is as relevant today as it was in the nineteenth century.

Dying itself is not painful (Worcester 1935) – it is only painful in situations where there is unrelieved pain prior to the last days of life. An appropriate assessment of the situation taking into account the frailty, natural dehydration of frail older people, and any specific distressing symptoms must be made and a syringe driver only used if symptoms are severe. Often occasional s/c medication is all that is necessary in frail older people.

A small percentage of deaths in LTCFs can be quite sudden and, despite the person being in their 90s, is seen as "unexpected." An "acute" event like a silent pneumonia can often prompt admission to an acute hospital and sadly the person's dies in unfamiliar surroundings. The dwindling dying trajectory however is the most common type of dying in LTCFs, and generally speaking if properly acknowledged, the death will occur in the LTCF.

5 Different Models and Initiatives to Enhance Palliative Care in LTCFs

It is well documented that palliative care education on its own does not change practice in the often hierarchical structures of LTCFs (Froggatt 2001) that have for many years adopted a rehabilitation culture. However, we know that when education is done alongside implementing a specific tool, for example, advance care planning documentation, there is a greater chance of developing a palliative care approach to care.

Many LTCFs eagerly respond to new initiatives in relation to improving palliative and end-of-life care especially when supported by an outside agency such as a local university or hospice. Effectiveness of a project depends not only on the enthusiasm of the LTCF staff to develop their practice but also the support given by manager/management. Projects benefit when there is both a "top-down" and "bottom-up" approach. However, the current trend of short-term funding of programs is unlikely to bring about long-lasting change unless a funded sustainability initiative has been proposed at the beginning of the project (Hockley and Kinley 2016).

A number of tools, quality improvement initiatives, and models have been developed. These are now described, firstly, from a focus on the implementation of individual aspects of palliative care such as advance care planning or pain assessment in advanced dementia and, secondly, the implementation of a system that addresses multiple aspects of palliative care.

5.1 Individual Tools

If given the task to choose what might be the "key" developments of a palliative care approach in care homes, it would be impossible to list all such initiatives. Nonetheless, there are a number of tools that are gathering evidence of their effectiveness and are described below.

5.1.1 Advance/Anticipatory Care Planning and DNACPR Decisions

Advance/anticipatory care planning (ACP) is reported to decrease inappropriate hospital admissions of frail elderly residents with palliative care needs (Hockley and Kinley 2016). Documentation may take the form of an advance statement of wishes and preferences, an advance decision to refuse treatment (a legal document refusing specific treatment), and/or a surrogate decision-maker in the appointment of a Lasting Power of Attorney for Health and Welfare. These documents are then available to guide care if the individual loses the ability to make decisions or communicate their wishes. However, there are multiple preconditions related to successful ACP in LTCFs which occur at different levels of the organization (Gilissen et al. 2017).

Who in the LTCF Should Undertake These Conversations?

Until recently, the dominant culture in LTCFs has been a "striving to keep alive," and it is not always straightforward for staff to embrace discussions around ACP – especially when they have limited healthcare knowledge.

Most frail older people know they are facing the last year/s of their life. The very fact that they have now been admitted for 24-h care because they can no longer manage to care for themselves at home is every indication to them that this is likely to be their last move; to deny this is to discredit their autonomy and their ability to know their own body. Many residents are very open to discussions in relation to their wishes at the end of life (Stone et al. 2013). However, for many LTCF staff, often young with little healthcare training, conversations about care at the end of life can be extremely daunting.

Learning how to undertake such conversations is really important, and considerable support and education is often required. Learning can be very effective when seeing other people undertaking such a conversation (either through role modeling by an experienced clinician or through watching videos) and/or through role play alongside some communication skills training such as Sage and

Thyme (http://www.sageandthymetraining.org.uk/about). Sitting in with an experienced professional is probably the most useful.

In the UK, discussions about what a resident might want to achieve before becoming very frail, and whether they have thought about who they might want close-by at the end, can be undertaken by experienced social care workers. However, any detailed health-related discussions such as an event that might result in an action like going to hospital must be undertaken by properly qualified healthcare professionals.

With the increasing likelihood that many frail older people are likely to die within months of admission to a LTCF, conversations in relation to wishes toward the end of their life are most important. Such conversations are very individual (often requiring at more than one conversation) and must be documented accordingly.

Relatives are key to these conversations, and while they might like to think they know what their family member wants, sometimes they can be misguided. It is important to include where possible both resident and family in such conversations.

When Should Such Conversations Take Place?

The timing of conversations about the care in the last weeks of life including discussions regarding "do not attempt cardio-resuscitation" (DNACPR) needs to be adopted into routine practice of the facility. Most LTCFs will review residents' care plans on a monthly and 6-month basis; these therefore become the ideal times. For residents who have been in the LTCF a number of months/year/s, then the 6-month review (unless there is a sudden deterioration) is perfectly acceptable opportunity for such a conversation to be added to the end of the general discussion. For someone being admitted to a LTCF, especially if they are frail and ill, the timing is likely to be different.

It is important that the doctor/nurse establishes within a week of admission whether a DNACPR decision is to be signed. More detailed conversations about care at the end of life need to be undertaken once the resident and family have settled into the care home – and likely not to take place until the end of the 1st month in the care home.

There are a considerable number of forms and pamphlets that have been developed and are widely available. However, it is the importance of the conversation that is paramount – and the process should not be a "tick box" exercise. It is really important that such conversations are undertaken by staff who feel competent, having had the opportunity of sitting in with doctors/senior nurses to witness how it is done; such role modeling is very important if care home staff are to become competent.

5.1.2 Monthly Multidisciplinary Meetings

Good coordination of care especially in the last year of life is vital if the needs of frail older people in care homes are to be identified and managed appropriately. Monthly multidisciplinary meetings in the care home bring together all those who not only know the person but also those who have expertise to advise and ensure that care is properly coordinated.

In the UK, the Gold Standards Framework (http://www.goldstandardsframework.org.uk), promoting the development of a palliative care approach both in peoples' own homes and care homes, has advocated the importance of monthly multidisciplinary meetings for over 10 years now.

A simple palliative care register completed at a monthly multidisciplinary meeting in the LTCF prompts staff about different aspects of care, i.e., advance care planning/DNACPR, symptom control issues, and family communication. One of three triggers indicating that a resident is nearing the end of life is the "surprise question" (Thomas 2011):

> would I be surprised if [Mrs B] died in the next. . .three months, six months, year?

This question is asked at the meeting in conjunction with two other triggers: deterioration over the previous month/s and specific clinical

indicators related to certain conditions. As a result of this questioning, the resident is categorized as likely having day/s, week/s, or month/s to live. Importantly, it is often the formal care workers in daily contact with the frail older person who are best able to answer this "surprise" question despite often having little advanced health education. It is important that they are present to discuss their specific residents. Once it is considered likely that the LTCF staff believe the person to be nearing the end of life – even though that might still be month/s away – it is important that there is open communication with the rest of the staff, to the resident (as appropriate), and family.

Such a monthly multidisciplinary meeting not only helps to build teamwork and trust across the different professions as well as good coordination of palliative care. Working with services provided during the day, at night, and at weekends is key to providing seamless quality palliative care in LTCFs.

5.1.3 Pain Assessment/Management Tools

Some diseases and conditions create varying degrees of pain for individuals. Older people often suffer in silence with their pain as they believe arthritis and other musculoskeletal conditions are part of growing old and therefore to be endured. LTCF residents have been found to have considerably more pain compared to the same population living in their own homes (Husebo et al. 2012).

Systematic pain assessment on admission and the use of relevant documentation can contribute to effective pain assessment and management. We know that pain has a combination of physical, emotional, social, and spiritual elements which Dame Cicely Saunders called "total pain." However, with 80% of frail older people in LTCFs having dementia or severe cognitive impairment, pain in these people needs to be assessed differently to that of people with cancer pain. It is often more complex to assess/manage pain in people with advanced dementia than it is in people with cancer (see Case Study C).

Case Study C: Pain Assessment in a Person with Advanced Dementia Unable to Verbalize Her Pain

During a year's study in a particular LTCF, I had got to know the majority of the 40 residents very well indeed. Mrs. C and her husband had been residents for a couple of years – she was a charming but muddled lady in her mid-80s with advanced dementia, while Mr. C had recently been diagnosed with advanced prostate cancer. One day when coming into the LTCF, instead of Mrs. C being up and about dusting the staircase, I noticed her sitting by the front door rubbing her knees. This was a change to Mrs. C's normal activity of walking around the house making sure that everything was spick and span.

At the time, although this was not the focus of the study, I had become interested in the difference between assessing pain in people with advanced dementia and assessing pain in people with advanced cancer in a hospice/community. I had read about the importance of assessing the nonverbal response to pain in people with advanced dementia and in particular the Doloplus2-scale (Lefebvre-Chapiro and the Doloplus Group 2001). The rubbing of the knees was new, and I was interested to find out her level of pain.

The manager happily told me who Mrs. C's carer was, and we proceeded to Mrs. C's room in order to undertake a pain assessment. Using a scale of 0–10, I asked Mrs. C "if '0' is no pain at all and '10' is the most excruciating pain you have ever had in all your life, what score would you give the pain in your knees?" Almost immediately Mrs. C told me 8/10. Ashamedly, because she didn't look as though she was in that much pain, I wondered whether she had become muddled and had really meant 2/10. To confirm my musings, the carer and I

(*continued*)

went away and completed the Doloplus2-scale together.

The Doloplus2-scale pain assessment tool (see Table 4) checks ten reactions at four levels (0–3) divided into three domains: somatic reactions, behavioral reactions, and psychosocial. A total score of 5 or more is likely to represent pain. When the carer added up our scoring of Mrs. C's pain, it came to 15. We realized together that Mrs. C had very real pain. We slowly titrated the analgesics that included starting oral morphine. Gradually over 3 weeks, the morphine was increased until Mrs. C was up and doing her dusting again. She remained stable on MST 30 mg bd alongside paracetamol for a number of months walking around and doing her dusting. She died reasonably suddenly in the LTCF about 4 months later.

There are many different pain assessment scales for use with people with advanced dementia unable to express their pain verbally (Lichtner et al. 2014). There are probably four that have had repeated scrutiny in relation to validity and reliability testing:

- *PAINAD*: This tool (http://geriatrictoolkit.missouri.edu/cog/painad.pdf) has five domains and is a relatively simple tool for nurses/care staff to use (Warden et al. 2003). Tool reliability is good for interrater reliability, but internal consistency is only moderate, and stability has not been demonstrated. http://prc.coh.org/Review%20of%20Tools%20for%20Pain%20Assessment/Review%20of%20Tools%202004/PAINAD/PAINAD_Indepth.pdf
- *ABBEY*: The ABBEY (Abbey et al. 2004) scale is similar to the PAINAD in that it is easy to complete. However, reliability and validity have been shown not to be strong. http://prc.coh.org/PainNOA/ABBEY_D.pdf
- *PACSLAC*: the Pain Assessment Checklist for Seniors with Limited Ability to Communicate (Fuchs-Lacelle and Hadjistavropoulos 2004) has been developed in Canada. It covers four domains: facial expressions × 13, activity/body movement × 20, social/personality/mood × 12, and others × 15. Prospective evaluation has added to the tool's reliability and validity. http://prc.coh.org/PainNOA/PACSLAC_D.pdf
- *Doloplus2-scale*: The Doloplus2-scale (Lefebvre-Chapiro and the Doloplus Group 2001) was specifically developed by geriatricians in France for people with advanced dementia who were no longer able to verbalize their pain. Although more complex to use, its reliability and validity are strong. http://prc.coh.org/PainNOA/Doloplus%202_Tool.pdf (Torvik et al. 2010).

Further studies evaluating the above tools and their efficacy and ease of use in the assessment/management of pain in frail older people with dementia by LTCF staff would be useful.

5.1.4 Documentation for the Last Days of Life

Dame Cicely Saunders (1918–2005) is well known for saying, "How someone dies remains in the memory of those who live on." This is extremely important in LTCF settings where often the majority of staff have little healthcare training. Some sort of documentation to help guide these last days is of vital importance.

Developed and adapted from the Liverpool Care Pathway (Ellershaw and Wilkinson 2003) for specific use in care homes, the *Integrated Care Plan for the Last Days of Life* (Hockley et al. 2005; Watson et al. 2006), further developed to more recent documentation called the *Integrated Personalised Plan for the last days of life* (http://www.stchristophers.org.uk/care-homes/research/ipp) (IPP), has managed to ride the storms of controversy in relation to the Liverpool Care Pathway. A recent audit report outlines the first 50 completed IPPs and the success of its use in care homes in south London (Coleman et al. 2017).

The importance of at least 90% staff in a setting where such documentation is being used was highlighted by Ellershaw and Wilkinson (2003)

Table 4 Doloplus2-scale (http://prc.coh.org/PainNOA/Doloplus%202_Tool.pdf)

DOLOPLUS-2 SCALE — BEHAVIOURAL PAIN ASSESSMENT IN THE ELDERLY

NAME : Christian Name : Unit : DATES

Behavioural Records

SOMATIC REACTIONS					
1• Somatic complaints	• no complaints	0	0	0	0
	• complaints expressed upon inquiry only	1	1	1	1
	• occasionnal involuntary complaints	2	2	2	2
	• continuous involontary complaints	3	3	3	3
2• Protective body postures adopted at rest	• no protective body posture	0	0	0	0
	• the patient occasionally avoids certain positions.	1	1	1	1
	• protective postures continuously and effectively sought.	2	2	2	2
	• protective postures continuously sought, without success.	3	3	3	3
3• Protection of sore areas	• no protective action taken	0	0	0	0
	• protective actions attempted without interfering against any investigation or nursing	1	1	1	1
	• protective actions against any investigation or nursing	2	2	2	2
	• protective actions taken at rest, even when not approached	3	3	3	3
4• Expression	• usual expression	0	0	0	0
	• expression showing pain when approached	1	1	1	1
	• expression showing pain even without being approached	2	2	2	2
	• permanent and unusually blank look (voiceless, staring, looking blank)	3	3	3	3
5• Sleep pattern	• normal sleep	0	0	0	0
	• difficult to go to sleep	1	1	1	1
	• frequent waking (restlessness)	2	2	2	2
	• insomnia affecting waking times.	3	3	3	3
PSYCHOMOTOR REACTIONS					
6• washing &/or dressing	• usual abilities unaffected	0	0	0	0
	• usual abilities slightly affected (careful but thorough)	1	1	1	1
	• usual abilities highly impaired, washing &/or dressing is laborious and incomplete	2	2	2	2
	• washing &/or dressing rendered impossible as the patient resists any attempt	3	3	3	3
7• Mobility	• usual abilities & activities remain unaffected	0	0	0	0
	• usual activities are reduced (the patient avoids certain movements and reduces his/her walking distance	1	1	1	1
	• usual activities and abilities reduced (even with help,the patient cuts down on his/her movements)	2	2	2	2
	• any movement is impossible, the patient resists all persuasion	3	3	3	3
PSYCHOSOCIAL REACTIONS					
8• Communication	• unchanged	0	0	0	0
	• heightened (the patient demands attention in an unusual manner)	1	1	1	1
	• lessened (the patient cuts him/herself off)	2	2	2	2
	• absence or refusal of any from of communication	3	3	3	3
9• Social life	• participates normally in every activity (meals, entertainment, therapy workshop)	0	0	0	0
	• participates in activities when asked to do so only	1	1	1	1
	• sometimes refuses to participate in any activity	2	2	2	2
	• refuses to participate in anything	3	3	3	3
10• Problems of behaviour	• normal behaviour	0	0	0	0
	• problems of repetitive reactive behaviour	1	1	1	1
	• problems of permanent reactive bahaviour	2	2	2	2
	• permanent behaviour problems (without any external stimulus)	3	3	3	3
	SCORE				

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in their original book and has underpinned the work of Coleman et al. (2017). The individual care home setting has managed to be more rigorous in achieving such training than in the acute hospital setting with the myriad of staff to be taught. Training should include the use of a "case scenario" alongside the documentation so that training isn't being taught via a PowerPoint presentation in isolation of real-life situations. It is important to note that any care given is only

as good as the person giving the care, and while "using the IPP does not in itself assure quality of care, the use of such a plan can provide homes with evidence that their care is consistent" (Coleman et al. 2017, p. 41).

5.1.5 Valuing and Supporting Staff Support After Death: Reflective Debriefing Sessions – UK

For many young untrained staff, talking about and caring for people who are dying are frightening and the powerful triggers to any of their own unresolved grief (Holman et al. 2011). With the increasing number of frail older people dying in LTCFs, meaningful support through reflective debriefing sessions has been found to be helpful (Hockley 2014).

Staff often become very close to residents – especially if the resident has been in the LTCF for a number of months or even years. Reflecting on the death in a structured way is a useful support for staff and an innovative way of learning from practice – a tool has been developed (Hockley 2014). The aim of a reflective debriefing sessions is:

- To use the experience of caring for a resident who has died as a basis for learning about end-of-life care
- To be a place where "death and dying" can be safely and openly discussed and where support can be actively shown
- To construct knowledge about end-of-life care of frail older people dying in LTCFs in order to develop a palliative care culture in these settings
- To increase team cohesion between different shifts and across different roles that include not only nurses and carers but different ancillary staff who have known the resident and/or family

Sessions are held monthly with an emphasis on a "no blame" culture. The deaths of residents who have died during the previous weeks are formerly discussed. Such a session lasts about 45 min (a maximum of an hour). If there is no death during the month, then these sessions can be used for informal teaching on any subject that the LTCF manager thinks will be helpful. The essential point is for the sessions to be planned in the diary at a specific point each month of the year so it becomes routine practice and not just something that might happen if there is a significantly bad death. It is important that the LTCF manager be present wherever possible at the reflective debriefing sessions.

The outline of a session is as follows:

- For someone within the group to give a short portrait (no more than a couple of minutes) of the person who has died and the knowledge they had of the family
- What led up to the death – was it sudden or anticipated, etc.
- How did staff fell things went – What went well? What didn't go so well?
- What could have been done differently?
- What needs to change in the LTCF as a result of the reflection?

Each reflection can inform practice and should be used not only as a building block to learning but as a celebration of good practice. Reflection is not a passive contemplation but an active, deliberate process that requires commitment, energy, and a willingness to learn as a team.

5.2 Tools Incorporating Whole System Change to Create a Palliative Care Approach

Not surprisingly, the "individual initiatives" that have been highlighted above do in time promote a palliative care culture to emerge. However, there are initiatives that champion a "whole system" development in one project. Establishing a system which addresses a number of different aspects of palliative/end-of-life care alongside an educational initiative is probably one of the most effective ways to encourage a greater palliative care approach in LTCFs. However, it is sustaining such

initiatives that is of vital importance and will be discussed in Sect. 6.

5.2.1 The Gold Standards Framework for Care Homes: UK/Europe

The most notable whole system change in relation to palliative care/care homes in the UK has been the Gold Standards Framework in Care Homes (GSFCH) (http://www.goldstandardsframework.org.uk/care-homes-training-programme). Professor Keri Thomas, founder of the GSF program, saw the need in the early 2000s for better collaboration and communication in relation to palliative and end-of-life care in the community (Thomas 2003), furthered the vision to encompass a program for care homes (GSFCH) (Badger et al. 2009; Thomas 2016).

The GSFCH program is a 2-year accredited program divided into three parts: a *preparatory phase*, *an implementation phase*, *and a consolidation phase*. The *preparatory phase (6 months)* is extremely important phase encouraging not only the staff, residents, and families to take part but also the local GP/s and specialist palliative care team/s external to the care home.

Care homes from a regional area are encouraged to sign up for the course and as part of the payment will be given all the documentation/folders/videos, etc. Each care home manager appoints GSFCH "champions" who will attend 4 training days during the *implementation period (9–12 months)* and be responsible for disseminating the information to the rest of the care home staff in between each of the 4 days. The number of "champions" is never less than two and will vary depending on the size of the care home. The *consolidation period (6 months)* helps care home staff to work on aspects that they are unsure about and at the same time prepare a portfolio for accreditation. An "after-death analysis" audit is undertaken on a number of residents' deaths before commencing the course and compared to those during/after the completion of the GSFCH program.

The GSFCH provides care home organizations with a number of key aspects of documentation in relation to advance care planning "Thinking Ahead"; prognostic indicator guide; the monthly multidisciplinary supportive care register; the PACA, a summary of resident and carer needs and concerns; the PEPSI COLA Aide Memoire, an holistic assessment tool; and significant event analysis that is completed following a death and helps staff reflect and feel supported.

In 2008, St Christopher's Hospice developed a Care Home Project Team to "reach out" to local care homes (http://www.stchristophers.org.uk/education/training-and-research/care-homes/). It became the first GSFCH regional center in the UK and over a 5-year period reached out to all the 71 care homes with on-site nurses in the area, encouraging them to take part. By the end of 5 years, the percentage of care home residents dying in hospital had reduced from 44% to 22% (Hockley and Kinley 2016).

As a result of GSFCH program, the UK National Health Service developed documentation "Route to Success" to encourage local regions to develop the palliative care needs of their residents in care homes (http://www.nwcscnsenate.nhs.uk/files/7714/3040/1087/Route_To_Success_Care_Homes_updated_Apr2015.pdf?PDFPATHWAY=PDF/). Different localities then developed different tools such as the "Six Steps to Success" and "Steps to Success" programs. While making it locally relevant, some programs have lacked resources when it comes to accreditation, ongoing support, and sustainability.

5.2.2 The PACE Program: Europe

The PACE program (www.eupace.eu) is a randomized controlled trial looking at whole system change in the adoption of a palliative care approach in LTCFs across six European countries (Van den Block et al. 2016; Smets et al. 2018). The PACE program was developed following a number of quality improvement initiatives in care homes and is framed around six steps: advance care planning, mapping changes in a resident's condition, monthly multidisciplinary meetings, pain and symptom assessment, care in the last days of life, and reflective debriefing sessions for staff following a death. The intervention is

complete, and outcomes from the PACE program are awaited.

5.2.3 Palliative Approach Toolkit for Residential Aged Care Facilities: Australia

Deborah Parker and colleagues from Blue Care Research and Development Unit and the University of Queensland developed the "Palliative Approach Toolkit for Residential Aged Care Facilities" – an evidence-based knowledge translation product for staff in aged care facilities in Australia (https://www.caresearch.com.au/caresearch/tabid/3629/Default.aspx). The Toolkit is a set of clinical care, educational and management resources, and a "comprehensive 'how to' guide featuring a step by step approach to implementing a new model of palliative care. It includes policies and procedures, education and training for staff" (Parker 2013). The success of the project was realized when the Australian Government Department of Health funded a national rollout of the Toolkit under the Encouraging Better Practice in Aged Care (EBPAC) initiative between October 2013 and December 2014 (https://www.caresearch.com.au/Caresearch/Portals/0/PA-Tookit/Training%20Support%20Materials/PowerPoint%20Presentation.pdf).

5.2.4 Namaste Care Program: Improving the Quality of Life for Residents with Advanced Dementia: USA and UK

The Namaste Care program was developed by Joyce Simard in the early 2000s in the USA (Simard 2013). Joyce had worked as a social worker in LTCFs and was interested in the importance of meaningful activity to improve the quality of life for people with advanced dementia. She had set up innovative meaningful activity for those with mild to moderate dementia ("The Club") but noticed that many people with advanced dementia just sat on the edges of such activity with little engagements or otherwise didn't attend, remaining alone in their bedrooms.

Namaste is an Indian greeting which means "to honor the spirit within." Namaste Care is a multidimensional program that includes physical, sensory, and emotional elements. The purpose of Namaste is to give comfort and pleasure to people with advanced dementia through sensory stimulation, especially the use of touch. It aims to restructure the care for people with advanced dementia who are often immobile/confined to a wheelchair and incontinent failing in their speech.

Namaste runs for 2-h in the morning and 2-h in the afternoon, 7 days a week, and aims to increase engagement through the five senses (hearing, sight, touch, taste, and smell). It requires no additional staffing. The Namaste Care worker assigned to run the program for that day will work with all those in the facility with advanced dementia as defined above. It is likely that there will be 6–8 such residents within a facility of 60 people. Once they have been helped with breakfast, instead of remaining in their room, these residents are brought to the Namaste Care "space" (whether an adapted dining area or a dedicated space). Here they will be greeted by name, made very welcome and checked for discomfort and pain. The Namaste Care worker will engage with each as appropriate during the next 2 h – doing a hand massage, helping with a drink, combing a resident's hair, applying cream to the face, giving a footbath, and offering cut-up fruit and tasty titbits.

When it is felt a resident would benefit from being part of program, a family meeting is held to understand from them things that will bring pleasure and trigger memories for their family member. This meeting is also an opportunity to acknowledge the resident's deterioration from dementia in the positive context of offering more appropriate care. Finally, the meeting is an opportunity to establish the overarching goal of a peaceful, dignified death in familiar surroundings in the care home.

Namaste Care has now been implemented in LTCFs in a number of countries including the USA, Japan, Australia, and the UK. A toolkit is freely available from the St Christopher's Hospice website (http://www.stchristophers.org.uk/education/resources). There are several core elements of the program (see Table 5).

A recent study evaluating Namaste Care in six care homes found that, where there is strong

Table 5 Core elements of the Namaste Care program (Stacpoole et al. 2016)

1	"Honoring the spirit within"	The guiding principle of Namaste Care is a respectful and compassionate approach to individuals with advanced dementia
2	The presence of others	Namaste residents are brought together as a social group with a dedicated Namaste Care worker, so each resident feels "included" in their community
3	Comfort and pain management	Comfortable seating and pain assessment/management are the essential first step toward enabling Namaste residents to relax, engage, and express how they feel
4	Sensory stimulation	The program incorporates stimulation of the five senses (touch, hearing, sight, smell, taste). Music, color, therapeutic touch and massage, aromatherapy oils, and food treats are all part of the multisensory environment created in the Namaste room
5	Meaningful activity	In Namaste, personal care is provided as a meaningful activity, even though the Namaste residents will usually have had their morning wash. The focus is on pleasure rather than personal hygiene. Hands and face are gently washed with a warm flannel and patted dry with a soft towel. Moisturizing creams are applied, and the Namaste Care worker uses this opportunity to make eye contact and talk affirmatively with the resident. Hand and face washing is part of everyone's life experience and usually results in a sense of well-being. The Namaste Care worker will explore individual wishes and preferences and adapt activities to meet people's needs
6	Life story	Knowledge of the resident's life story is key to adapting the program of activities and interventions so that they are meaningful for each person
7	Food treats and hydration	The Namaste Care worker offers drinks and food throughout the session (being mindful of any swallowing difficulties). This creates extra opportunities to improve hydration and nutrition and contribute to the residents' health and well-being
8	Care worker education	Care workers involved in Namaste require education about dementia and all aspects of the care program. The care workers need support to feel confident
9	Family meetings	Holding a family meeting when a resident is going to start the Namaste Care program creates a further bond between the family/friends and the care staff, opening up the conversation about end-of-life care. Families are encouraged to take part in the Namaste sessions when they visit
10	Care of the dying and after-death care	The care that residents enjoy in the Namaste Care program can be transferred to the bedroom when the person is unwell and when they are dying
11	After-death reflection	Dedicating time to remembering a resident after their death supports the care staff emotionally. Reflecting on what went well, and any difficulties, provides an opportunity for care staff to learn from the experience and improve the care they give to residents when they are dying

leadership, adequate staffing, and good nursing and medical care, the Namaste Care program can improve quality of life for people with advanced dementia in care homes by decreasing behavioral symptoms (Stacpoole et al. 2015).

Implementing such a program actively demonstrates a person-centered relationship-based holistic culture for people with advanced dementia. Those with advanced dementia are not isolated but included in a program that is set to bring them enjoyment through the senses focusing on the palliative care needs including pain and agitation in the end stages of dementia. The Namaste Care worker reports any distress and lack of engagement of those at a session – people cannot engage if they are uncomfortable. The beneficial effect of Namaste Care on the family and staff has also been shown to be significant (Stacpoole et al. 2017).

6 Components of Successful Implementation of Initiatives

Implementing quality improvement initiatives is an interplay of three elements (Kitson et al. 1998, 2008):

- The "context" where the development is to take place (McCormack et al. 2002)

- The quality of the "evidence" that backs up what is being implemented (Rycroft-Malone et al. 2004)
- The level of "facilitation" required based on the "context" and "evidence" (Harvey et al. 2002)

For each of the above elements, different "situations" prevail (Kitson et al. 1998) which makes the element "not so effective" ("low") or "very effective" ("high"). In their model, Kitson and colleagues suggest that for successful implementation of a quality improvement initiative, there has to be a minimum of two "highs" associated with the three elements. For example, in the *context* of many LTCFs, there is no on-site multidisciplinary team, the majority of staff have little healthcare education, and many lack a learning culture. It can therefore be deduced that many LTCFs have a "low" *context* and any LTCF quality improvement initiative therefore needs to have a "high" evidence base + "high" facilitation.

The importance of understanding the multidimensional aspects of implementing quality improvement initiatives in LTCFs cannot be emphasized enough. A recent quality improvement initiative implementing the GSFCH framework ("high" evidence) using "high" facilitation showed four times the number of LTCFs gaining GSFCH accreditation compared to normal facilitation (Kinley et al. 2014b).

The importance of how an initiative is facilitated is often vital to its success. Just giving a LTCF a certain toolkit with little information on how to implement the change will be likely to fail. Where there is no effective facilitation, then any outcome will rely heavily on the care facility ability to "take hold" of the project and its ability to implement it.

Facilitation of 'whole system change' tools discussed in the previous section (such as GSFCH, PACE, Namaste) when supported well by specialist palliative care can be extremely beneficial – not only do colleagues in specialist palliative care increase their understanding of the chronic illness trajectory of frail older people in LTCFs, but such collaboration enables LTCFs to be connected and supported while they develop their own palliative care approach.

6.1 Sustainability When Undertaking Quality Improvement

Evaluations of many quality improvement initiatives in LTCFs have been encouraging. However, the importance of sustaining what has been implemented cannot be emphasized enough especially in light of the current high turnover of staff in LTCFs.

Whether it is just a simple tool or whole systems change, the importance of building in some sustainability initiative into the wider project is extremely important. Sustainability is not without cost but sustainability can be cost effective. Many initiatives, even when LTCF staff and management are keen to develop a palliative care approach, can fail because of lack of sustainability and support of the LTCF once the project is over. This raises a debate about the value of funding short-term initiatives/projects without a long-term vision (Hockley and Kinley 2016).

Little evidence exists regarding sustaining interventions in practice in LTCFs, but where these organizations have contributed financially toward to a sustainability initiative once the implementation has been completed, it has continued to empower, support, and develop staff (Kinley et al. 2017).

7 Future Issues and the Need for Innovation

By 2050 there will be more people in the world over the age of 60 than under the age of 15 years old (UNFPA 2012). It is important to start thinking differently about LTCFs if we are to improve the palliative care needs of frail older people. It is vital that LTCFs are seen as places where frail older people can live out the remaining months/year/s in the knowledge that their end can be in the place where they have got to know and trust the staff.

Increasingly, LTCFs are innovating how they care; whether it is developing a more homely atmosphere for frail older people with advanced dementia (http://hogeweyk.dementiavillage.com/en/) or

encouraging greater emphasis on student involvement and training in order to attract and retain staff (Kirkvold 2008).

Further innovation in relation to palliative care and LTCFs involves technology. Countries, especially those with large rural areas, have developed videoteleconferencing technology (VTC) to support the palliative care needs of LTCF residents' alongside staff training. The need to evaluate such services is important.

Finally, here in Scotland, development is underway to build a teaching/research-based care centre (The Vision for a Teaching/Research-based Care Centre). Based on the "hospice model" of holistic person-centered relationship-based care for people with advanced progressive incurable diseases, it will provide a centre of clinical excellence alongside being a resource for training and coordination of research across the region. With the majority of frail older people requiring 24-h care having a diagnosed dementia or severe cognitive impairment, the emphasis will be on advanced dementia with plans to innovate in relation to proactive respite care and support of families.

It would appear that developing palliative care in LTCFs is now very much on the political agenda. There is a danger however that LTCFs become overwhelmed by all the different education courses, quality improvement initiatives, and research. It is important for there to be a coordinated approach to work with LTCFs in a locality so that they are not inundated with different projects but that a "homely" atmosphere be maintained.

8 Conclusion

William Osler's quote "pneumonia is the old man's friend" was written prior to the considerable developments that have occurred in medicine over the last 70 years within which time geriatrics/gerontology and palliative care have both created their own specialties. The coming together of these specialties in the care of frail older people in residential care facilities is a vital area requiring expansion while recognizing Osler's wise words.

Mutual learning between those passionate with the care of frail older people in residential care settings and those experienced in the palliative care needs of people facing the end of life, while bearing in mind not to impose what has been learned from a cancer "model of palliative care" onto residential care settings, will bring remarkable elegance to the care of frail older people.

This chapter has described a number of initiatives – "stand-alone" as well as "whole system" change initiatives. The emphasis must be on sustainability of such initiatives and the support of staff in residential care settings. An important "white paper" details the areas for practice development and research for people with advanced dementia being cared for in residential care settings. This alone if acted upon will break the isolation that staff caring for the 24-h needs of frail older people often feel.

Competent multidisciplinary working to support the palliative care needs of people in residential care settings will not only reduce inappropriate hospital admissions but is likely to enhance staff support, reduce turnover, respect what really matters to frail older people and their wishes at the end of life, and improve their quality of death.

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Hospital Care

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_50

Abstract

Hospitals are where we find the most seriously ill people in our society. Patients go there to receive lifesaving and life-prolonging treatment, but they are also where many will deteriorate and die. Care for these people and their families is therefore core business for hospitals, and this is being increasingly recognized internationally. Hospitals are also facing the challenge of how best to meet the needs of a population that is becoming ever older and frailer. When in an acute care facility, patients with advanced disease require palliative care in its broadest sense, and when their needs are complex, they deserve reliable and timely access to specialist support.

This chapter will look at the provision of palliative care in the acute setting, from the perspective of a dedicated team, working in a small provincial city in the South Island of New Zealand. It will explore how this service has developed and how it operates and thrives within its unique healthcare setting. A broad range of challenges and opportunities are discussed as well as issues such as information technology, team sustainability, and education provision. Ultimately the aim is to promote a culture change in health that promotes universal access to holistic care at the end of life.

1 Introduction

Specialist palliative care is well recognized internationally as a core component of health service delivery. People with palliative care needs often move from one care setting to another, and the skills and expertise that are provided and supported by those with specialist training need to be readily available. The ideal system is supported and configured to ensure that quality and compassionate care at the end of life is available in a timely way to everyone who needs it, wherever they are located.

The reality is however that in the minds of many (including healthcare professionals, administrators, and funders), palliative care is what happens in hospices and in people's homes, not in acute hospitals. It is often assumed that palliative care is delivered only by nurses who have a calling to provide an alternative option for care when death is inevitable. Grateful and generous communities donate money and provide time as volunteers to supplement government funding. It is viewed as separate and different to the multidisciplinary, quality-driven, holistic, and supportive services that are needed across the wider health system, including in hospitals.

Hospitals are where people who are living with and ultimately dying from chronic progressive illnesses and conditions seek treatment for (usually) short periods during an acute episode or exacerbation (Clark et al. 2014). This is certainly the case in New Zealand, as it is in many other developed countries. Community care has expanded and developed to encompass those who are very unwell and disabled and many acute problems are able to be managed very comprehensively without admission. However, hospitals are where people often look to in times of crisis, and staff should be able to recognize when a person is at risk of dying and respond accordingly. This is achieved best when their department or service recognizes the importance of this issue and is configured appropriately with access to all the necessary resources, policies, and guidelines.

Expectations vary as to what hospitals can provide, but most patients will be hoping that treatment will work and that they will be returned to health. Supporting this belief are the ever-expanding array of specialties and subspecialties which flourish as medicine evolves and more treatment options become available. Hospitals are often where it becomes apparent that cure is not possible, that the person's future is far from certain, and that the priority now is the relief of suffering.

Hospitals are also where a large proportion of our population die. In the period 2000–2013 in New Zealand, 33.9% of all deaths occurred in publicly funded hospitals. This figure is closer to

50% for Australian hospitals (Ireland 2017). The majority of these deaths are able to be anticipated given the progressive nature of the person's medical condition or conditions.

Studies conducted in Australia, the UK, and Belgium have concluded that at any one time, 13–36% of hospital inpatients meet the criteria for palliative care need. A New Zealand estimate from 2013 using the Gold Standards Framework criteria is entirely consistent at 19.8% (Gott et al. 2013). The proportion of in-hospital deaths with a palliative care status identified in hospital databases (from that same Australian study) sits at 44% in 2013–2014 which is up from 37% in 2009–2010. Looking more broadly, it is apparent that the majority of deaths are preceded by a period of deterioration over weeks to months where there was the opportunity to instigate a palliative approach and involve specialist services if required. This issue was cited in a 2008 paper by Project Muse where it was stated that 75–80% of decedents have a dying process that typically occurs over a few weeks to many months (Wilson et al. 2008). Despite these statistics, many are still surprised that such a large proportion of the care provided in hospitals is for patients nearing the end of their lives. Such information should be used to inform end-of-life care policy in hospitals (Clark et al. 2016).

Acceptance of the need for a palliative philosophy in acute care is far from the norm. As far back as 2001, it was stated that "the hospital environment reflects the business of life in society, which still denies the naturalness and inevitability of death. The culture of practice in the acute care setting is inherently related to life supporting and life prolonging activities" (Middlewood et al. 2001). The inclusion of palliative care can be an uneasy fit, but it "has presented an alternative philosophy to guide the care for dying patients... there is a need to integrate palliative care services into the acute care setting to assist the transition of goals from investigative and treatment orientated care to improving quality of life" (Middlewood et al. 2001). This issue of integration has become one of the central functions of palliative care services and will be covered later.

2 Normalizing Death and Dying

The overriding focus for doctors continues to be on returning patients to health using the diagnostic and treatment skills in which they were trained. However, essential to ensuring that palliative care is both available and of high quality is the recognition that dying is inevitable for each and every patient and agreeing that expert and timely care should be delivered with compassion. When it is apparent that a patient is not responding to active treatment or they do not want life-prolonging measures, doctors "step onto the threshold" of a new place, the place of realizing that this person is not improving, not taking the normal path, and perhaps preparing for the end of life and/or even imminent death. Dying brings health professionals face to face with their own mortality. For most this is a frightening landscape. It can be a place of discomfort on many spheres, not just physical. Palliative care operates right on this threshold. Dying often brings everyone into a liminal space, uncharted territory. In hospitals enabling this acceptance to occur is particularly challenging.

The rapid pace of hospital diagnostics and treatments now needs a reduced pace and a slow and listening presence. Assessing where the discomfort is, helping patients and families navigate this landscape and all the uncertainty it brings. Uncovering where the fear lies and transitioning people to a place of understanding and hope, through confident care and management of symptoms, are the essence of the palliative care approach.

The wider nursing and multidisciplinary team in hospitals is strongly influenced by the medical paradigm. This medically oriented hierarchy within hospitals tends to give weight to the narrative set by doctors, and it can be hard for nurses or others to break into this with their own observations and assertions or to give voice to the person's unique concerns and priorities regarding their future care.

The acknowledgement of palliative care brings a fresh perspective to any acutely unwell patient's care. It makes available a different way of

thinking particularly with regard to goals of treatment and the role of the carer and wider family/whānau. (**Whānau**: extended family, family group, or a familiar term of address to a number of people. In the modern context, the term is sometimes used to include friends who may not have any kinship ties to other members (Moorfield 2015) (ISBN 978-0-947491-36-9 (online)).). Hospital palliative care teams can assist with difficult decisions, weighing up the risks and burdens versus benefits of treatment options in real time. They can assist with the transition from active treatment to a palliative approach, uncovering what is most important to the person. This is the unique set of skills that those with specialist training in palliative care and palliative medicine bring to the acute care setting.

In New Zealand, five recurring themes regarding the provision of care to palliative patients in the acute setting have been identified. These are as follows: symptom control and burden, communication with health professionals, decision-making related to patient care and management, inadequate hospital environment, and interpersonal relationships with health professionals (Robinson et al. 2015). These are areas of care provision that can be deliberately addressed by hospital palliative care teams. Ideally, palliative care should be "at the table" when vulnerable patients are discussed. This may go some way to ensuring that a palliative approach is actively considered and that teams are reminded to glean the person's wishes in the light of any clinical concerns or worsening prognosis.

3 New Zealand Context

In New Zealand, hospitals are operated and funded by district health boards who are also responsible for delivering a full range of services in community settings. This is overseen by the New Zealand Ministry of Health (MOH) (Cumming et al. 2013). There is a strong imperative to provide a seamless care experience for consumers, and this is made more achievable given that there is no competition for patient numbers and no conflicting interests across care settings.

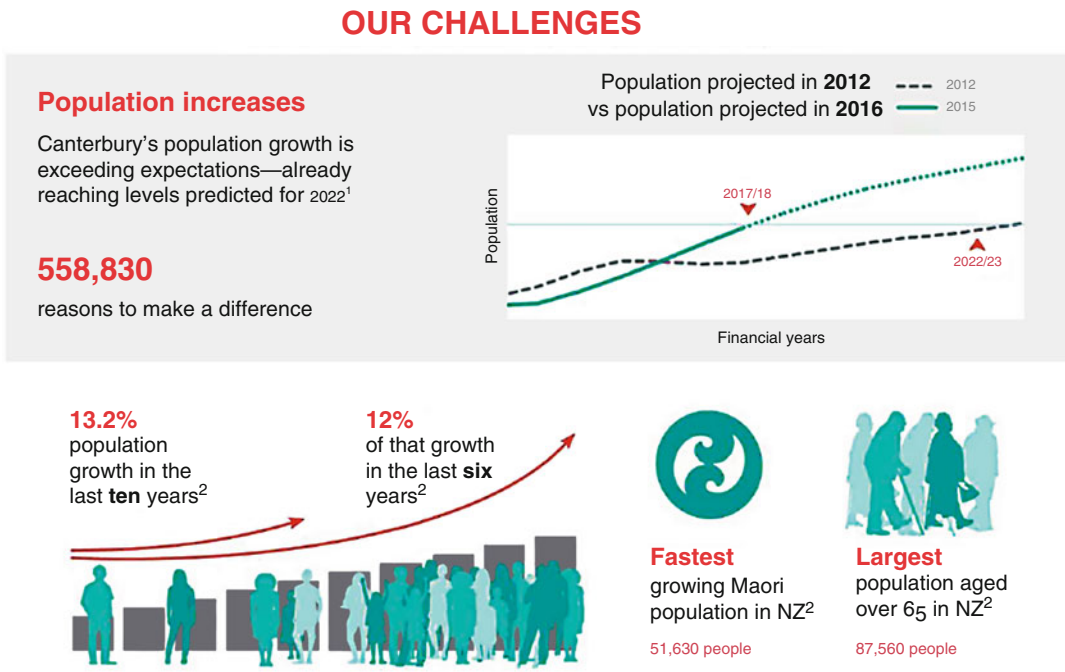

Fig. 1 Challenges of population growth in Canterbury

The insights detailed in this chapter are based on the experience of establishing a hospital palliative care service in Christchurch, Canterbury. Canterbury is located on the east coast of the South Island of New Zealand. The total population of NZ is 4.8 million. The Canterbury District Health Board (CDHB) encompasses one major population group with an overall population of 558,830. The following graphic is taken from the CDHB Annual Report 2016/2017 and illustrates current population challenges, including the high proportion of residents aged over the age of 65 years (http://www.cdhb.health.nz/About-CDHB/corporate-publications/Documents/Canterbury%20DHB%20Annual%20Report%20year%20ended%2030%20June%202017%20%28PDF%2C%202MB%29.pdf).

The Christchurch Hospital is a tertiary-level teaching hospital with approximately 650 beds. There is a second hospital in the north of the city with approximately 300 beds. The hospital palliative care team accepts referrals from both hospitals and consults on a regular basis. There is also a rural hospital with approximately 70 beds in Ashburton in the south of the region. There is a close relationship with the much smaller DHB on the West Coast (WCDHB) which has a highly dispersed mainly rural population of approximately 32,600. A large range of specialist services on the West Coast are provided by the CDHB, and some, including palliative care, are enhanced and supported by the CDHB through agreements and alliances.

Projections of the need for palliative care in all settings in New Zealand were published in 2016 (McLeod 2016). These are based on historic patterns from 2000 to 2013 and demonstrated that palliative care was needed for 73.5% of all deaths in public hospitals. Deaths in acute hospitals are often sudden and unexpected, but there are also a large number where the death can be anticipated and prepared for (Gott et al. 2013). It is anticipated that the South Island will experience an increase in total deaths of 44% over the period 2016–2038, as the population ages and the "baby boomers" begin to reach the end of their lives. As a consequence, it is projected that the need for palliative care will increase by 47% – an increase of 35% in public hospitals and a much bigger increase of 75% in aged residential care.

When considering the need for palliative care services, it is noted that this analysis is done on the basis of place of **death** and not place of **care**. The need for hospital palliative care at older ages is therefore dependent on the extent to which people are hospitalized. It is also a concern that aged residential care facilities will not be expanded as extensively as the predictions suggest, putting additional pressure on home care. Hospitals may also see an increase in admissions for the elderly as a result.

The introduction and sustainability of specialist palliative care in New Zealand hospitals have been very challenging, despite it being a clear recommendation in the palliative care strategy for over 15 years (Minister of Health 2001). In the analysis from 2016 (http://www.cdhb.health.nz/About-CDHB/corporate-publications/Documents/Canterbury%20DHB%20Annual%20Report%20year%20ended%2030%20June%202017%20%28PDF%2C%202MB%29.pdf), the need for palliative care in different settings was assessed, and it is interesting to note that a high proportion of deaths occur outside of hospitals, relative to other countries (Broad et al. 2013). Contributing to this might be the fact that only 25.8% of cancer patients died in public hospitals, in contrast to approximately 56% of cancer patient deaths in England and Wales. It is interesting to note that the largest increase in place of death for cancer patients in New Zealand has been in residential care (Palliative Care Council 2014). In addition to this, an overarching priority of the New Zealand MOH is to provide care "close to home," drawing attention away from acute care as the default option (http://www.health.govt.nz/publication/better-sooner-more-convenient-health-care-community). These factors combined may be contributing to a lack of focus on allocating sufficient resources to hospitals for end-of-life care.

3.1 Definitions

All health systems are complex, and navigating them can be challenging, both as health

professionals and as consumers. Talking about death and dying is also not easy, and confusion can occur when the phrase *palliative care* is used both for the type of care provided to people with a life-limiting or life-threatening condition and for some, **but not all**, of the health professionals tasked with delivering that care. Palliative care organizations are well placed to be involved in developing local models of care and promoting integration across care settings.

Definitions can be confusing, and in order to clarify the situation, the New Zealand Palliative Care Glossary was developed (2nd edition, MOH 2015) to assist with promoting the Framework. Terms such as a "palliative care approach," "primary palliative care," and the "palliative care system" are included, and socializing these concepts has been occurring incrementally.

Palliative Care Approach: an approach to care which embraces the definition of palliative care. It incorporates a positive and open attitude toward death and dying by all service providers working with the person and their family and respects the wishes of the person in relation to their treatment and care.

Primary Palliative Care: is provided by all individuals and organizations who deliver palliative care as a component of their service and who are not part of a specialist palliative care team.

Specialist Palliative Care: palliative care provided by those who have undergone specific training and/or accreditation in palliative care/medicine, working in the context of an expert interdisciplinary team of palliative care health professionals. It may be provided by hospice- or hospital-based palliative care services where people have access to at least medical and nursing palliative care specialists.

Specialist Palliative Care Service: a team or organization whose core work focuses on delivering palliative care, for example, a hospice or hospital palliative care team.

Palliative Care System: comprises specialist palliative care services, primary palliative care providers, and the other factors that enable them to deliver palliative care, such as communication and coordination between providers. It is not simply the existence of primary palliative care providers and palliative care services that comprises the palliative care system; it is the links between them that tie together "a system."

Supporting the delivery of primary palliative care are specialist services. These include

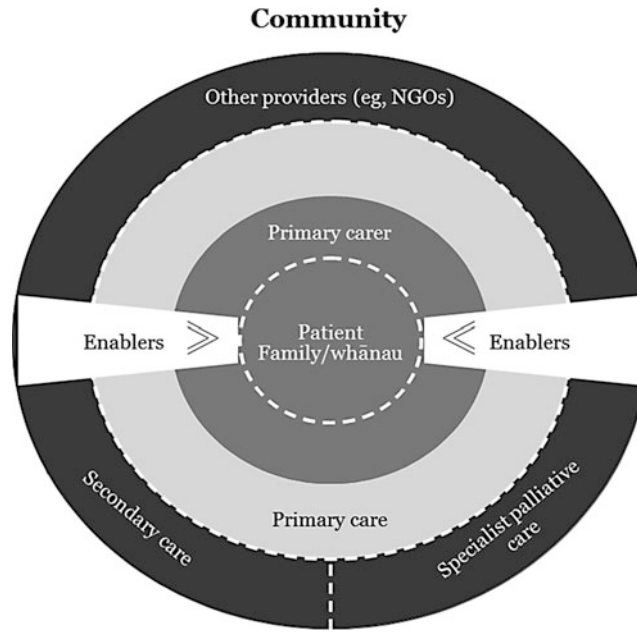

Fig. 2 Support for the patient and family/whanau https://www.health.govt.nz/system/files/documents/publications/resource-capability-framework-adult-palliative-care-services-v2.pdf

hospices and community palliative care teams AND hospital palliative care teams. Hospice inpatient and community services are very well embedded across New Zealand, and they are still considered the face of palliative care in society.

3.2 Models of Care

In 2012, the Resource and Capability Framework for Integrated Adult Palliative Care Services in New Zealand (the Framework) (Ministry of Health 2012) was developed. This outlines a model of care which explicitly recognizes that the majority of palliative care in New Zealand is delivered and coordinated by those without specialist training in palliative care, working outside a hospice or palliative care service/team, i.e., primary palliative care. The current arrangement across both the CDHB and the WCDHB is aligned with this Framework. The following graphic is taken from the Framework document.

The delivery of specialist palliative care in the acute care environment has grown organically in New Zealand, as has been the case around the world. It is contingent on supportive and sympathetic organizational leadership and a shared vision for integration of care across settings. This was fortunate to happen in CDHB leading to the creation of the Christchurch Hospital Palliative Care Service in 1999. The same cannot be said across the country with the establishment of hospital services proving very hard to realize in some DHBs.

The service in Canterbury started with a part-time physician and the recruitment of a full-time specialist nurse a few months later. Now the service employs two physicians, a nurse practitioner, two nurse specialists, registered nursing cover for planned leave, and a full-time registrar training position. The team is located within the Canterbury Regional Cancer and Haematology Service and is funded as a component of the medical and surgical division of the Hospital.

It remains the case that some hospitals in New Zealand still have **no** specialist palliative care presence at all. This is problematic and disappointing and has been allowed to happen because of the lack of a clear MOH directive for DHBs in this regard. Some hospital services are limited to in-reach nurses from hospices, with or without DHB input and often with restricted medical oversight.

Although the interdisciplinary consult liaison team is the usual model of care in hospitals, there are other models utilized in other countries. For example, there are dedicated palliative care units within some hospitals in the UK funded by the National Health Service (NHS). These units have led directly to an increase in home death rate, a reduction in deaths in the acute care hospital setting, and better integration of community, hospital, and palliative care unit team facilitating admissions and discharges and have raised the profile of palliative care within the trust (Grogan et al. 2016). (Trusts are organizations within the National Health Service which serve either a geographical area or a specialized function (such as an ambulance service). In any particular location, there may be several trusts involved in the different aspects of healthcare for a resident.).

Regardless of model, the key aspect of hospital palliative care is providing a higher level of expertise in complex symptom management, psychosocial support, communication, grief, and bereavement. Ideally, this process involves a full multidisciplinary approach and requires negotiation, coordination, communication, and collaboration as well as clinical knowledge and expertise.

The overarching goal is integration across the "whole of system" (Ministry of Health 2017a, b). This is increasingly necessary given the growing burden of chronic conditions. Ensuring that care at the end of life and following bereavement is equitable, of high quality, and available to everyone, **wherever they are located**, can only be achievable by empowering, teaching, and supporting "primary palliative care" providers in all settings, including hospitals. The issue of integration will be covered later in this chapter, but it is worth noting that following the release of the Framework (Ministry of Health 2012), momentum to configure specialist services with improved integration as a focus has indeed increased across New Zealand.

In the South Island, this imperative of integration is led by the South Island Alliance, covering

all five DHBs. Since 2014, palliative care has been represented on the Alliance by the Palliative Care Workstream (https://www.sialliance.health.nz/our-priorities/palliative-care/).

The graphic below illustrates the functions of the SIA with "population health" and "experience of care" being two of its core principles. Of particular relevance to those working in and promoting universal access to palliative care is that "people die with dignity" is one of the eight key priorities (https://www.sialliance.health.nz/UserFiles/SouthIslandAlliance/Image/Outcomes%20Framework_020715.jpg).

4 Hospital Palliative Care Services

As noted earlier, approximately one third of all deaths occur in hospital in New Zealand. Recent trajectories predict this will remain steady over time (http://www.cdhb.health.nz/About-CDHB/corporate-publications/Documents/Canterbury%20DHB%20Annual%20Report%20year%20ended%2030%20June%202017%20%28PDF%2C%202MB%29.pdf; Palliative Care Council 2011). Regardless of whether the risk of dying has been acknowledged, consumers quite rightly expect that alongside active treatment of an advanced progressive condition, attention is paid to pain and any other distressing symptoms and that communication around diagnosis, prognosis, and options for care and treatment is conducted sensitively and with compassion and respect.

While there is an expectation that all health professionals provide supportive and palliative care, it would be fair to say that many do not have sufficient knowledge or understanding to do so effectively, or they feel out of their depth with initiating a palliative approach, particularly in complex situations. Hospital palliative care as a specialist area developed in response to a recognition that many people were dying in acute hospitals without ready access to expert symptom control and a timely referral to palliative care is increasingly recognized as an essential service within the hospital system.

The symptom burden of hospitalized patients is high. "Many patients in hospital with uncontrolled symptoms including pain, nausea, vomiting, constipation, anorexia and dyspnoea" (Jack et al. 2003). The impact of hospital palliative care team has been studied with positive results. "Analysis of the data showed statistically significant improvements in the symptoms of pain, nausea, insomnia, anorexia and constipation following interventions by the team. Discussion regarding diagnosis significantly change the insight of both patients and relatives, and appropriate placement was facilitated. This study has demonstrated the significant contribution that could be made to patient care by a hospital palliative care team" (Ellershaw et al. 1995).

Within hospitals, the primary model of care delivery is the interdisciplinary consultation team (Kelly and Morrison 2015). This is generally referred to as a "consult liaison service." The palliative care team needs to work alongside the treating team and respond to the prevailing discomfort around death and dying, offering clinical support, reassurance, and education. Teams build on the care provided by the primary clinical team to enhance the capability and capacity and quality of the overall service provided while emphasizing the normality of dying. Ideally, teams need not only to be competent but also accessible and nonjudgmental. Within the palliative care team, experience levels and areas of expertise will differ requiring collaboration and support. It is preferable at times for two team members to see an individual patient.

Where hospital services are present, thought needs to be given to two aspects which may extend the "consultation liaison model." The first is "admitting rights" which is the ability to admit patients under a palliative care specialist. The other is about "prescribing rights" which is the acceptance that palliative care team members (doctors or nurse practitioners) can prescribe and amend medications. The situation in the CDHB has not changed since the service was established with the team being able to prescribe freely, in consultation with the treating team, but all patients are admitted under another specialist with

palliative care providing advice and support. This model has served us well but has been challenged a few times over the years.

4.1 Clinical Roles and Functions of Hospital Teams

It is our observation that hospital teams vary considerably in size and personnel depending on available resources. Appendix B of the Framework has outlined the essential composition and clinical functions in the New Zealand context, and teams have used these as a guide and as a vehicle for discussions with funders and managers (Ministry of Health 2012).

The constitution of a hospital-based palliative care team also varies depending on the will and influence of clinical leaders within the individual organization. Many hospital palliative care services began with one nurse or one doctor, sometime in-reaching from a local hospice. One person does not make a team, and successful services depend on their being a team structure for mutual support, sustainability, and professional safety. It is generally recognized that medical and nursing involvement is required **at a minimum**, ideally supported by some administration hours, sufficient to assist the team with the typing, data collection, and general administration.

The hospital team functions are as follows:

- Five days a week on-site service (with after-hours telephone cover)
- Consultation, advice, and liaison with referring multidisciplinary team (MDT)
- Advanced assessment (initial and ongoing) and care planning – medical, nursing, psychosocial, and spiritual
- Liaison – community (primary care) aged care, hospital teams, hospice (inpatient and community services), and pain services
- Input into family meetings
- Input into discharge planning
- Input into advance care planning
- Input into end-of-life care pathway implementation

Nonclinical functions were also included in the framework. These were considered critical to enhance the knowledge and skills of primary palliative care providers and to ensure leadership and strategic direction for palliative care:

- Clinical education – both formal/structured and informal
- Supervision/training (medical and nursing)
- Leadership and strategic planning
- Quality improvement
- Research/audit
- Clinical data collection
- Access to clinical supervision
- Appropriate networks and engagement (local, regional, and national)

An ideal service would be able to offer consultation liaison services 7 days a week and the option of in-person specialist review after-hours for complex or emergency cases. To date this comprehensive coverage has not been possible in any New Zealand hospital, and even providing after-hours telephone cover is proving difficult for most hospital teams. Provision of after-hours telephone advice has been achieved recently in Christchurch and involves the sharing of senior staff across the hospital and the hospice/community services. This arrangement is based on a close working collaboration that has developed over years.

It is apparent that hospital palliative care teams often demonstrate the benefits of a flat hierarchy. This is where the views of the whole team are equally valuable and decisions are made after attending to members' views and ensuring that there has been open and honest dialogue. As a minimum, this requires hospital teams to consist of nurses AND doctors as members and a strong alignment with allied health in the wider hospital to include social, cultural, and spiritual care. Some teams include social worker and/or counselor/psychologist as members of the specialist team, and this can compensate for when there is inexperience in these areas in the wider hospital.

It is important to emphasize that there is a need for hospital teams to operate in a time-constrained

environment which can be challenging. Trust and rapport with patients and families must be established very quickly, in what is a busy and fast-paced environment. The median time from referral to discharge or death for the Christchurch service is 4 days, and this is inclusive of weekends where the team are not on site.

Anecdotally, the case mix for hospital palliative care is somewhat different to hospice and community services, with acute deaths and non-malignant conditions more strongly represented. In Christchurch Hospital, the proportion of new referrals who have a non-cancer diagnosis sits at approximately 40%, a number that has been consistent over the last 5 years. The proportion of new referrals who die during an episode of care has also been stable over time at 25%. Three quarters of referrals therefore are discharged from hospital to community settings, making it an imperative that the process of transfer of care is robust and well-planned (Unpublished data from Christchurch Hospital Palliative Care Database, New Zealand).

Further analysis of the Christchurch data has confirmed the impression that a higher proportion of patients seen by our service die in hospital if they have a nonmalignant condition. Eighteen percent of cancer new referrals to the palliative care team died during that first episode, compared to 49% of non-cancer new referrals. This difference is striking. These patients (and their families) may not be aware of the seriousness of the situation at the time of admission or the possibility that they might be close to death. This raises many issues in regard to community and health system preparedness that is likely to become more important as the general population ages (Unpublished data from Christchurch Hospital Palliative Care Database, New Zealand).

Ward-based referrals are not the only activity undertaken by hospital palliative care teams. Across all disciplines, clinics are a core component of specialist services in acute hospitals. Increasingly these are not led by doctors but by specialist nurses conducting clinics in areas such as oncology, diabetes, wound care, and infectious diseases. Hospital-based palliative care clinics are variably utilized, and this is often a reflection of capacity. It also depends on whether ambulatory care is provided by the local community-based/hospice service. It can be confusing for patients and referrers if there are multiple options for outpatient intervention in palliative care (particularly in a publically funded health system like New Zealand), and it is important not to have unnecessary duplication of resources.

In Christchurch, palliative care services work collaboratively with a number of other specialty areas with clinics and multidisciplinary support processes that complement each other and promote integration. Having combined clinics to address particular areas can work very well and include but are not limited to nephrology (for end-stage kidney disease), motor neurone disease, and heart failure.

Pediatric palliative care is a specialty area on its own, and most adult specialists (medical and nursing) do not feel it is appropriate to be offering advice to their pediatric colleagues. However, the volume of patients in pediatric practice is low, and it takes much longer to accumulate a broad experience base. There is enormous value in some situations for providing collaboration and support. It is an issue that is very worthwhile considering.

Access to bereavement support including formal counseling is ad hoc and often absent. Hospices generally have well-developed services and link very effectively with other community providers. Some hospital-based services such as intensive care and pediatric oncology have policies that include bereavement support, but it is the exception rather than rule. This is the subject of a current project in our DHB.

4.2 Nonclinical Roles

The knowledge and wisdom of individuals within the hospital palliative care team are often utilized by other teams around the hospital to discuss complex patients and debrief over difficult issues, especially in cases where there is particular sensitivity or emotion. This is perhaps because of having expertise in communication skills but also because as a discipline palliative care sits slightly outside the traditional medical model and

therefore brings a different perspective and a sense of neutrality. This listening ear can be highly valued in the stressful environment of acute medical care.

The influence of hospital palliative care extends beyond the patients and the clinical teams caring for them. Ideally the reach should be directly into the realm of quality and patient safety as this is at the heart of what we do. Hospitals receive regular feedback on their services, and criticism is often leveled at issues around poor end-of-life care and communication. Building a profile in the organization where the service is valued for providing guidance and advice is invaluable. This can involve assisting with the processing of complaints in a constructive and meaningful, driving institutional change around policy and priority setting for dying patients.

The requirement for "noncontact time" (the time spent on issues not relating directly to patient care) is specifically identified within the employment contract of doctors in New Zealand. This is very relevant for palliative care where education, service development, research, and continuing professional development must be undertaken. Other staff, most specifically nurses, also require noncontact time for these endeavors. For everyone the ability to prioritize this above clinical work is extremely challenging.

4.3 Staff Training

Advanced medical training to specialist level across Australia and New Zealand is delivered through the Royal Australasian College of Physicians (RACP). New Zealand has a nationally funded program, and palliative medicine registrars work in hospital palliative care for a minimum of 6 months to develop their palliative care skills in an acute setting. This is a mandatory requirement for training. All palliative medicine specialists employed by the CDHB have a role in undergraduate medical student teaching both in the hospital and in the hospice.

Nursing students have little exposure in most undergraduate programs to opportunities to improve generic symptom assessment and treatment skills as well as communication skills. Allied health staff have even less. Palliative care forums worldwide continue to advocate for increased training in all undergraduate programs.

Postgraduate university posts for palliative medicine and palliative care nursing are gradually becoming more common but are still inadequate for the research that is required and for providing sound evidence for clinical decision-making. This is particularly the case in New Zealand. The CDHB is fortunate to have a specialist in post who is also employed as a Senior Clinical Lecturer for the University of Otago.

While numbers are still small, the introduction of nurse practitioners (NP) approximately 15 years ago in New Zealand has assisted in increasing advanced assessment skills and increased pharmacology knowledge among palliative care nurses. This has been valuable in the acute hospital environment as well as rural and community settings and has raised the bar regarding clinical reasoning, knowledge, and prescribing of medications by nurses. The NP role supports the philosophical stance of palliative care in many hospital teams – that nursing, allied health, and doctors consult on the same group of patients. Allowance is made for the clinical experience of the individual practitioner in relation to the complexity of the case, but otherwise there is no differentiation.

Hospital palliative care teams need to prioritize their own ongoing learning which may include journal clubs, hospital grand rounds, complex case management reviews, mortality meetings, cancer multidisciplinary meetings (MDMs), etc. Combined continuing medical education (CME) with other disciplines such as oncology are also highly beneficial and usually easily accessible in the hospital environment. Such meetings also provide opportunity to discuss patients with complex symptoms. Within the hospital system, specific meetings can be set up to review imaging and discuss patients with complex pain issues. This has happened in Christchurch and is proving invaluable in the treatment of patients with pain who require a broader team discussion. Appropriate patients may then be selected for palliative procedures such as cementoplasty/

vertebroplasty, ablation techniques, and nerve blocks as well as palliative surgery and radiotherapy. These meetings provide opportunity for specific ongoing learning as procedures are refined or new innovations become available.

As hospital teams grow, the risk emerges of referring teams getting conflicting advice, depending on who from palliative care responds on each occasion. This needs to be managed proactively as it can erode trust in the wider team. Having agreed symptom management guidelines that the whole team adheres to sets a platform for the main problems that are encountered. Complex cases, where creative thinking may be required, need to come back to the team so that a consensus is developed. Every effort should be made to ensure that each team member does not work independently, with synergy of practice being of paramount importance, while still valuing each other's unique skills and ideas.

Another issue that causes concern is when the advice of palliative care is in conflict with the treatment plan of the referring team. This is not an uncommon situation and requires diplomacy and care to minimize confusion and polarization. Ultimately a consensus is usually reached as long as the needs and preferences of the patient are put at the center. The palliative care perspective is not always correct of course, so mutual respect and humility are very useful attributes.

4.4 Prompt Response to Clinical Need

As hospital palliative care services have been established, so have referral criteria to manage the flow of referrals and to guide referrers. In New Zealand the Framework identifies three main criteria for specialist referral. These are as follows:

1. The patient has active progressive and advanced disease or life-limiting illness.
2. The patient has a level of need that exceeds the resources of the primary palliative care provider. The Framework states that palliative care services "should provide direct management support of patients their families and whānau where more complex palliative care needs exceeds the resources of the primary care provider."

   There has also been agreement that the level of input is "needs based" rather than based on diagnosis or prognosis and in some cases where that level of need becomes extraordinary examples include:

   "Uncontrolled or complicated symptoms, specialised nursing requirements related to mobility functioning or self-care, emotional behavioural difficulties related to the illness such as uncontrolled anxiety or depression."
3. The patient agrees to the referral if competent to do so (or an advocate agrees on their behalf).

On the basis of these criteria, a referral for a specialist palliative care assessment can be activated. The referral is made according to **patient need**. Sometimes patients with a longer or unknown prognosis are referred, and this is entirely consistent with the model of care. It has been recommended that individual service referral criteria in New Zealand are based on the national guidelines. As noted in the Framework, "the subsequent level of involvement/intervention, treatment plan and care package be negotiated with the patient, carer and referring team" (Ministry of Health 2012).

Patients can also be discharged from palliative care services either through patient choice or because their needs have been met and ongoing care can be effectively managed without regular input from specialist services. Discussion with and referral back can be made at any time.

Another recommendation is that teams articulate a target response time for new referrals to be seen once the referral has been received. Not infrequently, referred patients will be in acute pain or close to death. These are sometimes referred to as "late" referrals and to a certain extent are inevitable. Teams should make themselves as approachable as possible to help mitigate this issue, and responding quickly with advice and support is essential. Local policy is that patients are seen the same day if at all possible. While this may not always be achievable, it should be the

ideal as responding to acute need/demand for acutely unwell patients is core business for hospital palliative care. In many cases, the issues affecting the person and/or their family have been present for some time before the referral is generated, so waiting any longer only compounds distress for patients, families, and staff.

Triaging of referrals is a complex and fraught issue. The task of making a referral is often delegated to junior staff who may not appreciate the full picture and struggle to articulate the purpose or urgency. Speaking to the most appropriate member of the referring team (which may be a senior) is often required. To complicate things further, there are often additional concerns that have not been identified by the referring team. Wherever possible, patients should be prepared for a palliative care referral and have agreed for it to occur. The presence of a specific support person may be required. Working alongside referrers on a daily basis is essential to improve their capacity to identify and respond to palliative and end-of-life issues. Over time, referral practices improve and true teamwork emerges.

4.5 Complex Decision-Making and Ethical Challenges

Palliative care skills are generic and required in all locations; however, working in the acute hospital environment allows clinicians to be involved at the coalface for active treatment decisions as they are unfolding during an acute admission. The availability of specialist palliative care support when a patient is in the emergency department or being admitted to intensive care as well as for acute assessment teams such as in general medicine, general surgery, oncology, cardiology, hematology, and older person's health is highly beneficial. Being accepted as part of the wider team requires mutual trust and respect; benefits are significant, and they can work both ways. Palliative care as a specialty needs to stay current with practice trends and developments for the benefit of all patients and also improves interdepartmental communication and collaboration.

Patients with palliative care needs derive many benefits from hospital admissions. Robinson et al. reported that "families felt relieved when they were admitted to hospital. This was seen as relief from the responsibility of decision making associated with caring for someone with a serious illness" (Robinson et al. 2015). Primary teams defer to the hospital palliative care service particularly when patients with complex symptoms or psychosocial issues are admitted when they lack the confidence to manage the case alone (Ireland 2017). Access to specialist palliative care in the hospital environment has a demonstrated effectiveness in reducing the symptom burdens of dying person, whether these be physical or psychosocial (Le and Watt 2010). There are also established benefits for carers (Higginson and Evans 2010). This occurs despite that fact that a member of the hospital palliative care team cannot be at every ward-based multidisciplinary meeting or mortality meeting, just like they cannot be present at every cancer MDM, but the profile of palliative care within the acute hospital should ideally be such that teams can call on a team member to provide a palliative care viewpoint or option in most situations where that is needed.

A regular reason for referral is when ethical challenges arise or where there is conflict between the wishes of the treating team and those of the patient and/or family unit. These cases are distressing for health professionals, and the palliative care team can act as a "sounding board" or "wise ear." This is a form of collegial support which is increasingly important in the acute environment.

It should also be routine that a health professional with advanced knowledge in end-of-life care will assist in the development and socialization of policies and processes linked to complex decision-making. This can be achieved by contributing to initiatives such as the transition from active treatment to a palliative approach, determining and documenting goals/ceiling of care, advance care planning, medical guidance plans for incompetent patients, and policies regarding resuscitation decisions and documentation. It also requires an understanding of how to discuss these delicate issues with consumers.

4.6 Education, Mentoring

The training and education of healthcare professionals who work in acute hospitals are paramount and linked closely to the issues of transitioning patients from active treatment to a palliative approach and end-of-life care. Medical staff trained in the biomedical model with curative intent should be introduced to the basic concepts of palliative care early in their training and be given the opportunity to think about their own mortality and the importance of compassion, empathy, person-centered care, communication, and self-care.

Face-to-face education sessions for ward-based staff are expensive to deliver for resource-constrained hospitals, and this has led an increasing demand for online learning packages. These are also more easily accessible for healthcare professionals working across 24-h shifts, but such programs are time-consuming to produce. Even once implemented, these tools cannot completely eliminate the need for personal contact with experts in the field, especially when teaching sensitive and challenging content that may trigger deeply personal responses that need to be carefully managed.

It is important to maximize informal teaching opportunities and to mentor ward nursing and medical staff and students. This is part of the day-to-day work of hospital palliative care teams. This ongoing requirement can be a heavy workload for inherently numerically small hospital teams but is absolutely necessary.

An excellent opportunity for palliative care education is as part of any communication skills training that happens within the hospital. Teaching and role-playing of breaking bad news/end-of-life care consultations with patients and families are also required. The introduction of advance care planning programs in acute care in recent years has also provided the opportunity for healthcare professionals to improve their communication skills and to encourage them to better acknowledge that people have unique preferences, goals, priorities, and fears when it comes to care at the end of life. Both of these should be taught in the hospital setting, and opportunities for collaboration should be sought with other specialty groups to give weight to the importance of the topic in the eyes of the learners and the organization. Collaborating on teaching also spreads the load which is important for small services with stretched resources.

There is a very high turnover of clinical staff in acute hospitals, not limited to just doctors and nurses, so keeping everyone familiar with the place of palliative care, the role of the service, the availability of resources, and opportunities for education needs to be constantly refreshed. Part of the challenge is to empower staff without de-skilling them. This requires resisting the temptation to do everything ourselves!

New Zealand is an increasingly multicultural society with significant numbers of the registered and unregistered workforce having trained overseas. English may also not be their first language. This may lead to cultural, clinical, and ethical challenges regarding care at the end of life that require targeted education and support.

4.7 Guideline and Pathway Development

Throughout the world, various palliative care guidelines have been developed (e.g., NICE Guidelines in the NHS (https://www.nice.org.uk/guidance/qs13)) to assist in one of the most important purposes of palliative care – the education and support of healthcare professionals. Developing guidelines based on best practice and research is challenging with the relative paucity of robust studies in palliative care. The Christchurch Hospital Palliative Care Guidelines were developed approximately 15 years ago. They were initially only available for hospital-based staff on the intranet, but in more recent times, they have been refined and made available to all health professionals on the CDHB Internet site (http://cdhb.palliativecare.org.nz/). They have been widely accessed and referenced by individuals and services both across NZ and internationally.

Another platform for improving access to localized and relevant information has been HealthPathways (https://www.healthpathwayscommunity.org/About.aspx). In the CDHB there

1. Baseline assessment

A health practitioner undertakes a baseline assessment when they think a person may be entering their last days for life. This change in condition acts as a prompt to ensure conversations occur with the person and with their family/whānau.

If a person in their last days of life has a level of need that exceeds the resources of the primary palliative care provider, that provider should refer them to specialist palliative care.

Table 1: Baseline assessment summary

Te taha tinana: *Physical health*	
1.1	Recognition the person is dying or is approaching the last days of life
1.2	Identification of the lead health practitioner
1.3	Assessment of physical needs
1.4	Review of current management and initiation of prescribing of anticipatory medication
1.7	The person's awareness of their changing condition
1.11	Provision of food and fluids
1.12	Availability of equipment to support the person's care needs
1.13	Consideration of cardiac devices
1.14	Advice to relevant agencies of the person's deterioration
Te taha hinengaro: *Mental health*	
1.5	Assessment of the person's preferences for care
Te taha whānau: *Extended family health*	
1.6	Identification of communication barriers
1.8	The family/whānau's awareness of the person's changing condition
1.9	Discussion of cultural needs
1.15	Provision of information to the family/whānau about support and facilities
Te taha wairua: *Spiritual health*	
1.10	Provision of opportunity for the person and family/whānau to discuss what is important to them

Fig. 3 Baseline assessment at last days of life

is a version for general practice teams and community care and another version for the hospital. HealthPathways have been adopted in many other areas in New Zealand and localized as needed but based on the same principle of a shared platform of information across all settings of care.

A number of location-specific pathways have been developed by the palliative care team. The most notable ones are in the emergency department and the intensive care unit. Both of these areas are highly experienced at dealing with serious life-threatening illness and death but wanted to appreciate and understand the nature and benefits of palliative care in order to improve their services and ensure that transfers were safer and more in line with ward- or community-based care. It has been a mutually beneficial process and is an ongoing work in progress.

New Zealand has also recently released Te Ara Whakapiri: principles and guidance for care at the end of life and the Te Ara Whakapiri Toolkit (April 2017) (Ministry of Health 2017c). The two documents are suitable for all healthcare settings, including acute care, and a process of implementation is currently underway. The program was developed in response to the withdrawal of the Liverpool Care Pathway for the Dying Patient in 2015. The following graphic is taken from the section of the guidance that covers the baseline assessment that is conducted on all people identified as dying, regardless of their location. Te Reo Maori, the language of New Zealand's indigenous peoples, is used throughout the document as a recognition of the need for culurally appropriate care at the end of life.

4.8 Liaison with Community Services

A key aspect of providing seamless palliative care is being able to transfer patients to community-based services upon discharge from hospital. This requires knowledge of what they can provide and

their level of expertise. It also requires close links with specialist palliative care service(s). This interface is improved if there is good sharing of electronic patient data to ensure all information is accurate and up to date and shared in a timely fashion. Ideally this should be inclusive of patients in their own homes, those residents in aged residential care facilities (care homes) as well as any other locations such as supported care homes for those with intellectual disability, and those in prisons or other facilities.

Effective liaison also requires a relationship of trust so that when setting up discharge arrangements from hospital, there is confidence in what follow-up services will be there to for each patient and family. This may be as simple as ascertaining whether the patient can be seen promptly by the community palliative care team and/or district nurse. Hospital teams can act as a "bridge" with the community, and fully understanding the capacity and capability of the local providers is essential to avoid inflated expectations.

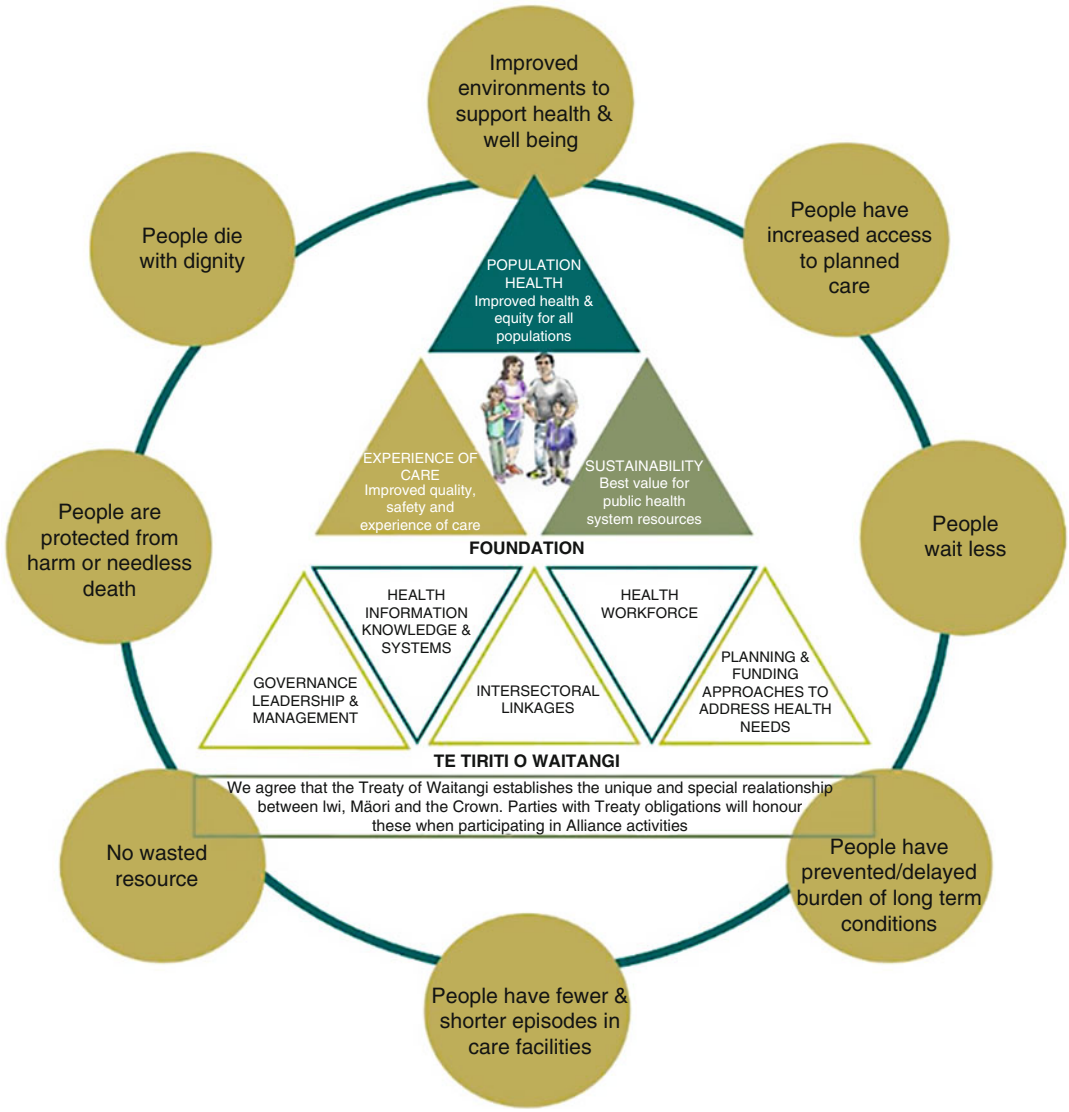

Fig. 4 Best for people, best for system outcomes framework https://www.sialliance.health.nz/system-outcomes-framework-graphic/

Sometimes patients cope better than expected, and sometimes they need to fail in order to understand the extent of their limitations. All of these issues need to be communicated effectively with our community colleagues.

It is imperative in the New Zealand system that the general practice team (also known as the primary healthcare team) is considered at all times. Having a general practitioner (GP) who is supportive is critical to the functioning of the primary palliative care team as the model of care. This is because specialist palliative care in the community is contingent on a collaborative GP relationship.

Models of community care and the organization of palliative care services will vary from country to country and within regions. As part of the model of care in Canterbury, the DHB has an agreement between the hospital and the community (Nurse Maude (https://www.nursemaude.org.nz/)) to work as a single specialist unit – *Canterbury Integrated Palliative Care Services*. Even though the two arms are funded separately, the vision, planning, and operational goals are aligned to eliminate gaps and waste and to enhance the consumer and health professional experience.

Even within a small country such as New Zealand, models of care vary; however, organizations such as the South Island Alliance (SIA) are promoting a more uniform approach. The SIA is funded and supported by the five South Island DHBs which has enabled the region to work collaboratively to develop more innovative and efficient health services than could be achieved independently. The SIA has been a driving factor in improving access, quality, and service development in a wide range of clinical areas.

In order to ensure a connected community of care, access to real-time information such as current medications, results, specialist assessments and letters, acute care plans, advance care plans, goals of care documents, etc. is becoming a universal expectation internationally. Making this happen with diverse IT systems, privacy concerns, and IT logistics is a significant barrier to providing comprehensive integrated palliative care. Improving IT systems and software programs are bridging these gaps; however, having information accessible to all the relevant health professionals in real time is proving to be an ongoing challenge. The SIA is helping spearhead IT integration across the South Island within the limitations of the systems available. Change can be difficult for staff, but benefits are steadily being realized.

4.9 Information Technology

As mentioned above, data sharing and transfer of patient information across healthcare settings is of paramount importance and is an increasingly complex endeavor. Hospital palliative care teams can usually access all the same information as colleagues from other areas within the acute environment, but this does not always translate to the same access for specialist doctors, nurses, and allied health staff working in community settings. This inevitably leads to delays, errors, and frustrations. Working collaboratively with IT services is essential in ensuring that the care of dying patients is seen as just as important as those being treated actively.

In 2013, the Health Information Standards Organisation in NZ developed a suite of national data definitions for specialist palliative care (Health Information Standards Organisation 2013a, b). These have helped drive consistency in hospice services, but as yet there have been no resources available to standardize, measure, and report on activity, demographics, and trends in hospital practice. This issue has been much more proactively addressed in other countries but will not be reported here.

An important way of maximizing productivity for small services is to invest in IT innovations such as Telehealth (videoconferencing). This has been a very successful vehicle in the CDHB especially for rural consultations, for complex case meetings which are conducted regionally, and for staff support.

4.10 Building and Sustaining the Team

New Zealand as well as most other countries has a shortage of skilled palliative care medical

and nursing staff let alone allied health staff. "Growing your own" where possible appears to be the best option available. As mentioned earlier, the RACP has a training program to specialist and diploma level, and these are well utilized. Many New Zealand hospitals are accredited for palliative medicine training, but the number of funded positions is insufficient to meet current and future needs. This issue will no doubt be familiar internationally. In regard to nursing staff, a trust fund is available in New Zealand for two placements per year where a registered nurse can train in palliative care for a 2-year period. Working in the hospital setting is part of the training program, but places and funding are limited, and efforts to improve the situation have not yet been forthcoming.

The recruitment of a "team" is dependent on many factors not least the availability of skilled personnel with appropriate qualifications and experience. Growing the specialty within nursing and succession planning for services is an ongoing challenge. More creative ways to upskill registered nurses in palliative care are required. Working in hospitals is different to hospices, and although many of the necessary skills can be gleaned in hospice or community care, the swift-moving and highly pressured environment in acute care can make it hard for nurses in particular to feel that their input is having any influence.

Leadership in the team is also important to consider and foster. One of the benefits of having a flat structure within hospital teams is being able to share leadership responsibilities, to cover personnel when others are away, and to take collective responsibility for accepting challenging cases. Leadership in any team sets the direction, philosophy, and culture of the service, but the entire team must "share the vision."

Formal orientation to a new position within a hospital team is critical, with clear directions and guidance as to how referrals are managed, how workload is contained, how to seek help, and how to keep skills and knowledge current. Even small teams need orientation packs for new or visiting team members. Teams develop very intricate patterns of behavior that can be mystifying to the outsider; therefore, writing down what your team does helps new personnel to integrate more smoothly and operate effectively.

Maintaining a team in the acute hospital environment requires close professional working relationships and high levels of trust in each other's work as well as the checks and balances of paper ward rounds, patient review meetings, audits, and ongoing research projects. It also requires each individual team member to take responsibility for the emotional, psychological, and spiritual demands inherent in a busy hospital palliative care practice. Reflective professional supervision should be encouraged and funded (as is the case in the CDHB) as well as informal debriefing among the team members as needed. It is a forum where the complexities of the interpersonal interactions that underpin the provision of healthcare can be explored in a supportive and confidential setting (https://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2016/vol-129-no-1434-6-may-2016/6884). Regular team business meetings can also be helpful and occasional team-building activities. These are essential to create sustainability.

Ideally team members should be supported to utilize their individual strengths and strong enough to tolerate their differences. This is particularly challenging at times of growth and when managing change such as a new manager or leader.

There is no doubt that small teams can fall into the trap of spreading themselves too thinly. An example of this might include the common request for a palliative care physician to be present at every cancer MDM. There are more than 12 individual meetings in the CDHB, each lasting at least an hour and run sometimes every week. Meeting this request is impossible, and each case must be looked at individually to maximize the resource.

Small teams are very vulnerable – both in regard to the myriad of unrealistic expectations placed on them by others but also to the teams' own internal dynamics. Palliative care attracts health professionals with a strong vocation and a desire to venture where others are unable or unwilling to tread, and this can make team members overly sensitive to a fear of failure to meet their own high standards.

It is important to foster relationships with management that are attuned to these pressures, expectations, and dynamics so that they can empower and support hospital teams to develop and thrive, despite the pressure placed upon them. This can make the difference between a team that is able to adapt and change successfully and one that is only able to "tread water" and survive.

5 Raising the Profile and Promoting Culture Change

Having a clear and visible profile within the hospital requires individual commitment and managerial support. Some examples of how this might be achieved include making and taking the opportunity to present at departmental meetings and hospital grand rounds, contributing to hospital newsletters, developing policies and pathways, and participating in strategic projects and hospital-wide meetings. The function of hospital palliative care is not only to provide excellent clinical advice and support but also to be politically astute and active. Being seen to be involved in the workings of the wider hospital system is critically important.

Hospital palliative care teams, when working well, influence and change the culture within the organization around care of the dying. They legitimize dying as being "OK" even within a curative model, and they allow other health professionals to ask for help in both an end-of-life situation and to assist in managing difficult symptom management and complex social needs. They also advocate for patients especially those who are vulnerable. Hospital palliative care teams promote a way of thinking that turns around the notion prevalent in acute care of "what can we do to the patient" to "what is best for the person." Having a palliative care presence in hospitals challenges a model of care that may no longer be appropriate.

There are many examples of patients having more than one team or multiple teams involved in their care and no one team taking the lead. The patient who is left languishing without any direction or plan lost in the complex world of acute hospital care. These are the situations in which patients or family members feel they have little choice other than to lodge complaints against "the system." Added to these are the environmental factors of acute care hospitals. Due to pragmatism and cost, multi-bedded rooms with few, if any, alternative spaces make it extremely difficult for any personal or reflection time let alone private conversations with family members or other healthcare professionals. Discussing spiritual care or fears around dying is extremely challenging in the acute care environment for patients, family, chaplains, pastoral care, and palliative care team members. Therefore, hospital palliative care teams need to use their position within the healthcare system to advocate for patients and to influence change.

6 Palliative Care and Hospital Costs

Despite the fact that death and dying are ubiquitous in hospitals, acceptance of the value of a palliative care presence is far from universal. This may be, in part, due to the reticence of hospices to venture into the acute environment, wishing to preserve the identity and separateness of the hospice philosophy of care. It may also be due to an assumed lack of evidence that they are of benefit. This, however, is not actually the case. Palliative care teams have been shown to improve quality of life for patients with advanced cancer and in a recent study to extend survival (Temel et al. 2010). "Furthermore, palliative care programs can reduce hospital costs by ameliorating pain and other distressing symptoms that increase hospital lengths of stay and cause medical complications; can reduce overuse of unnecessary, ineffective or marginally effective services; and can develop transition plans that result in safe hospital discharges with lower likelihood of readmission" (Morrison et al. 2011).

Cost savings attributable to palliative care services in hospitals have been extensively reported in international studies (Kelly and Morrison 2015; Morrison et al. 2008; Simoens et al. 2010). The paper by Ireland in 2017 examined access to palliative care services during a terminal hospital

admission and concluded that intervention rates and hospital costs were reduced. Involvement from palliative care was associated with significantly lower hospital costs in the order of $5000–8000 (Australian dollars) for all patient groups, but most particularly for those with non-cancer diagnoses. Shorter terminal episodes and greater palliative care-related cost reductions have been identified for patients with diagnoses other than cancer. The paper states that the total costs of these episodes were reduced by 28% for cancer patients and 36% for other patients with much lower rates of ICU admissions and operative procedures being the chief drivers of cost reductions. A prospective multisite cohort study published in 2017 noted that reduced length of stay is the biggest driver of cost saving from early consultation for patients with advanced cancer. Patient- and family-centered discussions on goals of care and transition planning initiated by palliative care consultation teams were felt to be at least as important in driving cost savings as the reduction of unnecessary test and pharmaceuticals identified in other studies (May et al. 2017).

It is worthy to include a note of caution when extrapolating such specific findings to individual situations. "Funding models are a very important consideration and they need to be well understood to ensure best practice and minimise perverse incentives. Before we can conduct cross-national comparisons of costs and impact of palliative care, we need to understand the funding and policy context for palliative care in each country of interest" (Groeneveld et al. 2017).

7 Integrated Palliative Care

Integration is required to ensure that palliative care is available and effective for all who need it. This needs to occur across all settings of care and is dependent on collaboration, trust, respect, and mutual support.

A definition of integration is included in a recent systematic review in Europe. "Integrated palliative care involves bringing together administrative, organisational, clinical and service aspects in order to realise continuity of care between all factors involved in the care network of patients receiving palliative care. It aims to achieve quality of life and a well-supported dying process for the patient and the family in collaboration with all the caregivers, paid and unpaid" (Garralda et al. 2016).

The recommendations from this project are well worth reflecting on, and they address the issue from three levels.

At a policy (macro) level, the focus is on:

1. National policy development
2. Earmarked funding
3. Measurable outcomes
4. Public engagement

At an organizational (meso) level, the following requirements are emphasized:

1. Identify gaps (often communication).
2. Include the multidisciplinary team.
3. Ensure seamless working across systems.
4. Acknowledge that **one size does not fit all.**
5. Promote formal structures specifically targeting integrated care.

At an individual patient/family (micro) level, the report also emphasizes the following;

1. Personalized communication to enable patients to express their preferences for their care, e.g., via formal advance care planning
2. Identification of patients before crises occur, e.g., goals of care
3. Involvement of family/whānau
4. Integration of care across agencies
5. Established communication systems

Many of these points resonate with work that has been occurring in New Zealand, but there is still a long way to go. The work of agencies such as the Health Quality and Safety Commission (https://www.hqsc.govt.nz/our-programmes/patient-deterioration/), the Advance Care Planning Cooperative (http://www.advancecareplanning.org.nz/), the Canterbury Initiative (http://www.canterburyinitiative.org.nz/) (including

HealthInfo and HealthPathways), and the South Island Alliance (https://www.sialliance.health.nz/UserFiles/SouthIslandAlliance/Image/Outcomes%20Framework_020715.jpg) are helping palliative care organizations with promoting integrated care at the end of life and service development.

8 Conclusion

An important indicator of how effectively a health system is operating is how well it cares for the most vulnerable members of society. The dying are extremely vulnerable, and it is pleasing to see that New Zealand features highly in a global context with a ranking of third in the 2010 report by the Economist Intelligence Unit (http://graphics.eiu.com/upload/eb/qualityofdeath.pdf). Despite this, coverage and integration are incomplete, and hospitals remain a major area for improvement.

Within Christchurch Hospital, in addition to medical and nursing partners, it has been beneficial to identify champions in areas such as pharmacy, social work, occupational therapy, acute pain management, counseling, and mental health. These have helped to support the wider interdisciplinary team with their care of routine and complex cases, and collectively they serve to raise the bar in regard to interdisciplinary team commitment to quality palliative and end-of-life care. This is part of creating a shared vision for care of the dying across the whole health system.

Back in 1994, it was recognized that having "palliative care in a hospital. . ..is an issue of justice and equity, and gives structure to compassion" (Lickiss et al. 1994). As indicated throughout this chapter, more recent studies have validated this over and over, providing a clear and welcome message for providers, commissioners, and funders of health services. It is summarized very eloquently in this final paper. "In the intense pressure for health services to do things differently and more cost effectively, specialist palliative care teams may have a central role in delivering better care and outcomes while reducing acute care use in last weeks of life, and should be resourced and commissioned to do so" (Murtagh 2014).

Given the aging population and the ongoing expectation that hospitals will remain central to the delivery of care at the end of life, hospital palliative care must not be forgotten. The relatively poor profile of palliative care in acute settings and in society in general, the observation that high proportions of nonmalignant patients are only being recognized as dying in the final stages, and the vulnerability of small teams are just some of the challenges that need to be faced. Palliative care is not an optional extra. Targeted effort is required to drive improvements in outcomes for patients and families and to ensure that **all** health professions are equipped to look after palliative patients in their care.

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Palliative Care in the Intensive Care Unit (ICU)

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Rebecca A. Aslakson and J. Randall Curtis

Contents

Abstract

Palliative care is a medical specialty and philosophy of care that focuses on reducing suffering among patients with serious illness and their family members, regardless of disease diagnosis or prognosis. As critical illness is often life-threatening and confers significant disease-related symptom burdens, palliative care and palliative care specialists can aid in identifying goals of care, reducing symptom burden, and improving quality of life among intensive care unit (ICU) patients and their

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_51

family members. Palliative care in the ICU can be delivered by the ICU team itself, specialist-trained palliative care consultants, or a combination of both. Though initial reports describing end-of-life care practices in the ICU were published in 1976, the modern era of palliative care research in the ICU began in the early 2000s. Since 2010, the Improving Palliative Care in the ICU (IPAL-ICU) Advisory Board has published a series of articles exploring opportunities and barriers to palliative care delivery in the ICU, particularly across different ICU types, ICU providers, and ICU patient populations. Furthermore, initiatives to improve delivery of "family-centered care" in the ICU frequently also correlate with palliative care practices. To date, over 40 palliative care and palliative care-related interventions targeting ICU patients and families have been trialed and published with results showing mixed effectiveness on outcomes such as ICU length of stay, patient and family symptoms, and family member satisfaction; several randomized trials provide important insights into interventions that improve patient and family outcomes as well as those that do not.

1 Introduction

The chapter aim is to discuss the history, delivery models, evidence base, opportunities for, and barriers to palliative care delivery in the intensive care unit.

Critically ill patients often require the most sophisticated technological treatments that modern medicine can offer and are at significant risk of death during or after the intensive care unit (ICU). In addition, ICU patients are at risk for significant morbidity with physical and psychological suffering that can occur both during and after ICU care (Angus et al. 2004; Teno et al. 2013; Wunsch et al. 2010; Cox et al. 2007, 2009; Choi et al. 2014; Puntillo et al. 2010; Herridge et al. 2011; Dowdy et al. 2005; Iwashyna et al. 2010; Davydow et al. 2008, 2009; Nelson et al. 2006a; Needham et al. 2012). Family members and caregivers of ICU patients are also at risk of increased morbidity, especially psychological morbidity (Needham et al. 2012; de Miranda et al. 2011; Swoboda and Lipsett 2002; Van Pelt et al. 2007; Anderson et al. 2008; Siegel et al. 2008; Cameron et al. 2016). The ICU is also a frequent place of patient death, often following a decision to withhold or withdraw life-sustaining treatments when those treatments no longer meet the patient's goals of care as identified by the patient, family member, and/or clinicians (Angus et al. 2004; Teno et al. 2013; Prendergast and Luce 1997). Finally, due to the burdens of critical illness, many ICU patients are unable to make medical decisions (Nelson et al. 2006a; Prendergast and Luce 1997; Silveira et al. 2010). Consequently, family members, caregivers, or other surrogate decision-makers must often work with the ICU team to make complicated, nuanced decisions that ideally attempt to balance a patient's previously expressed wishes with an evolving and often repetitive and cumulative barrage of critical illness-related insults to patient mortality, morbidity, and short- and long-term quality of life (Schenker et al. 2013; Scheunemann et al. 2015; White et al. 2007, 2012; White and Curtis 2006; Zier et al. 2012; Nelson et al. 2017). As critical illness confers significant disease-related symptom burdens, complex values-based decision-making and surrogate decision-making, and nontrivial risk of death, palliative care provided by ICU clinicians and palliative care specialists can aid in reducing symptom burden, facilitating decision-making, and improving quality of life among ICU patients and their family members (Kelley and Morrison 2015; Aslakson et al. 2014a).

2 Recent History of Palliative Care and Ethical Controversies in the ICU

By the late 1960s, the advent of life-supporting technologies – particularly ventilators – and the recognition of a survival benefit conferred through close physiological monitoring and intense nursing for critically ill patients led to the inception of ICUs (Luce 2010). ICUs rapidly

became not only a physical care location but also a nexus for a progressively multidisciplinary team with expertise in selection and delivery of the complex treatments required to optimize patient survival despite severe, life-threatening illness. Indeed, the ICU with its combination of cutting-edge technologies and specialized care teams enabled patient survival through many previously fatal medical conditions. Yet, since inception, ICUs inherently illuminate the boundaries of modern medical care and consequently compel patients, family members, clinicians, and the medical community as a whole to confront and debate if and when aggressive medical treatments are personally, pragmatically, and ethically acceptable.

The advent of ICUs and ICU care has spurred multiple decisional, ethical, and legal conundrums, often involving palliative and end-of-life care-related issues and frequently surrounding the withdrawal or withholding of medical technologies (Luce 2010). By the mid-1960s, ethicists and ICU clinicians began to question the value of sustaining a patient's physiologic life when that patient had sustained a severe, irreversible neurologic insult; by 1968, the Harvard Commission published criteria for brain death and from those criteria evolved treatment pathways for when and how brain dead patients could or should be separated from physiologically supportive technologies, such as ventilators (School, A.H.C.o.t.H.M. 1968). By 1976, a prominent *New England Journal of Medicine* article acknowledged that ICUs are a frequent place of patient death and that ICU clinicians "promulgate and discuss publicly explicit policies about the deliberate withdrawal or non-application of life-prolonging measures" and that it is an "open secret" that "such measures are in fact regularly withheld or withdrawn" (Fried 1976; Optimum care for hopelessly ill patients, 1976). From the 1970s through the early 2000s, life-supporting technologies inherent to the ICU also instigated a series of legal cases in the United States to explore and define whether and when life-supportive technologies could be withdrawn or withheld; the legal cases involving the care of Karen Quinlan and Nancy Cruzan underlie modern ICU practices about if and when life-sustaining treatments can be withheld or withdrawn based on a patient's previously expressed wishes (In re Quinlan 1976; Cruzan v. Director, Missouri Department of Health 1990). Even in modern critical care practice, ethical, legal, and professional debates continue about what ICU-based technologies – such as extracorporeal membranous oxygenation (ECMO) – constitute the boundary of acceptable medical care and in what circumstances those technologies could or should be deployed (Fan et al. 2016).

There has been important regional variation in how decisions have been made regarding withholding and withdrawing life support. For example, a study across Europe conducted in the early 2000s found that much higher proportion of deaths were preceded by withdrawing life support in Northern Europe compared to Southern Europe, while withholding life support was more common in Southern Europe (Sprung et al. 2003). Withdrawal of life support is also less common in many countries in Asia, Africa, and South America. Some of these differences are undoubtedly driven by religious influences (Sprung et al. 2007). However, it is important to note that there is also considerable variability within countries or even among physicians in a single ICU suggesting that lack of consensus and limited education play an important role in this variability (Mark et al. 2015). A recent study suggests that differences are decreasing across Europe, which may be the result of increased consensus and education.

Given these tensions surrounding if and when medical technologies are medically feasible, ethically acceptable, and pragmatically likely to facilitate patient and family medical goals, it is not surprising that early palliative and end-of-life care-related interventions and trials have involved ICUs and ICU patients, family members, and clinicians (Aslakson et al. 2014b). By the late 1980s, a hospital in the state of Michigan in the United States began to evaluate whether a "comprehensive supportive team" for "hopelessly ill" ICU patients, primarily those with hypoxic encephalopathy and advanced dementia, could improve the quality of care and end-of-life care through focused provision of physical comfort,

psychosocial support, and family support (Field et al. 1989; Carlson et al. 1988). Through the early to mid-1990s, further ICU-based, palliative care-related interventions, often led by nurses, trialed whether enhanced communication strategies – informational booklets, daily phone calls to family members, and/or goal-related communication between ICU clinicians and family members – could improve family member-related outcomes such as satisfaction, anxiety, and/or informational awareness. By the late 1990s and early 2000s, the modern era and definitions of palliative care and palliative care practices commenced and consequently spurred a cohort of trials attempting to integrate palliative care principles, and sometimes palliative care specialists providers, into routine ICU care.

3 Defining Palliative Care in the ICU for the Coming Decade

Palliative care is a rapidly growing interprofessional specialty as well as an approach to care by all clinicians who care for patients with serious illness. The key domains of palliative care in the adult ICU, which have been defined by patients and families (Nelson et al. 2010a) as well as by expert consensus (National Consensus Project for Quality Palliative Care 2013; Clarke et al. 2003), include effective management of distress from physical, psychological, and spiritual symptoms; timely and sensitive communication about appropriate goals of intensive care in relation to the patient's condition, prognosis, and values; alignment of treatment with patient values; attention to families' needs and concerns; planning for care transitions; and support for clinicians. Palliative care is often optimally provided together with life-prolonging care, a coordinated approach that has been supported by major societies representing critical care professionals (Lanken et al. 2008; Selecky et al. 2005; Truog et al. 2008; Carlet et al. 2004; Cox et al. 2007, 2009; Choi et al. 2014; Puntillo et al. 2010) and by the World Health Organization (2018) and that is embraced by patients and families (Nelson et al. 2010a). Therefore, palliative care is not a mutually exclusive alternative, nor simply a sequel to failed attempts at life-prolonging care, but rather an integral component of comprehensive care for critically ill patients from the time of ICU admission.

4 Delivery Models of Palliative Care

Palliative care can be in many different clinical settings and can be provided by the following (Nelson et al. 2010b; Quill and Abernethy 2013; Committee on Approaching Death: Addressing Key End of Life Issues; Institute of Medicine 2015):

- Frontline, nonspecialist providers (termed primary or generalist palliative care)
- A specialist, interdisciplinary team with advanced training and skills in symptom management and communication about goals of care, prognosis, and treatment options (termed specialty or consultative palliative care)
- Some combination of both (termed mixed)

This conceptualization is particularly relevant for delivery of palliative care in the ICU (Fig. 1). The ICU team itself is inherently interdisciplinary

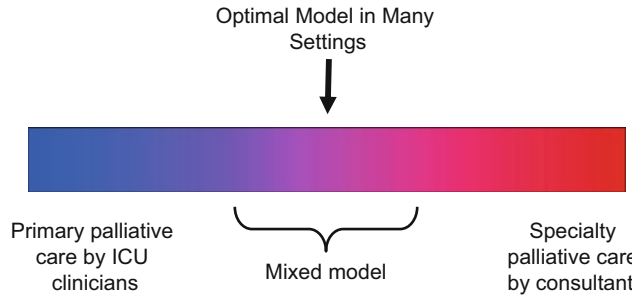

Fig. 1 Conceptualization of palliative care delivery model spectrum – optimal model is based on availability of specialty palliative care and on ICU primary palliative care expertise

and often includes doctors, nurses, social workers, chaplains, respiratory therapists, and pharmacists who are trained and specially skilled to address the unique needs of critically ill patients and their families (Nelson et al. 2010b). In mixed palliative care in the ICU, the primary palliative care provided by this ICU team is further supplemented by care provided by the specialty palliative care interdisciplinary team (Nelson et al. 2010b).

Core elements of palliative care, such as basic symptom management and discussion of goals of care in relation to the patient's prognosis and preferences, should be part of routine critical care practice and within the competency of all ICU clinicians. However, sometimes the optimal care of a critically ill patient may call for more advanced palliative care skills and specialist expert input. Goal setting with a family experiencing unusual distress or internal conflict, symptom management for patients with refractory symptomatology, supporting a bereaved family, or providing continuity of care after the patient is discharged from the ICU are examples of clinical challenges for which a critical care clinician may wish to obtain expert consultation from a palliative care specialist team (Quill and Abernethy 2013). In addition, sometimes a palliative care specialist can serve as a "third party" to help mediate conflict between the ICU team and the patient or family.

After more than a decade of rapid expansion, expert palliative care through a palliative care consultation is now available at the majority of US hospitals, although smaller and/or for-profit hospitals are less likely to have palliative care consult services. Availability of hospital-based palliative care consult services is much more variable in Europe, Asia, and South America although developing in many areas, and where they are developed, they often have less interaction with the ICU than in the United States. Specialty palliative care services have often developed from within oncology, geriatrics, or primary care and may consequently have less experience and integration in the ICU setting. However, as interest in improving palliative care in the ICU increases, this setting can offer an opportunity for palliative care specialists to increase their presence, both in supporting better primary palliative care through ICU clinician education and provision of supportive tools and also in providing specialty palliative care consultation for patients and family members with unmet palliative needs after primary palliative care.

Workforce shortages for palliative care specialists may limit availability of palliative care consultations, at least in the near term (Goldsmith et al. 2008). In addition, excessive reliance on specialty palliative care could fragment care, potentially complicate therapeutic relationships between patients and ICU care clinicians, as well as diminish impetus for ICU clinicians to cultivate and maintain primary palliative care skills (Accreditation Council for Graduate Medical Education 2018). Indeed, a key issue for palliative care in the ICU is to determine how best to utilize existing specialist palliative care resources as well as how to optimally integrate those resources into existing primary palliative care practices and pathways.

Previous palliative care trials in the ICU have frequently used triggers to identify which patients should receive specialist palliative care (Aslakson et al. 2014b). In past trials, triggers have included both diagnoses, such as hypoxic encephalopathy, multiple organ failure for multiple days, or advanced dementia, as well as non-specific assessments such as ICU clinician belief that a patient is "likely to die" and/or intra-ICU team conflicts regarding a patient's likely survival and/or quality of life following critical illness. Ultimately, the provision of primary versus specialist palliative care should be fluid over time, unique to each ICU, and based on multiple factors including unit culture toward palliative and end-of-life care, ICU clinician primary palliative care competence and capacity, the availability of palliative care specialist resources, ICU patient and family desire for specialist palliative care, and/or systematic triggers or goals championed by ICU and/or hospital clinicians and leadership.

When specialty palliative care clinicians are interested in increasing their impact in the ICU setting, either through supporting primary palliative care or providing specialty palliative care consultation, it is very important that the

palliative care clinicians become familiar with the functioning and culture of the ICU. In our experience, two key barriers to effective palliative care consultation in the ICU setting include ICU clinician suspicion that palliative care clinicians will advance an agenda of withholding or withdrawing life support and belief among some ICU clinicians that they already provide high-quality primary palliative care. Understanding such barriers is essential to overcoming them. For example, in the ICU where ICU clinicians are suspicious of the agenda of palliative care clinicians, reassuring ICU clinicians about the lack of such an agenda is essential. However, in the ICU where ICU clinicians believe they provide high-quality primary palliative care, the key to overcoming this barrier is to highlight areas of palliative care that the ICU clinicians are less focused on, such as anticipatory bereavement support and supporting palliative care needs after ICU discharge.

5 Palliative Care Needs Both Within and After the ICU

In this chapter, we focus on studies conducted in adult ICUs in North America and Europe, where existing data demonstrate important opportunities to improve all core components of palliative care in the ICU. For example, multiple studies confirm that symptom distress is prevalent at high levels of severity among critically ill patients (Puntillo et al. 2010, 2014; Puntillo 1990). Communication between clinicians and families is often delayed and fragmented (White et al. 2007; Azoulay et al. 2000; McDonagh et al. 2004). When families meet with ICU physicians, they frequently have insufficient time to share their perspectives on the patient's goals and values or express their own concerns (McDonagh et al. 2004). ICU physicians may miss opportunities for empathic response to emotions, leaving families too distressed to absorb or integrate information they need for surrogate decision-making (Curtis et al. 2005; Selph et al. 2008). Some patients spend their last days in the ICU because planning for care in a more suitable or preferred setting is inadequate. In addition, transitions from one setting to another (e.g., acute care, critical care, long-term care, and home care) are increasingly frequent but often without adequate support for patients and families (Teno et al. 2013). Among those who require prolonged mechanical ventilation, data show that during the year following ICU discharge, patients will make multiple transitions across a variety of facilities, spending an average of 74% of all days in a hospital or post-acute care facility or dependent on a high level of home healthcare (Unroe et al. 2010). Finally, the need to support ICU clinicians more effectively for the emotional strain of ICU practice is evident from the widespread problems of burnout, depression, moral distress, and conflict across disciplines on the critical care team (Azoulay et al. 2009; Studdert et al. 2003a, b; Breen et al. 2001).

The burden of critical illness for patients and family members continues after the ICU. Decreases in hospital mortality from critical illnesses, such as sepsis, acute respiratory distress syndrome (ARDS), and major cardiac or neurologic events, have not diminished the relevance of palliative care in the ICU but rather underscored the importance of anticipating and attending to the palliative care needs of those who survive intensive care as well as those who succumb. As ICU survivors increase in number and investigators examine the experience of these patients and their families more fully, the burdens of survivorship are coming into clearer view (Needham et al. 2012). A broad array of physical and psychological symptoms along with impairments of function and cognition continue to impair the quality of patients' lives (Cox et al. 2009; Choi et al. 2014; Herridge et al. 2003, 2011; Iwashyna et al. 2010; Davydow et al. 2008, 2009; Adhikari et al. 2011; Dowdy et al. 2006; Pandharipande et al. 2013; Boyle et al. 2004). During the 1st year after ICU discharge, ARDS survivors commonly report debilitating insomnia, fatigue, and pain along with emotional lability, depression, and anxiety (Cox et al. 2009). In addition to ongoing functional limitations and decrements in physical quality of life, these survivors have psychological sequelae for as long as 5 years (Herridge et al. 2011). A systematic review of depression in general ICU survivors found that the median point

prevalence of clinically significant depressive symptoms within 14 months of ICU discharge was 28%, and depression in the early post-ICU period predicted longer-term depressive symptoms (Davydow et al. 2009). ICU survivors also struggle with chronic pain that is associated with decrements in health-related quality of life (Boyle et al. 2004). New and clinically significant cognitive impairment follows critical illness for a broad range of survivors (Pandharipande et al. 2013). Some ICU patients surviving acute critical illness remain critically ill on a chronic basis, with protracted or permanent dependence on mechanical ventilation and other intensive care therapies (Nelson et al. 2010c). For this "chronically critically ill" patient group, symptom burden is heavy, functional and cognitive outcomes are very poor, and 1-year mortality is over 50%, exceeding that for many malignancies (Nelson et al. 2004, 2006a; Jubran et al. 2010). Families struggle with their own symptoms and with strains of caregiving (Cox et al. 2009; Needham et al. 2012; de Miranda et al. 2011; Swoboda and Lipsett 2002; Van Pelt et al. 2007; Choi et al. 2011; Pochard et al. 2005). Among family members of critically ill patients, anxiety and depression are common and may persist long after the ICU, along with post-traumatic stress disorder and complicated grief (Anderson et al. 2008; Siegel et al. 2008; Pochard et al. 2005). Thus, a distinctive "postintensive care syndrome" is now recognized not only in patients but also in families (Needham et al. 2012). Effective integration of palliative care during the treatment of acute and chronic critical illness may help patients and families prepare more fully for challenges to come in the days, months, and years after discharge from intensive care.

In addition, the use of intensive care for patients approaching the end of life continues. Approximately one in five deaths in the United States occurs during or shortly after intensive care, with more deaths occurring in the ICU than in any other setting in the hospital (Angus et al. 2004). In the United States, patients over age 65 with severe chronic illness are less likely to die in the hospital and more likely to receive hospice care than they were a decade ago, but ICU treatment during the last month of life has concurrently increased (Teno et al. 2013; Goodman et al. 2011). For patients over age 65 receiving ICU treatment, particularly among those who are mechanically ventilated, the risk of death within 3 years of discharge is nearly three times that of matched controls in the general population (Wunsch et al. 2010). These trends are likely to continue as aggressive medical and surgical treatments are offered to a growing population of older adults with multiple comorbid conditions. For now and the foreseeable future, palliative care will thus remain an essential element of critical care practice, both during and after ICU admission.

6 The Modern Era of Palliative Care in the ICU: Evaluating the Evidence Base

Data for this chapter were drawn from systematic and comprehensive narrative reviews as well as a recent research agenda on palliative care in the ICU (Aslakson et al. 2014a, b, 2017; Khandelwal et al. 2015; Scheunemann et al. 2011). Interventions can be grouped into broad domains based on the intervention target – ICU patient, family members, ICU clinician team, system, and/or multilevel (Table 1) – although some interventions are "bundled" with multiple targets. Interventions can also be organized based on content and goals. It is important for palliative care specialists interested in supporting patients and families in the ICU to understand this evidence base for both primary and specialty palliative care in the ICU.

Structured approaches to communication. Interventional research to date has focused mainly on testing proactive, structured approaches to clinician communication with families, implemented either by the interdisciplinary ICU team or by consultants specializing in palliative care or biomedical ethics (Aslakson et al. 2014b; Curtis et al. 2016; Andereck et al. 2014; Carson et al. 2016). This research has been summarized in several comprehensive reviews (Aslakson et al. 2014b; Khandelwal et al. 2015; Scheunemann et al. 2011). Most studies were conducted in a single center using a pre-post design. In those studies, the communication

Table 1 Examples of ICU-based palliative care interventions and representative studies

Primary target	Examples	Summary of findings	Sample of references
Patient	NONE		
Family	Intervention booklet for family; intensive nurse-, social worker-, or physician-led communication; standardized or structured family meetings; family support coordinator or navigator; family presence during ICU rounds	Mixed – no effect or change in family satisfaction or depression scores, reduced ICU length-of-stay, reduced nonconsensus between ICU clinicians and families; increased DNR and comfort care orders; increased order choosing "aggressive" interventions; improved frequency of communication with ICU providers; decreased ICU costs	Daly et al. 1994; Lilly et al. 2000; Lilly et al. 2003; Azoulay et al. 2002; Burns et al. 2003; Curtis et al. 2016
Clinician team	Education about ethics; education about communication skills; Palliative care team rounds with ICU team	Increased proportion of ICU patients receiving palliative care consultation; reduced ICU length-of-stay	Holloran et al. 1995; Villarreal et al. 2011
System	Palliative care or comfort care order set	No change; increased pastoral care involvement; reduced hospital length-of-stay	Treece et al. 2004; Hall et al. 2004
Multi-level	Palliative care consultation; ethics team consultation; transition of patient out from ICU team to "comprehensive support care team"; ICU clinician education about communication and more frequent and intensive communication with family; clinician education about palliative care communication with designation of local champions and standardized comfort care order sets; communication facilitator	No change; reduced ICU and hospital length-of-stay; reduced treatment intensity; reduced depression, anxiety, and PTSD prevalence among family members; improved nurse quality of death and dying scores; increased frequency of family conferences; increased frequency of prognosis being discussed in family conferences; increased DNR status designation	Carlson et al. 1988; Field et al. 1989; Schneiderman et al. 2000; Campbell and Guzman 2003; Schneiderman et al. 2003; Campbell and Guzman 2004; Lautrette et al. 2007; Norton et al. 2007; Curtis et al. 2008; Curtis et al. 2011

interventions were associated with significant reductions in resource utilization (e.g., shorter ICU length of stay) without increases in mortality, as well as with decreases in discord among decision-makers for ICU patients. However, in one of the largest pre-post studies conducted in five ICUs in two academic medical centers which tested the effect of regular, structured family meetings for patients in the ICU for 5 days or more, there was no significant reduction in ICU length of stay or other utilization outcomes (Daly et al. 2010). Importantly, a multicenter, randomized trial testing a protocol-based strategy for family meetings together with a brochure addressing bereavement found that family members had significant decreases in depression, anxiety, and post-traumatic stress disorder at 3 months after the death of a loved one in the ICU (Cox et al. 2012). Informational brochures have also been independently evaluated and shown in a multicenter, prospective randomized trial to improve family comprehension and satisfaction with information provided by ICU clinicians (Azoulay et al. 2002). These studies suggest that a structured approach to communication with patients and family members in the ICU is one of the most important targets for primary and specialty palliative care interventions.

Support for families and surrogate decision-making. A number of interventions have been

designed to support families of ICU patients through increased involvement of the families or more explicit support for surrogate decision-making (Aslakson et al. 2014b; Scheunemann et al. 2011; Curtis et al. 2016; Carson et al. 2016). Examples include an intervention promoting greater involvement of family members in patient care rounds, a critical care family assistance program, a social worker specifically counseling and supporting ICU families, an ICU family clinic, a communicator facilitator to support ICU families, and a palliative care specialty-trained communicator to convene prognosis-related meetings for family meetings of chronically critically ill patients. Although results vary across studies, these studies suggest such interventions are promising and require further evaluation.

Decision support tools. Several tools have been developed to support surrogate decision-making in the ICU. For example, a short video to support decision-making about resuscitation increased surrogates' knowledge of CPR and the proportion of patients with DNR directives at the time of ICU discharge or death (McCannon et al. 2012). An ICU admission assessment tool to help identify surrogate decision-makers and clarify decision-making standards was associated with shorter LOS and lower total hospital charges for patients requiring mechanical ventilation for 4 days or more (Hatler et al. 2012). A decision aid for surrogates of patients on prolonged mechanical ventilation was associated with less discordance between physicians and surrogates as well as with improved quality of communication as perceived by families and lower hospital costs (Cox et al. 2012). Decision support tools are likely an important area for future research.

ICU diaries, order sets, and "death rounds." Some additional tools have been evaluated to support patients, families, and clinicians. A randomized, controlled multicenter study in Europe evaluated an intervention in which healthcare staff and family contributed to a handwritten diary including photographs that recorded events and experiences on a daily basis during the patient's ICU stay and was provided to the patient 1 month after ICU discharge (Jones et al. 2010). As measured at 3 months after the ICU, this intervention significantly reduced the incidence of new-onset post-traumatic stress disorder among survivors of critical illness when compared to usual care. Another tool included the development of standardized order sets to support clinicians, prepare families, and ensure patient comfort during limitation of life support (Treece et al. 2004). Regular sessions for ICU clinician debriefing after patient deaths have been evaluated for supporting clinicians (Hough et al. 2005). Evidence supports use of these types of tools to support patients, family members, and ICU clinicians.

Multifaceted quality improvement. Multifaceted quality improvement approaches have also been used to improve palliative care in the ICU. The largest and most rigorous study to date was a multicenter, cluster randomized controlled trial that tested a multicomponent intervention comprising education of ICU clinicians, identification of local palliative care "champions" in the ICU, standardization of palliative care order sets, and feedback to ICU clinicians about palliative care-related outcomes. Although this intervention was initially successful at the investigators' own center (Curtis et al. 2008), the multicenter cluster randomized trial found no differences in outcomes including quality of dying as assessed by families or nurses, family satisfaction, ICU length of stay before death, or time from ICU admission to withdrawal of life-sustaining therapies (Curtis et al. 2011). These studies suggest that such interventions may be more successful when generated by and targeted for the needs of each institution.

Tailoring of palliative care interventions for sub-specialty ICUs. A few studies and expert opinion-informed guidelines have addressed further unique palliative care barriers and needs in sub-specialty types of ICUs. Existing data describe cultural tension surrounding palliative and end-of-life care among surgical providers and in surgical intensive care units (Buchman 2010; Buchman et al. 2002, 2003; Cassell et al. 2003a; Olson et al. 2013; Schwarze et al. 2010, 2013). Not surprisingly, studies demonstrate lower utilization of specialist palliative care providers among surgical patient populations (Rodriguez et al. 2015), and a systematic review of palliative care in surgical populations notes

relatively few trials and that most existing trials are small and of low to moderate quality (Lilley et al. 2016). Nonetheless, expert opinion supports thoughtful tailoring of palliative care interventions to surgical intensive care units (Lilley et al. 2017; Mosenthal et al. 2012). In addition, existing data regarding specialist palliative care interventions in surgical intensive care units is promising. A single center, before-after study tested a multifaceted interdisciplinary intervention to integrate palliative care into standard care in a trauma ICU. After the intervention, symptom management and goals of care were discussed more frequently on rounds, and while ICU mortality was unchanged, the intervention was associated with shorter length of stay in the ICU and hospital for patients who died. A similar intervention in the same institution for liver transplant surgical ICU patients was associated with earlier consensus around goals of care, earlier and more frequent use of DNR and withdrawal of life-sustaining treatment order, and shorter surgical ICU length of stay, with unchanged mortality. Further expert statements address tailoring of palliative care in both neurocritical care units and burn critical care units (Frontera et al. 2015; Ray et al. 2017).

7 Opportunities and Challenges for ICU Palliative Care Improvement

Ongoing challenges for optimal integration of palliative care in ICU settings have been identified and it is important that palliative care specialists interested in supporting critically ill patients, family members, and clinicians understand these challenges (Kirchhoff and Beckstrand 2000; Nelson 2006; Fassier et al. 2005). In a survey of a large, nationally representative sample of nurse and physician directors of US adult ICUs, respondents reported on perceived barriers at the level of the patient/family, clinician, and institution (Nelson 2006). Important barriers included unrealistic expectations on the part of patients, families, and clinicians about patient prognosis or effectiveness of ICU treatment, inability of patients to participate in treatment discussions, insufficient training of physicians in relevant communication skills, and competing demands for clinicians' time. Similar perspectives have been articulated by critical care professionals in Europe, along with distinct issues facing these clinicians including cultural variations across different European countries as well as a history of more decision-making by clinicians, and less involvement of families, as compared to North American settings (Fassier et al. 2005).

Special challenges for efforts to integrate palliative care in surgical ICU settings care have been noted. These include surgeons' strong sense of personal responsibility for patient outcomes (Buchman et al. 2002; Cassell et al. 2003b), disparate surgical provider opinions about the adequacy of communication regarding prognosis (Aslakson et al. 2010), and what has been described as a "covenantal" relationship in which the surgeon commits to protect the patient and the patient commits to endure the operation and sequelae (Buchman 2010; Cassell et al. 2003b). In a national survey of surgeons, more than 40% reported conflict with intensive care physicians and nurses with respect to appropriate goals of postoperative care (Olson et al. 2013). In addition, many responding surgeons described difficulties in managing clinical aspects of poor outcomes, communicating with the family and patient about such outcomes, and coping with their own discomfort about these outcomes (Olson et al. 2013).

8 Surrogate Decision-Making

The vast majority of ICU patients are incapacitated and dependent on family or other surrogates for medical decision-making (Nelson et al. 2006a; Prendergast and Luce 1997). Qualitative studies are increasingly illuminating the perspectives, concerns, and needs of these surrogates (Schenker et al. 2013; Boyd 2010; Evans et al. 2009; Apatira et al. 2008; Schenker et al. 2012). Most surrogates favor timely discussion of prognosis by ICU clinicians as necessary for decision-making as well as for emotional and practical preparation for the possibility that the patient could die (Apatira et al.

2008). Surrogates appear to recognize and accept that uncertainty about prognosis is unavoidable yet still wish to discuss expected outcomes (Herridge et al. 2003). At the same time, they experience intrapersonal tensions, acknowledging that information about an unfavorable prognosis may be painful as well as helpful (Schenker et al. 2012, 2013). Surrogate behaviors in response to these tensions include focusing on details rather than the larger picture, relying on personal instincts or beliefs, and, at times, rejecting prognostic information (Schenker et al. 2013; Nelson et al. 2017). Awareness of surrogates' perspectives may help ICU and palliative care clinicians more fully address their concerns and needs, thereby facilitating effective shared decision-making. Palliative care specialists can play an important role in helping ICU clinicians understand and address these concerns and needs.

ICU clinician approaches that maximize family-centered communication, provide support for families, and incorporate active listening are associated with increased family satisfaction, improved surrogate decision-making, and psychological well-being of surrogates (McDonagh et al. 2004; Curtis et al. 2005; West et al. 2005; Stapleton et al. 2006). Palliative care specialists can play a key role in supporting these approaches. Based on qualitative research and expert opinion, clinicians are encouraged to help surrogates "plan for the worst" while "hoping for the best" (Back et al. 2003). Other communication strategies suggested by existing evidence include explicit expression of empathy (Selph et al. 2008; Pollak et al. 2007); affirmative exploration of family concerns and comprehension with adequate time for listening by clinicians (White et al. 2007; Azoulay et al. 2000; McDonagh et al. 2004); assurance that the patient will not be abandoned or allowed to suffer should life-sustaining treatments be withdrawn (West et al. 2005; Stapleton et al. 2006); support for critical decisions made by family members, such as whether the patient would want to limit or continue life-sustaining therapies (Stapleton et al. 2006; Back et al. 2005); and, when possible, advance care planning discussions between surrogates and high-risk patients prior to the need for ICU care or the next episode of critical illness (Majesko et al. 2012).

9 Operationalizing Core Palliative Care Components as Measures of ICU Quality

As interest in value-based care rises, ICU and palliative care clinicians are increasingly working together to implement palliative care quality measures in the ICU. Key domains of ICU palliative care quality have been identified and made operational as specific measures that focus on care processes and outcomes (Mularski et al. 2006; Aslakson and Bridges 2013). Focusing primarily on processes, the "Care and Communication Bundle" was developed and tested as part of a national performance improvement initiative by the Voluntary Hospital Association (VHA), Inc. (Nelson et al. 2006b). The measures in this bundle are triggered by time periods in the ICU, with emphasis on proactive, early performance of key processes (e.g., identify medical decision-maker and resuscitation status before Day 2 in the ICU, offer social work and spiritual care support before Day 4, and conduct an interdisciplinary family meeting no later than Day 5). Specifications are precise (e.g., the family meeting measure defines "interdisciplinary" as including at least the attending physician; a member of another discipline such as a nurse, social worker, or chaplain; and the patient and/or his or her family, as documented in the medical record, and must include discussion of prognosis, goals of care, and the patient's and family's needs and preferences) (Nelson et al. 2006b). Similar Day 1 and Day 3 communication measures were tested in a statewide ICU collaborative project in Rhode Island (Black et al. 2013). Significant increases were seen in compliance with these measures, while improvements in compliance varied across ICU type with less improvement in open, nonteaching, and mixed medical-surgical ICUs. Most patient-specific outcome measures were unchanged, although there was an increase in patients discharged from ICU to inpatient hospice. Additional studies evaluating performance on ICU palliative care quality

measures show wide variation both within and across hospitals and even within individual intensive care units, as well as low performance levels overall on most items and little improvement over recent years (Penrod et al. 2011, 2012; De Cato et al. 2013).

The quality of ICU palliative care should also be evaluated by structure and outcome measures in addition to process measures (Curtis et al. 2006; Pronovost et al. 2001). The relationship of ICU palliative care process measures to desired patient and family outcomes requires further investigation.

10 Resources Available to Support Integrating Palliative Care and Critical Care

Training opportunities for ICU clinicians. Several interventions have focused on training ICU clinicians to deliver palliative care more effectively. Some approaches include communication skills training (Lilly et al. 2000, 2003; Lautrette et al. 2007; Norton et al. 2007) and education on ethics and conflict resolution (Schneiderman et al. 2003; Browning et al. 2007). These training programs are often conducted or supported by palliative care specialists. For intensivists and hospitalists in the United States, the Harvard Medical School Center for Palliative Care offers an annual two-and-half-day course that provides clinicians with information and skills needed to offer high-quality palliative care to critically ill patients and their families. "Critical Care Communication" (C3), another intensive course focusing specifically on communication skills, was offered to physicians training in critical care at the University of Pittsburgh. In workshops for pediatric critical care providers, the "Program to Enhance Relational and Communication Skills" used "parent-actors" to simulate pediatric, values-based, and/or end-of-life conversations (Browning et al. 2007; Meyer et al. 2009). The VitalTalk program offers specific communication training on palliative care and communication skills and also offers a smartphone-based supplemental application. A 1-day workshop was developed specifically to train bedside critical care nurses in skills they need for active and effective participation along with physicians in interdisciplinary meetings with ICU families (Krimshtein et al. 2011). Of nurses receiving this training and surveyed before and after it ($n = 74$), the average proportion self-rating skills as "very good/excellent" rose significantly, and almost all nurses reported that, after training, they had an increased awareness of special contributions they could make and felt more able to initiate interdisciplinary family meetings. The End-of-Life Nursing Education Consortium (ELNEC), an international education initiative to improve palliative care, has developed a critical care-specific course for nurses. A before-after study in three medical and surgical ICUs in a single community hospital tested a 90-min program of interdisciplinary team training to enhance communication with ICU families (Curtis et al. 2013). Along with clinicians' confidence in communication with families, family satisfaction with ICU communication improved significantly. Yet, this randomized trial of a communication skills building workshop for residents and nurse practitioners did not show an improvement in the patient- and family-level outcomes. These studies identify questions and challenges with showing improvements in patient and family outcomes with educational interventions. One-day communication training programs for ICU clinicians have also been offered at some European intensive care congresses over the past decade including the European Society of Intensive Care Medicine, although such training programs seem less common in Europe and other parts of the world than the United States.

Web-based resources. Extensive resources for use in ICU palliative care improvement efforts are readily accessible, and palliative care specialists could consider offering these resources to their ICU colleagues. Many of these are available on the Website of The IPAL-ICU Project, which is sponsored by the National Institutes of Health and the Center to Advance Palliative Care (CAPC). This Website is password-protected and requires an institutional or individual membership to CAPC to be able to access the materials. Yet, once accessed, those materials are extensive and

include a library of relevant references, a variety of practical improvement tools (e.g., family meeting planner and documentation template, data collection instrument for quality monitoring, pocket cards for guidance on symptom management and communication), materials for patients and families (e.g., family meeting brochure), and links to curricula for professional education. In addition, the IPAL-ICU Advisory Board has published an expanding series of articles addressing key issues for efforts to improve palliative care in different types of critical care settings (Nelson et al. 2010b, 2011, 2013, 2015; Puntillo et al. 2014; Mosenthal et al. 2012; Ray et al. 2017; Lustbader et al. 2012).

Professional practice recommendations. Multiple societies representing critical care professionals have published practice recommendations and/or guidelines related to important aspects of ICU palliative care, and these are evidence-based and extensively referenced (Lanken et al. 2008; Selecky et al. 2005; Truog et al. 2008; Carlet et al. 2004; Davidson et al. 2017; Mularski et al. 2013; Mahler et al. 2010; Barr et al. 2013; Yancy et al. 2017; Holloway et al. 2014). Palliative care specialists may be able to use these practice recommendations and guidelines to support improved primary and specialty palliative care in the ICU. For example, the American College of Critical Care Medicine has published consensus recommendations for end-of-life care in the intensive care unit (Truog et al. 2008), as well as clinical practice guidelines for support of the family in the patient-centered intensive care unit (Davidson et al. 2017) and for management of pain, agitation, and delirium (Barr et al. 2013). Similarly, the American Thoracic Society (ATS) published a clinical policy statement on palliative care for patients with respiratory diseases and critical illnesses (Lanken et al. 2008). The American College of Chest Physicians (ACCP) published a position statement on palliative and end-of-life care for patients with cardiopulmonary diseases (Griffin et al. 2007). In addition, both ATS and ACCP have specifically addressed the management of dyspnea (Mularski et al. 2013; Mahler et al. 2010). The American Heart Association (AHA) and American College of Cardiology Foundation included palliative care in their management plan for patients with severe heart failure (Yancy et al. 2017), and the AHA and American Stroke Association have published a statement advocating for palliative care for stroke patients (Holloway et al. 2014). Finally, among five recommendations published as part of the 2014 "Choosing Wisely" campaign, the Critical Care Societies Collaborative recommends that clinicians not "continue life support for patients at high risk for death or severely impaired functional recovery without offering patients and their families the alternative of care focused entirely on comfort" (Halpern et al. 2014). These and other resources can help ICU and palliative care clinicians to strengthen their knowledge and skills and support integration of primary and specialty palliative care as a routine part of critical care practice.

Synergy with family-centered care interventions. Over the past decade, efforts to improve family-centered care in the ICU have burgeoned concurrent to those to improve delivery of palliative care in the ICU (Davidson et al. 2017). Indeed, as psychosocial support of family members is a key component of palliative care, so the two are different facets of the same entity, and interventions to improve family-centered ICU care cannot help but to advance palliative care – often primarily palliative care – content and to improve integration of palliative care practices and providers into ICU care practices.

11 Conclusion and Summary

Palliative care evaluates and treats patient symptoms, provides psychosocial support for patients and families, and identifies and integrates a patient's personal goals into medical treatment. Over the last two decades, intervention studies have explored how to better provide palliative care together with critical care, including incorporating palliative care specialists and supporting critical care clinicians in the delivery of primary palliative care. Moreover, efforts to improve family-centered care in the ICU are synergistic with those to improve palliative care. Evidence supports the benefits of palliative care in the critical

care setting, although the most effective and efficient ways to achieve these benefits are not yet clear. Critical care professional society statements call for delivery of primary palliative care by ICU clinicians as well as provision of specialist palliative care, when needed. Existing educational tools and resources enable ICU clinicians to improve their palliative care knowledge and skills and to help palliative care clinicians identify opportunities to support critically ill patients, their families, and their ICU clinicians. Future research is needed to better determine how best to provide palliative care to critically ill patients and their families both in the ICU and beyond.

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Palliative Care in Rural Settings

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_47

Abstract

To ensure the provision of end-of-life care is relevant to individual communities, it must not only reflect the needs of the dying person and their family but also the diverse geography and cultures in which they live. Studies consistently report that rural residents perceive themselves as different to their urban counterparts and clearly hold distinct views on what it means to die well. Currently there is no international consensus on the definition of rurality and remoteness. Rural settings are not homogeneous, and there is considerable individual, cultural, and ethnic diversity both within and between rural locations. Rural communities are close-knit, and known for their social solidarity, community commitment, and loose support networks. While there are many benefits of rural residency, significant challenges exist in the provision of quality end-of-life care. The needs of rural residents are shaped by decreased access and availability of services. While this potentially has a negative influence on outcomes, it is offset by local support networks. Rural palliative care is mostly primary care, with limited access to specialist multidisciplinary palliative care services. Home is the initial preferred place of death for most rural residents; however, when home is not possible, rural hospitals and residential aged care are considered appropriate alternatives, providing they are within ones' community. The universal rural theme is that if rural residents are unable to die at home, then it is essential that their place of death is within their local community.

1 Introduction

To ensure the provision of end-of-life care is relevant to individual communities, it must not only reflect the needs of the dying person and their family but also the diverse geography and cultures in which they live (Bakitas et al. 2015; Cottrell and Duggleby 2016). In general, populations are becoming more urbanized, with the estimated proportion of rural dwellers falling from 70.5% in 1950 to 46% in 2015 (WHO 2014). The highest proportion of rural populations remains in the developing regions, such as sub-Saharan Africa. For example, 84% of Uganda's population is considered rural, compared to 30% in Canada (World Bank 2016). While the size of many individual rural populations is decreasing, they are also aging, often at a faster rate than urban populations. In developed nations, the phenomenon of "sea-change" and "tree-change," adds to the graying of some rural populations, as older urban dwellers leave the cities in search of the more relaxed rural lifestyle (Castleden et al. 2010). Between 2000 and 2030, the growth rate in Australia's population aged 65-years or older is expected to rise by 139%, with a 180% increase anticipated in rural areas (Australian Government Department of Health 2008).

Studies consistently report that rural residents perceive themselves as different to their urban counterparts and clearly hold distinct views on what it means to die well (Wilson et al. 2009a, b; Robinson et al. 2010). In relation to palliative and end-of-life care, rural areas typically have fewer health and social services, as compared to urban areas resulting in substantial differences in the provision of care. As a consequence, some people must move away from their rural community to receive the care required.

Most rural end-of-life research has been focused on healthcare services (intervention studies, needs assessment, program planning and evaluation, education and finances) and professional attitudes, education, and practices (Bakitas et al. 2015). There is also a focus on determining the urban/rural differences, rather than finding ways to explore the unique factors associated with rural

health and in particular rural palliative care (Boarders 2017). Currently, there is a paucity of studies documenting rural end-of-life care experiences and perspectives from the recipients of such care – the patients and their family caregivers (Robinson et al. 2009).

The objective of this chapter is to describe palliative care in rural settings. This is a challenge due to the significant heterogeneity between rural settings. While the rural literature contains a number of excellent rural studies undertaken in sub-Saharan Africa and Asia, overall it is biased toward developed nations, especially Canada, the United Kingdom, Australia, and the United States of America. While attempting to remain inclusive, this chapter is written from the perspective of one Australian rural palliative medicine specialist.

This chapter begins by defining "rural" and exploring the challenges of developing a universal consensus on definition. This is followed by a description of rural residents and the nature of palliative healthcare services in rural settings. The challenges and benefits of receiving and delivering palliative care in rural locations are explored. Place of death in rural settings is described. The chapter concludes with a discussion on the concept of the "good" rural death.

2 The Challenges of Defining "Rural"

Currently, there is no international consensus on rural definition or universal rurality or remoteness index. In the absence of homogeneity within health services and cultural context, it is difficult to compare rural areas, not only between countries but also within countries. "Rural" is a multifaceted concept and can be interpreted in a number of ways. Rural settings encompass large towns with services, smaller towns with limited services, villages, hamlets, and farms of varying degrees of isolation, with some locations metro-adjacent or easily accessible to services, and others isolated by geography or weather; some locations are inland and others coastal. Policy-makers and service providers base definitions on population size, population density or demographics, or distance from urban centers and services. For example, since the early 1990s, four different geographic classifications have been developed in Australia (AIHW 2004): Rural, Remote and Metropolitan Areas classification [RRMA, 1994], in which the index of remoteness is based on the straight line distance to service centers and the distance from other people based on population density; Accessibility/Remoteness Index of Australia [ARIA, 1997], based on the road distance from the closest service center; Australian Standard Geographical Classification [ASGC, 2001], which uses the average distance from each populated locality to the closest service center (population 1000–4999 persons), as well as the larger urban service centers; and Modified Monash Model [MMM, 2015], based on ASGS with the additional subdivision of regional Australia into four categories based on the population size. The classification applied has significant implications on funding, service provision, and financial incentives to attract general practitioners to areas of need.

The definition of rural is complex and cannot be limited to geography based on distances from urban service centers or population densities. The provision of palliative care in rural settings is not only influenced by geographical borders and boundaries. In a rural study conducted by Giesbrecht et al. (2016), formal and informal caregivers in rural Canada identified five forms of borders and boundaries that impact on the delivery, and receiving, of palliative care: political (national/federal and state/provincial borders), jurisdictional (formal borders within states/provinces created by different health authorities), geographical (especially in terms of distances and isolation), professional (boundaries between organizations and specialities that determined specific roles of service providers), and cultural (differences in cultural norms, practices, behaviors, and communications, especially those that distinguished differences between rural and urban dwellers and between Aboriginal and non-Aboriginal peoples).

"Rurality" is a term increasingly used to differentiate rural people as a distinct cultural group consisting of "small human communities,

whose values of mutual aid and shared history still focus on pride and a sense of belonging to a community, a territory, or family. Rural areas are characterised by dynamic and social, cultural and economic practices centred on proximity, conviviality, mutual aid and cooperation" (Ministere des affaires municipales et des regions du Quebec 2007). While urban dwellers may not acknowledge or appreciate rurality as a separate entity, rural people openly state "that there are important differences between dying in a rural community and dying in a large city" (Wilson et al. 2009b, p. 316).

3 The Characteristics of Rural Residents

Despite significant cultural and ethnic diversity between rural communities, rural people are united by the fact they live in rural areas and believe they have some unique perspectives on, and concerns about, dying well and end-of-life care. Rural and urban residents share the desire for autonomy, a pain-free death, and quality end-of-life care; rural residents frequently have an openness and awareness of death and dying (Wilson et al. 2009a) and have been described as "more accepting of death and less likely to intervene to delay death" (Kirby et al. 2016, p. 1).

Some rural residents perceive differences between those living on farms and those residing in rural towns. Those residents living on farms have been described as more independent, resilient, and adept at problem-solving than rural town dwellers. This resilience (flexibility and the capacity to recover quickly from adversity) and self-reliance (the ability to problem solve rather than relying on others) is not necessarily a personality trait but, more out of necessity, born out of personal experiences and expectations with farmers adept to multitasking and finding novel ways to solve multiple problems.

Rural people are also identified by their deep concern for their community and its members (Kirby et al. 2016). Strong relationships and informal community services are important factors that facilitate end-of-life care within rural communities. The high level of community support fosters a strong sense of belonging and attachment to the community (physical, social, and autobiographical). While "country" has special cultural significance for Aboriginal and Indigenous peoples, many rural dwellers prefer to receive care and die in their community as "being at home is like a brick being in the right place: this is my land and these are my people" (Devik et al. 2015, p. 7). While the rural environment can quickly become unsafe and one of isolation, it has the capacity to be a source of great comfort, security, reassurance, and identity, while for many rural people, the urban environment is viewed negatively (e.g., noisy, unfamiliar, and impersonal).

4 Nature of Rural Palliative Healthcare Services

Quality palliative care is considered the right of every dying person, regardless of where they live (WHO 2015). In 2011, 44.6% of all deaths in the United States of America occurred under hospice (palliative) care (NHPCO 2012). In sub-Saharan Africa, the estimated proportion is less than 5% (Grant et al. 2011). The proportion of rural residents receiving specialist palliative care is significantly lower than for urban residents. The palliative care needs of rural and remote residents "are related to context [. . ..] and are shaped by reduced access and availability of services" (Kirby et al. 2016, p. 1). Access to palliative care services differs widely across rural locations – both within countries and between countries, with the commonality being "gaps" in service provision.

As in any location, primary healthcare providers are pivotal to the provision of rural palliative care. While many of the needs of patients and family caregivers are universal, priorities differ between rural and urban dwellers and between developed and developing nations. The nature of service gaps is dependent on context, with many rural areas, especially in developing countries, lacking the basics of healthcare such as trained primary care health workers, basic medicines (such as morphine), and equipment. In Australia,

and other developed countries, increased costs associated with healthcare delivery, decreasing numbers of rural healthcare providers, and centralization of services have all impacted negatively on access to rural and remote healthcare services.

In a number of developed countries, such as Australia, Britain, and Canada, extensive work is being undertaken to address these problems and to ensure palliative care services are provided locally (AIHW 2014).

5 Challenges of Rural Residency

Much of the current rural literature emphasizes the unique challenges associated with rural residency. The obvious challenges relate to isolation and distance from specialist services in major urban centers; however, rural residents face other barriers to receiving quality end-of-life care, as outlined below.

5.1 Distance and Travel

For many rural residents, distance is the greatest negative influence on rural end-of-life care. Many rural patients travel for investigations, diagnosis, and treatment. Commuting can be stressful, exhausting, inconvenient, expensive (Lockie et al. 2010; Pesut et al. 2010; Duggleby et al. 2011; Grant et al. 2011; Devik et al. 2013), and even dangerous or impossible, depending on the weather (Castleden et al. 2010). Despite this, some regard travel for treatment a price for living in a beautiful place, and a compromise they have to make for living at home, that is, "to live in a place that contributes to their overall health" (Wiik 2011, p. 12). While the time taken to reach certain services may be comparable to some urban areas, the actual distances can be considerably more and often at higher speeds. One patient receiving palliative care in rural Australia compared the time taken to travel from her farm to the local hospital, with that of her children who live in the city: "Here you're 20-kilometres but it translates to 15-minutes. In [the city], five-kilometres translates into 15-minutes" (Rainsford 2017, p. 192). While traveling can be acceptable in the early stages of disease, with some residents treating it as "a day out" (Devik et al. 2015), distance and travel become more problematic as patients become more ill and fatigued, when symptoms become more troublesome and when patients enter the terminal phase. Traveling becomes not just an inconvenience but can be associated with physical distress.

Once patients can no longer travel, they often report being disconnected from their specialists (medical, nursing, and allied health), who have been a source of valued support. A time of grieving sometimes follows, for both the patient and their family.

The issues of distance and travel are not just about seeking healthcare support. Distance and travel also impact on family caregivers, regardless of whether they live locally or away. Family caregivers are faced with a number of scenarios while caring for their family member: the out-of-town family having to travel to visit their family member, often leaving their own children and responsibilities for extended periods of time, the local family traveling to the distant tertiary hospital or out-of-region hospice to visit their family member, the anguish of family members trying to decide whether to seek medical help locally or in more distant specialist facilities, and the costs of travel and accommodation when there is no family home to stay in when visiting or supporting family members in hospital or residential aged care. Traveling has been reported to impact negatively on the health of some family caregivers (Lockie et al. 2010).

Most families hope to be present at the time their family member dies. The fear of not being present can be significant and is compounded by the sense of geographical separation (Castleden et al. 2010). When family caregivers have to travel to out-of-region hospitals or hospices to be with their family member, the travel distances become more problematic. While rural family caregivers have a strong desire to be present at the time of death, they have to balance fulfilling their responsibilities at home or the farm with maintaining a bedside vigil away from home.

Traveling out of region, to access services not available locally, increases the risk of fragmented care (Duggleby et al. 2011). Without impeccable clinical handover and coordination of care, the quality of care can be compromised. The greatest support need of many rural patients with a terminal illness, and their family caregivers, especially in developed countries, is informational. Effective communication between healthcare professionals and patients/family caregivers reduces pain and distress, empowers carers to fulfill their responsibilities, facilitates smooth transitions of care, and allows patients and families to prepare for death (Rainsford et al. 2017). When surveyed, most patients and family caregivers report to be satisfied with the standard of communication by rural healthcare professionals (Devik et al. 2013); however, a number of communication difficulties are commonly reported. These include receiving conflicting or untimely information and uncertainty in identifying the lead physician.

However, opinions regarding the effect of distance on the quality of care are divided, with some rural residents seeing it as a major barrier to receiving home-based palliative care, and therefore achieving a home death (Dembinsky 2014), and others not viewing distance and rural residency a disadvantage (Devik et al. 2015). With advanced illness, the patients and family caregivers' sense of solitude (previously seen as an advantage of rural life) can become one of isolation (Duggleby et al. 2011). Geographic isolation can also contribute to the greater unmet emotional needs of rural caregivers, as they often lack the support of others going through similar experiences (Brazil et al. 2014).

5.2 Accessibility to In-Home Services

The availability of rural healthcare professionals to support patients dying at home becomes problematic the greater the travel distance and the more protracted the terminal phase. The most isolated rural locations are the least likely to have access to in-home care and support. Geographical distance limits accessibility to home-based services, especially for patients living outside the home visit boundary. Home visits become less frequent, especially in bad weather, and are often not available at short notice or after hours. Daily home visits to adjust medications, often required during the last days of life, are less likely to be available the further one lives from the service town. Some rural GPs provide on-call medical cover for rural hospitals. As rural generalists, this on-call cover can be in the emergency department, general wards, maternity, anesthetics, and/or operating theatres. In small towns, the on-call doctor is often the only doctor in town after hours and on weekends. While some doctors may be able to leave the hospital briefly to home visit a patient in close proximity to the hospital, they cannot leave town to visit patients living in surrounding villages or farms. In other rural locations, the service provided by GPs is on a part-time basis, with no daily access to medical support.

Mobile phones, computers, and internet access can help reduce the sense of rural isolation by maintaining contact with distant family and improving access to healthcare professionals; however, these technologies are often unreliable or not available in more remote areas (Lockie et al. 2010; Pesut et al. 2010). For some patients, a phone call is not sufficient and does not replace the physical presence of the nurse or doctor (Pesut et al. 2010; Hansen et al. 2012). In an Australian study, one husband living on a farm, felt "unsupported and alone" when the face-to-face presence of "qualified medical advice" was not available the night before his wife died (Rainsford 2017). Robinson et al. (2010) reported that some rural residents familiar with telehealth were not impressed with the service and found it unreliable and expensive. It cannot be presumed that all rural residents have sufficient literacy to use the technology and that phone and internet connections are available in all houses or in all communities.

Consistent with their urban counterparts, rural family caregivers often feel responsible for ensuring the dignity and comfort of their loved ones during their final days and experience distress, guilt, and anger when circumstances prevent them fulfilling this role (Revier et al. 2012).

While rural family caregivers take on the responsibility of providing direct care, many also take on the role of managing and coordinating care while being an advocate for their family member (Pesut et al. 2014); however, "few [are] physically, emotionally, or educationally prepared for the tasks and responsibilities of caregiving" (Revier et al. 2012, p. 5), especially as the illness progresses.

5.3 Lack of Local Specialist Services and Expertise

While travel distances restrict patients from visiting their specialists, the lack of local specialized personnel and facilities offering life-prolonging interventions is often considered a disadvantage of rural residency. However, as patients become more unwell, they and their family caregivers often acknowledge that the need for further complex interventions is no longer necessary, and in fact, helps ensure a better quality of dying. During a bereavement interview, one rural family caregiver commented that "not [being] hooked up to machines" facilitated a more dignified death for his father who achieved a home death on their farm (Rainsford 2017, p. 203).

Unlike metropolitan and some regional areas, most rural and remote locations do not have specialist palliative care services and are reliant on primary healthcare providers. In some locations, GPs and community nurses may be supported by a specialist palliative care nurse. The lack of a specialist service could be viewed as a limitation of the quality of palliative care for rural residents. While GPs often struggle with managing complex issues, such as complex pain and high dose opiates, they do deliver sound and effective palliative care, and rural patients and their family caregivers appreciate the care provided by their primary care professionals (Mitchell 2002). Rural primary care physicians are frequently highly praised for their honesty and presence at the time of death.

The benefits of primary care-led palliative care must not be overlooked. These benefits include increased continuity of care, which often continues when patients are transferred from home to hospital or residential aged care, being cared for by health professionals who have a long standing professional relationship and knowledge of the individual and their family (sometimes intergenerational), and access to continuing care and bereavement support for family members. As a member of the rural community, rural health professionals are also familiar with the broader issues and the unique rural culture within rural communities.

Compared to their urban colleagues, rural primary healthcare professions face additional challenges in providing quality evidenced based end-of-life care. Rural healthcare professionals often find themselves in the dual role of healthcare provider and community member. As members of the community they are not anonymous and are often faced with planning and providing end-of-life care for close friends, neighbors, and colleagues (Beckstrand et al. 2012). Added to this is the difficulty of taking study leave to attend educational programs to up-date knowledge and maintain competencies and skills. Travel distances are compounded by the difficulty of recruiting locums to fill in during periods of absence. Travel distances also limit opportunities for team meetings, which can compound the emotional and physical isolation of independent healthcare professionals. Many rural locations have a single "unofficial" palliative care champion, and in their absence the whole system may stagnate or even disintegrate.

Rural patients are more likely than urban patients to visit their primary care physician (or GP) and the hospital emergency room and less likely to be admitted to an inpatient hospice or make use of respite services (Brazil et al. 2013). For rural patients and their family caregivers, being cared for in their community and by people they know is often more important that receiving specialist care (Veillette et al. 2010).

5.4 Lack of Allied Health Support

A multidisciplinary team is central to the provision of quality palliative care. While medical, nursing, and informal family care are the backbone of rural palliative care, limitations in

accessing allied health support are often cited as a disadvantage of rural residency. In some circumstances, the lack of services and choice of commodities is just an inconvenience, for others the limitations, for example, home nursing, reduce the chance of patients dying at home.

Access to physiotherapy, occupational therapy, social work, counselors, and pastoral care varies depending on location and population. In some rural locations, when these services are available, they are often restricted to inpatient settings in the local rural hospital or are limited by the cost of private fees. Ongoing bereavement counseling is limited in most rural and remote communities. Community pharmacists are valued members of the multidisciplinary team; however, they are not present in all rural locations, and when available, after-hour services are either limited or nonexistent. Specific medications for symptom management are frequently not available at short notice.

6 Benefits of Rural Residency

Despite the challenges faced by rural communities, quality palliative care can be, and is, provided locally. In many ways, the benefits of rural living outweigh the disadvantages. The great sense of community is one benefit of rural living and a major contributor to quality end-of-life care. Another positive of rural living, voiced by many rural residents, is the beauty and tranquility of the rural lifestyle. Despite limited health services, many believe rural living has positive health benefits, and many could not contemplate living in a more urbanized location. Rural residents often speak of feeling "safe" in their isolation; however, when they, and especially those on isolated farms, are diagnosed with a terminal illness, due to the limited availability of medical, nursing and community support, the isolation can contribute to home becoming an unsafe place (Rainsford 2017).

6.1 Personalized Care

Features of care that facilitate quality rural end-of-life care include personalized care (Hansen et al. 2012), "knowing," and "being known" by the healthcare workforce (Pesut et al. 2011), and a willingness of healthcare workers to go beyond their professional duty. The concept of "being known" and "knowing others" is a unique feature of rural communities and extends into rural hospitals and residential aged care. Unlike many large urban institutions, there is often a small turnover of rural staff, within rural institutions, that facilitates personalized care. "Being known" promotes a sense of acceptance, where patients are known for who they are rather than being known for their illness. The workforce within rural community health, hospital, and residential aged care is usually members of the community and known to the patients and their families. This familiarity can assist patients and their families to have confidence in the care provided and can often ease the distress of transferring from home to hospital or residential aged care, for end-of-life care.

However, loss of privacy and anonymity and an expectation that friends will always be available are perceived as barriers (Pesut et al. 2011). Often the quality of care provided is dependent on the personality of the healthcare provider, with difficulties arising if personality conflicts arise, as often no alternative provider is available (Devik et al. 2013). Loss of anonymity can also be problematic if patients are self-conscious of their deteriorating state. Issues of confidentiality can also arise when family caregivers are forced into the dual relationship of family protector and community member. This can result in a spirit of independence as patients and their family caregivers may restrict both formal and informal support in an attempt to keep their personal circumstances private.

6.2 Informal Community Support

The informal support provided by family, friends, neighbors, and the community is significant, with some considering that family is the "most important" factor (Devik et al. 2013, 2015) and essential for culturally congruent care (Mixer et al. 2014). In many rural areas, the profile of informal rural caregivers reflects the social change in

family structure. As previously noted, many rural populations are graying and decreasing in size due to internal migration, as younger family members move to more urbanized areas in search of education and employment. Compared to urban areas, rural caregivers are now more likely to be younger and a non-first-degree relative (Burns et al. 2015).

Rural communities are often described as "very close knit with incredible volunteer bases, and very generous people… who are genuinely concerned about the community" (Castleden et al. 2010, p. 287). Informal community support is highly valued by rural residents and is perceived to be unique to rural communities and a significant advantage of rural residency. It is reported to have a positive influence on rural end-of-life care as it contributes to a sense of solidarity, as people take care of each other (Devik et al. 2015). Community support cannot be taken for granted and is highly reciprocal, with those who have contributed most to their rural community often receiving the highest amount of support from that community (Pesut et al. 2011).

Informal support is mostly direct and practical, such as food, transport, sitting with a patient, and domestic help; however, some support is indirect, with many community members unaware of the significance of a friendly smile or "hello."

There is an assumption that, due to reduced access and availability of services and support, rural caregivers would have higher levels of needs and greater unmet needs than their urban counterparts. However, rural communities are often resourceful when no specialist services are available. Local support networks are created in response to the unspoken responsibility and commitment to care for community members when one identifies as a member of the community. Compared to urban caregivers, rural caregivers perceive the same low level of carer burden and good level of support (Kirby et al. 2016). Rural caregivers are more positive about the caregiving experience than their urban counterparts, with most reporting the experience to be as expected or better than expected. Rural caregivers are also more likely to perceive their deceased family member to have been comfortable during the last 2 weeks of life (Burns et al. 2015). Despite the great sense of community support, the greatest unmet needs identified by rural family caregivers, in both developed and developing countries, remain the tangible or practical needs (Brazil et al. 2013, 2014; Grant et al. 2011).

For some patients receiving treatment in small rural health facilities, a special "subcommunity" can develop, where patients and their family caregivers find mutual support in other patients. For other rural patients and family caregivers, despite the strong sense of community, as disease progresses and patients lose mobility and independence, a sense of isolation can develop as often there is no one in the community who has experienced the same situation, "I am part of my community but I feel alone. Family and friends come to visit me, but I feel isolated as they are unable to understand what is happening to me and my wife" (Duggleby et al. 2011, p. 2).

Despite the perceived willingness to volunteer, it has been suggested that rural community members may volunteer out of obligation, rather than a true desire to be involved. Likewise, formal care providers may also feel pressured to provide services above and beyond that expected of their urban counterparts, because there is often no alternative (Castleden et al. 2010).

6.3 Formal Support

Depending on the locality, formal support can be readily available, limited, or nonexistent. Most rural patients, especially in developed countries, have access to primary palliative care through their general practitioners and community nurses. With the exception of those living in regional towns, most, if not all, rural patients are required to travel to receive specialist care. In contrast to the majority of urban medical practices, most rural GPs and community nurses live in the community where they work, with friendships commonly developing between healthcare professionals and their patients. Healthcare providers' obligations often extend far beyond the professional role with some providers going to extraordinary lengths to be available, and take great "pride in being able to make it work – through responsive,

creative, highly individualized care" (Robinson et al. 2010, p. 81).

In many rural areas, it is not unusual for residents to have their "own" GP. Some rural residents are supported by the same GP and community nurse over a prolonged period, often from the time of diagnosis. The advantages of "being known" and continuity of care enhance the sense of trust in the healthcare providers. The concept of "knowing" also extends to the healthcare providers, who are often known by, and know of, other service providers.

6.4 Convenience of Rural Residency

Despite the travel distances, once in town, there are conveniences often not found in cities. When family caregivers are "time poor," the lack of traffic congestion is a commonly reported benefit of rural residency. Parking at rural hospitals and medical centers is usually free and in close proximity to the front door.

7 Place of Death in Rural Palliative Care

In rural settings, relationships between place and one's self are often stronger than for urban residents, so one would expect that rural people would view dying at home an essential feature of the "good" rural death. Place of death is often considered in terms of geographical location (community) and physical space (home, hospital, residential aged care). Consistent with urban dwellers, surveyed rural residents do indicate that, if faced with a life-limiting illness, home is their preferred place of death, surrounded by family and friends (Veillette et al. 2010), and, in the case of Aboriginal and Indigenous peoples, connected to their land and family (McGrath 2007). However, inconsistencies exist in the current rural literature due to limited and small studies, heterogeneous rural definitions, and rural data embedded in mixed geographical studies (Rainsford et al. 2016a). Also, most rural studies are either population surveys reporting hypothetical preferences of healthy people or retrospective bereavement interviews/questionnaires of families and carers. Few studies report preferences directly from patients, i.e., those facing an end-of-life situation. Therefore, rural preferences for place of death are not clearly understood.

In contemporary rural studies, more than half of rural participants expressed a preference for dying at home; however, this is not a universal finding. Locations with stronger traditional cultures and values exhibit the strongest preferences for, and the highest numbers of, home deaths; however, these locations often have less access to hospitals, hospices, and residential aged care (Rainsford et al. 2016a). Rural residents are often considered disadvantaged by the lack of rural inpatient hospice facilities, with rural hospitals and residential aged care acting as substitutes for inpatient hospice (Menec et al. 2010). While wishing to remain home, studies indicate that many rural residents and their family caregivers accept the need to alternate between home and hospital, providing the length of hospital stay is kept to the minimum.

Currently, there is great variation in the rate of home deaths between rural settings. Rates range from just over 10% to 80%, with a large cluster around 25% (Rainsford et al. 2016a). Compared to urban residents, the chance of dying at home in rural areas is often dependent on the specific rural setting and cause of death. Rural residents who die of cancer in South Australia have been reported to have a greater chance of dying at home than urban residents (Hunt et al. 2001). Likewise, people living in rural England with COPD (Higginson et al. 2017) and living in parts of rural Europe with cancer (Cohen et al. 2010) are less likely to die in hospital than patients residing in urban locations. However, a Canadian study by Lavergne et al. (2015) reported no significant difference in the odds of dying in hospital for urban and rural residents with a terminal illness, organ failure, or frailty.

The most frequently cited reasons for leaving home are symptom control and carer distress. Factors influencing place of care/place of death in rural settings are not clearly identified in the literature but, when reported, include patients' functional status and clinical condition, carer and social networks, and health-system facilities. With

limited medical and nursing support at home to respond to changes in patients' conditions, the influence of rural residency has the potential to render rural homes, especially farms and outliers, more susceptible to become unsafe, earlier, and more frequently than most urban homes.

Deciding on place of death is a complex process, in which wishes and preferences are not necessarily the same. Rural patients change their preferences as illness progresses, with most accepting that a home death may not be possible. For many rural patients, hospital becomes their preference, and an acceptable alternative to home, especially in the last 48-hours and providing they are located within the patients' community (Robinson et al. 2010). Rural hospitals are often a substitute for inpatient hospice care.

Rural hospitals could be perceived as less safe than urban hospitals, due to the lack of specialist palliative care and expertise; however, this is often not the perception of rural patients. The familiarity and personal attention provided by rural hospitals, and the benefit of being known, creates a safe place within rural hospitals. At end of life, the inability of small rural hospitals to provide aggressive and often futile interventions is often perceived as an enabler to maintaining dignity. However, this experience is not universal. When local hospitals are perceived as unsafe, or under-resourced for "active" treatment, some rural residents choose to move away from their community, to specialist palliative care facilities or larger hospitals. Safety is not simply following procedures and policies. Safety is aligned with trust. Trust is based on prior knowledge of the hospital, and dependent on the moment-to-moment experience of care, not only for the patient but also their family. The biggest barriers to using hospital-based palliative care services for Indigenous peoples are the lack of cultural awareness by healthcare professionals and not being able to die "in country" (Kelly et al. 2009; Grant et al. 2011; Dembinsky 2014).

When available, residential aged care is a significant provider of rural palliative and end-of-life care for those aged 65 years and older; however, this option is not available in all rural regions. Availability of residential aged care varies significantly, not only within countries but between countries. In some Australian rural locations, it is not uncommon for patients who are unable to return home from hospital to be transferred to residential aged care for end-of-life care. Consistent with urban residential aged care, current workloads and staff shortages create challenges for registered nurses to be available, in a timely fashion, to attend to the acute palliative care needs of residents.

The congruence between preferred and actual place of care and place of death has been mooted as a quality outcome for palliative care, with health policies aimed at enabling people to die in their preferred place. Based on the current literature, the assumption is that for most people, the preferred place of care and place of death is home, being in a familiar place, surrounded by family and/or friends. With limited studies reporting the actual and preferred place of death, there is currently insufficient data to draw any conclusions as to the degree of congruence within rural settings.

Robinson et al. (2010) suggest that a death at home is not necessarily the most appropriate or desirable place in rural settings, due to often limited palliative care resources, especially after hours. The significant burden and cost (financial, physical, and emotional) to family caregivers, caring for a family member at home, is often overlooked. Patients may only be able to die well and have a "good death" if they leave their home or farm to die in the rural hospital. Therefore, it remains unclear if the "push" to increase the rate of home deaths in rural settings is justified.

If rural residents are unable to die at home, then most consider it important that they die within their community. Many rural residents will sacrifice access to specialist palliative care to ensure they are not displaced from their rural community. Dying within community is one factor contributing to the "good" rural death.

8 The Concept of the "Good" Rural Death

The "good death" is a difficult concept to define and is dependent on individual interpretations, perspectives, and priorities formulated by cultural, religious, and political values and beliefs.

There is significant overlap between urban and rural views, highlighting that all people, regardless of where they live, have some common needs and desire a "good death." The elements considered essential for a "good" rural death go beyond culture and ethnicity; however, the context and priority placed on each factor differ from the urban perspective (Kirby et al. 2016). The essential elements include those that maintain quality of life for the patient and their family and address the physical, emotional, social, spiritual, and cultural needs of the dying person and their family caregivers.

The dominant theme, from both developed and developing countries, is that a rural "good death" is one that is peaceful, free of pain, and without suffering (Rainsford et al. 2016b). The themes describing the "good" rural death parallel the urban view and include a "controlled" death, with control over symptoms, place of death, decision-making, manner of death, and independence (Wilson et al. 2009a, b; Veillette et al. 2010); a "timely" death, which is a death coming "naturally and after a long and well-spent life" (van der Geest 2004, p. 899) after having had opportunity to say goodbye to family; a "dignified" death by maintaining identity, self-worth, integrity, and control (Wilson et al. 2009a; Devik et al. 2013); a "social" death, such as to die within the community with family present (Wilson et al. 2009a, b); and a "noble" death such as through enduring the situation (Grant et al. 2003; Devik et al. 2013).

Rural residents consider family and community important, especially at end of life, because "the togetherness of the family members makes you feel they love you and are not abandoning you" (Grant et al. 2003, p. 163). In some cultures, the family and community play an important role after the death of a family member, by ensuring specific rituals are carried out.

The strong connection to one's rural/remote community means that dying within one's rural locality is frequently identified as a critical element in achieving a "good death." If it is not possible to die at home surrounded by family, then it is important to die within the rural community, as "home or home community… [is] the only place where the dying person [can] be close to the many people who have meaning for them" (Wilson et al. 2009b, p. 316). In Ghana, dying away from home is considered "bad" and disgraceful; however, partial restoration can be achieved by "bringing the dead body home" (van der Geest 2004, p. 909).

8.1 Physical Support (Pain and Symptom Management)

Good pain and symptom control is the overriding factor reported to ensure a "good death." Pain relief is central to maintaining quality of life through the dying journey, not just for the patient but also the family caregiver. Most dying people and families fear pain. While inadequate pain control is reported in developed countries, moderate to severe pain often dominates the lives of patients in rural sub-Saharan Africa, due to the shortage or absence of pain medication and healthcare workers (Grant et al. 2011). Anticipating medication requirements, when commuting long distances, is an important consideration for some rural patients (Pesut et al. 2010; Lockie et al. 2010).

8.2 Emotional Support

Strong emotional support is a facilitator of quality rural end-of-life care. Faith and hope are central to emotional well-being. Hope is often maintained through connection with family, friends, and being linked to something outside the illness. The serenity and peacefulness of many rural settings are an advantage of rural residency.

8.3 Social Support

As previously indicated, rural communities provide significant social support (both formally and informally) for patients and family caregivers. This support is an enabler of the "good death" and is dependent on good communication, information, the presence of healthcare professionals, and the support of other patients. The solidarity of

rural communities and mutual support of neighbors is unique to rural settings (Wilson et al. 2009a; Robinson et al. 2010).

8.4 Spiritual Support

Spiritual connection and faith foster hope, with faith seen as an enabler to persevering in life as death draws near. Faith is fundamental to rural Appalachians and their transition through end-of-life care (Mixer et al. 2014). In many rural communities, church support is not limited to spiritual issues, as congregations often also provide physical and financial support.

8.5 Cultural Influences on the "Good" Rural Death

In addition to the influence of rural residency, cultural beliefs and values influence how individuals view end-of-life care and preferences for management, interventions, conversations, and place of care and death. This chapter is written mostly from a western point of view, where there is an emphasis on individualism, autonomy, quality of life, privacy, science, and the nuclear family. Other cultures may place greater emphasis on interdependence, extended family, village community, and respect for elders and traditional healers. In more traditional rural settings, for example, Kenya, "powerful cultural traditions [make] it difficult for social needs to be met" (Grant et al. 2003, p. 163). In many developing countries, while Christianity has influenced the concept of the "good" and "bad" death, it has not replaced, but instead has been interpreted and applied to, traditional beliefs. These beliefs can significantly impact on the health and well-being of the community, descendants, and ancestors (Grant et al. 2003, 2011). The "good death" is often regarded as one that does not disrupt the life and health of the community (van der Geest 2004). In contrast, rural residents in developed countries often view the "good death" in light of a biomedical model, placing greater emphasis on autonomy, the process of dying, and minimizing any sense of struggle. Stoicism and the culture of "not complaining" are a feature of rural residents in both developed (Devik et al. 2013) and developing countries (Grant et al. 2003).

9 Summary

Regardless of place of residency, all people desire a "good death." The goal of palliative care is to ensure the dying person and their family is free of suffering and distress. However, the provision of palliative care in rural settings is variable and dependent on the degree of rurality. Currently there is no international consensus on the definition of rurality and remoteness. There is considerable individual, cultural, and ethnic diversity with regard to preferences for end-of-life care. Rural culture is distinct from urban culture, with rural residents holding unique perspectives on what it means to die well. Rural communities are close-knit and known for their social solidarity, community commitment, and loose support networks. While there are many benefits of rural residency, significant challenges exist. The needs of rural residents are shaped by decreased access and availability of services. While this potentially has a negative influence on outcomes, it is offset by local support networks. Rural palliative care is mostly primary care, with limited access to specialist multidisciplinary palliative care services. Home is the preferred place of death for most rural residents; however, when home is not possible, rural hospitals and residential aged care are considered appropriate alternatives, providing they are within ones' community.

10 Conclusion

To ensure palliative care is relevant to individual communities, it must reflect the needs of the dying person and their family, and the diverse geography and cultures of the community in which they live. While there are many similarities between urban and rural end-of-life care, there are many significant differences. Rural settings are not homogeneous. While studies indicate that rural

residents are mostly satisfied with the level of palliative care provided, there are huge, and often unacceptable, variations, especially in remote and developing regions. The universal rural theme is that if rural residents are unable to die at home, then it is essential that their place of death is within their local community.

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Informal/Family Caregivers

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Gunn Grande and Gail Ewing

Contents

Abstract

This chapter considers the importance of informal carers in enabling patients to remain at home towards the end of life, providing extensive hours of care and covering a range of caregiving tasks, including physical, emotional, and social care and monitoring. It highlights the considerable impact that caregiving has mainly on carers' psychological health, but also their general wellbeing, and it reviews the evidence on factors that predict worse impact, key elements of which are carers' own appraisal of their situation and their preparedness. The chapter describes how carers occupy two main roles: that of a co-worker and of being a client themselves, and the main areas with which they need support to enable them to support the patient as co-workers, and to look after their own health

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_52

and wellbeing as clients. It reviews the limited success interventions for carers have had to date, some of the challenges that need to be overcome, the importance of individualized, person-centered interventions, and some of the assessment tools that may help facilitate tailored support. It also highlights that assessment in itself is unlikely to be of benefit without clear procedures for discussion of and response to identified problems. Finally, it considers factors required for implementation of carer support within palliative care practice, including procedures for identifying carers, recording carer data and for intervention delivery, as well as organizational level support to sustain implementation including leadership, staff training, protected time, and carer champions. However, fundamental to achieving consistent carer support is the question of whether carers are true clients of palliative care services.

1 Introduction: The Importance of Carers

Informal carers make a substantial contribution to patient care. In the UK, it is estimated that informal carers of people of all conditions provide care to the value of £132 billion per year, close to the annual healthcare spending of £134 billion (Buckner and Yeandle 2015). In Australia, the cost of replacing the hours of informal caregiving with formal care would be equivalent to 60% of the spending on the health and social care work industry (Carers Australia 2015), while in Canada carers have been estimated to provide 80–90% of home care (Romanow 2002).

The size of the contribution of informal carers in palliative and end of life care is less clear. Caregiving hours are in this situation likely to be considerably higher compared to caregiving in general, thus representing a sizable input, but input from formal services is also likely to increase. A recent study from England found that informal caregiving amounted to more than twice the cost of formal healthcare among patients with advanced chronic disease and refractory breathlessness (Dzingina et al. 2017). Conversely, an Irish study found that informal caregiving accounted for 22% of total costs in the last year of life among patients receiving specialist palliative care (Brick et al. 2017). These estimates will depend on the caregiving context and what tasks are considered. Formal care input is likely to have been different in the two above studies. Further, Brick et al. (2017) only focused on carers' assistance with activities of daily living and out of pocket expenditure. Dzingina et al. (2017) considered hours "on call" in addition to more practical or physical caregiving tasks. Arguably, to gain a true picture of the value of caregiving (and impact on the carer), we need to consider caregiving in the broader sense, not just practical and physical elements but also their constant vigilance: a lot of carer time at home involves monitoring of the patient's condition and being on call. This in one sense mirrors the situation in inpatient care, where monitoring and being able to call on assistance when needed is an important aspect of care. Time spent looking after patients' psychological and social needs is also important in maintaining patients' psychological wellbeing and personhood, which arguably are important elements of holistic care.

Not surprisingly, the efforts of informal carers are crucial in enabling care to take place at home towards the end of life. The vast majority of patients prefer to be looked after at home towards the end of life, and although the percentage who actually wants to die at home may be smaller, these may still form the majority (Gomes et al. 2013a). Studies consistently show that the availability of carers is a major and consistent predictor of likelihood of dying at home: patients who have a primary carer, are married, live with relatives, have an extended family or carer network are more likely to achieve a home death than their counterparts (Gomes and Higginson 2006; Grande and Ewing 2008; Burns et al. 2013). Similarly, a substantial proportion of "inappropriate" hospital admissions may be carer initiated or due to carers' inability to cope (Reyniers et al. 2017; Gott et al. 2013, respectively).

Current healthcare policies often promote care in the community over inpatient care towards

end of life based on patient preferences and costs, where hospital inpatient care accounts for the majority of healthcare costs (Gardiner et al. 2017). However, sustaining care in the community is heavily dependent on carers' efforts, and this policy normally does not take into account the impact on carers and the size and economic value of their contribution (Gardiner et al. 2017). For instance, The National End of Life Care Programme (NEoLCP 2012) in England estimated that end of life community care was likely to be cheaper than acute hospital care, but this calculation only considered the costs of health and social care provision, not the costs of carers' contribution. Literature reviews indicate that the costs of palliative care is lower than standard care, but economic evaluations consistently fail to consider carers' time and out-of-pocket costs (Smith et al. 2013; Gomes et al. 2013b; Penders et al. 2017). Support for carers was explicitly excluded from the NHS Palliative Care Tariff recommended by the Palliative Care Funding Review (DH 2011) for England, despite the PCFR's emphasis on enabling patient death at home.

Proper recognition of carers' input, consideration of the impact on carers, and how we support them will be of increasing importance in the future. In the UK, the number of carers in the population increased by 16.5% from 2001 to 2015. More importantly, there was an increase of nearly 43% in carers providing 20–49 h and 33% in those providing >50 h per week (Buckner and Yeandle 2015). Our reliance on carers is likely to continue to increase in years to come, particularly for end of life care. Projections in the UK indicate there will be increases in people over 85, those with life limiting illness (Buckner and Yeandle 2015), in dependency in the final years of life (Kingston et al. 2017) and in the number deaths (ONS 2013). These demographic changes are likely to be mirrored at least across the developed world. Health and social care services are likely to struggle to meet these future demands, and carers are likely to have to make up much of the shortfall.

This chapter will give an overview of who carers are, what they do, what impact caregiving has on them and who may be worst affected, what support they need, what may help carers in terms of interventions, and how we embed carer support within palliative care.

2 Who Are the Carers?

Carers have been defined as "lay people in a close supportive role who share in the illness experience of the patient and who undertake vital care work and emotion management" (NICE 2004). They are usually first degree relatives, most often a spouse or adult child of the patient (Abernethy et al. 2009), but can also be more distant relatives, friends, or neighbors. In fact, the wider network of carers may have a more prominent role than is often realized. For instance, a population based study in Australia by Burns et al. (2013) found that of those reported providing "hands on care" for someone at end of life, only 44% were first degree relatives (a spouse, child, parent, or sibling) and 56% were extended family, friends, and others. Nevertheless, first degree relatives were more likely to do daily care and to care for a longer period. Therefore, the main burden of care is still likely to fall on the closest relatives.

Other characteristics are likely to define those who provide the most care. Abernethy et al. (2009) found that carers who provided more frequent care (daily or several times a week) were more likely to be women. Those providing more intermittent care compared to daily care were more likely to be younger (<60 years), have higher education, be in paid work and to be wealthier, as well as being more likely to be children, parents, other relatives, or friends of the patient.

3 What Do Carers Do?

Carers in general provide substantial hours of care per week. National data from England indicate that the majority of carers (62%) provide up to 19 h per week, although 24% provide 50 h or more (Buckner and Yeandle 2015). Carers of people with cancer have been estimated to provide

15–24.5 h per week (Van Houtven et al. 2010; Round et al. 2015, respectively). However, this is unlikely to reflect the intensity of caregiving towards the end of life.

To gain an overview of carer hours and tasks in the patient's final months of life, we conducted a national census post-bereavement survey of everyone who had reported the death of a relative from cancer in England during a two-week period in 2015 (Rowland et al. 2017). Respondents were asked to estimate how many hours they spent on a range of caregiving tasks in a typical week during the patient's last 3 months of life. A total of 1504 (28.5%) of 5270 relatives completed the survey and 91% provided information on hours of care. These carers reported spending a median of 69 h and 30 min on caregiving per week (interquartile range 28:37–115:15 h). Carers of people with cancer may therefore on average spend nearly 10 h per day 7 days per week on caregiving during the patient's final months. This may still not provide the full picture of informal care contributions: 60% of respondents reported receiving additional informal help in the patient's last 3 months, mostly from family, but also friends and neighbors, and the extent of this help was a median of 20 h per week (Interquartile range 7.3–50 h). While we do not have similar data for carers of people dying from other conditions, their contribution is also likely to be substantial.

Carers carried out a broad range of support tasks within their caregiving hours (Rowland et al. 2017). Most spent time on social and emotional support for the patient (83%), followed by shopping (79%), cleaning, preparing food/drink, general administration, organizing/attending appointments and helping with symptoms (all between 70–73%), personal care (64%), travelling with the patient (58%), and maintenance/miscellaneous jobs (55%).

Carers can also have considerable out of pocket expenditure in relation to caregiving. In a study of 13 European countries, Penders et al. (2017) found such expenditure in the last year of life to amount to 2–25% of median household income. In our national survey for England (Rowland et al. 2017), carers were asked to report total out of pocket expenditure during the deceased person's last 3 months. Seventy one percent reported such expenditure, with a median total expenditure of £370 among those reporting figures, including spending on travel, meals, medical equipment, and care supplies. Additionally, 17% reported "one off" expenses during the total time of caregiving with a median expense of £2000, including mobility equipment, furniture, or house adaptations. These expenditures relate to a country with public health service coverage and are likely to be considerably higher where people pay for private medical and nursing care.

4 Impact of Caregiving on Carers

Caregiving has considerable impact on carers' own psychological and physical health (Stajduhar et al. 2010). Studies have found carers to have worse psychological health compared with the general population (Dumont et al. 2006; Grov et al. 2005; Gotze et al. 2014; Kenny et al. 2010; Zapart et al. 2007), although some studies show them to have similar or better physical health than the norm (Grov et al. 2005; Zapart et al. 2007; Kenny et al. 2010). Compared with carers of people with non-terminal conditions, carers of palliative and end of life patients have worse emotional health and physical health (Williams et al. 2014; Wolff et al. 2007). They have even been found to have greater prevalence of anxiety and depression than patients themselves (Braun et al. 2007; Gotze et al. 2014; Grunfeld et al. 2004). In general, research seems to show that caregiving has the greatest and most consistent impact on carers' psychological health, and patterns seem to be similar at least across English-speaking countries and Europe (Dumont et al. 2006; Stajduhar et al. 2010; Wolff et al. 2007; Williams et al. 2014; Grov et al. 2005; Zapart et al. 2007; Kenny et al. 2010; Gotze et al. 2014).

The level of impact on the mental health among carers of palliative and end of life patients gives cause for concern. Studies using standard measures that enable identification of clinically significant levels of distress have found a prevalence of anxiety ranging from 34% to 47% among these carers during caregiving (Grov et al. 2005; Gotze et al. 2014; Grunfeld et al. 2004; Rumpold et al. 2016) and a prevalence of depression of 39%

(Braun et al. 2007). However, results may not be fully generalizable. These studies mainly have recruited carers for oncology/tertiary care (Grov et al. 2005; Grunfeld et al. 2004; Braun et al. 2007; Rumpold et al. 2016) or palliative care services (Zapart et al. 2007; Kenny et al. 2010; Gotze et al. 2014), and specialist services may produce better outcomes than generalist services. Conversely, patients referred to these services may also have more complex needs. Only Dumont et al. (2006) recruited carers both through generalist and specialist care, and found significant levels psychological morbidity to be between 41% and 62%. Only two studies have considered population data (Wolff et al. 2007; Williams et al. 2014). However, these used single item, non-standard scales of emotional impact which do not allow us to ascertain levels of clinical significance. Furthermore, most studies have included large proportions of carers of patients who are not yet in the final months of life and who may still be relatively well (Wolff et al. 2007; Grov et al. 2005; Zapart et al. 2007; Kenny et al. 2010; Gotze et al. 2014; Grunfeld et al. 2004; Braun et al. 2007; Rumpold et al. 2016), thus not indicating the full impact of caregiving on carers during the course of the patients' illness.

To gain insights into psychological morbidity and general health during end of life caregiving for a broader population of carers we investigated psychological and general health in our 2015 national census post-bereavement survey of carers of people who died from cancer in England (Grande et al. 2018). We asked for carers' retrospective reports of how they felt during the patient's last 3 months of life using the GHQ-12, a standard measure of psychological morbidity, and the EQ-VAS, an established single item scale for general health. We compared carers' reports with scores from the general population using the Health Survey for England 2014. Survey responses indicated that 83% of carers had clinically significant psychological morbidity compared with 15% in the general population, and their psychological morbidity scores were 5–7 times higher than population scores across all age groups. Carers also overall had worse general health than the general population, but differences were less marked than for psychological morbidity, and carer and population scores converged towards older age with carers age 75 and over in fact scoring better than the population. Given that these are retrospective carer reports, we have to treat the absolute scores with some caution. However, carers were surveyed 4 months post-bereavement to enhance accuracy of recall. Further, the GHQ-12 mainly focuses on psychological functioning, e.g., ability to concentrate or to make decisions, rather than more subjective general feelings. We can therefore probably conclude with some certainty that levels of psychological morbidity among carers during end of life care are very high relative to the general population.

However, it is important to recognize that many carers also can see caregiving as positive and rewarding alongside the challenges and problems experienced. We therefore must understand these positive aspects and how we can help preserve these, while seeking to ameliorate some of the negative impacts from caregiving. Reviews of caregiving (Funk et al. 2010; Li and Loke 2013) report that positive aspects of caregiving include gaining a sense of reward, personal growth, growing closer to the patient and demonstrating love, gaining a feeling of self-esteem and accomplishment, and finding life enriching and meaningful features within the experience. However, the Funk et al. (2010) review notes that these findings may reflect carer coping processes that use positive interpretation and identification of rewards as part of meaning-based ways of coping. Nevertheless, this should not invalidate these processes in any way or indicate that we should not seek to support these ways of coping.

5 When Are Carers More Likely to Suffer Negative Impacts from Caregiving?

Not surprisingly, the patient's disease burden (i.e., level of functioning and symptoms) appears to have negative impact on carers' psychological health, quality of life, and perceived burden (Stajduhar et al. 2010; Hirdes et al. 2012; Lee et al. 2013; Tang et al. 2013). Similarly carers have greater psychological morbidity (Burridge

et al. 2009; Tang et al. 2013; Grant et al. 2013; Hirdes et al. 2012) and worse health (Lee et al. 2013) as patients' approach death, where closeness to death is again likely to be associated with greater patient disease burden.

Hours of caregiving may also matter. A national survey of carers in general (Hirst 2005) found that increased hours were related to worse carer psychological health. Results are less clear for palliative care, however. Whilst some studies have found that longer hours of caregiving are associated with worse carer psychological health (Hirdes et al. 2012) and physical health (Kenny et al. 2010; Yoon et al. 2014), other hospice care studies have found no relationship (Washington et al. 2015).

Several demographic and contextual variables also affect impact of caregiving. A closer relationship with the patient may relate to more negative impact. Research indicates that spouses and/or (adult) children suffer greater psychological morbidity (Gotze et al. 2014; Hirdes et al. 2012; Tang et al. 2013) than less close relations. Spouses also report worse physical health (Park et al. 2012; Yoon et al. 2014) than other carers, but spouses may often also be older carers and therefore have worse physical health due to age. Good social network support is associated with reduced carer psychological morbidity (Gotze et al. 2014; Tang et al. 2013), health problems (Park et al. 2012), and perceived burden (Lee et al. 2013). Conversely, competing carer commitments may make caregiving more demanding. Stajduhar (2013) highlights that a growing number of carers, termed the "sandwich" generation, may be juggling caregiving for older parents with care for younger children and work which may be detrimental to their own health. However, more research is probably required into how the sum total of carers' commitments impact on carer health. Women generally report greater psychological morbidity during caregiving than men (Burridge et al. 2009; Stajduhar et al. 2010) and may also have worse physical health than male carers (Kenny et al. 2010; Park et al. 2012; Washington et al. 2015). Younger carers may suffer more psychological impact than older carers (Stajduhar et al. 2010), although Given et al. (2004) found middle aged carers to be more affected than younger and older carers, possibly representing the "sandwich generation." In contrast, older carers report worse physical health than younger carers (Kenny et al. 2010; Park et al. 2012; Yoon et al. 2014), but this may simply reflect the link between physical health and age. Carers with lower education on the whole seem to have worse psychological and physical health (Stadjuhar et al. 2010; Park et al. 2012) compared with those with higher education. Financial burden may be related to worse carer psychological morbidity (Gotze et al. 2014), and higher income or better financial support to better physical health and less perceived carer burden (Lee et al. 2013; Park et al. 2012; Yoon et al. 2014).

However, carers' own personal reactions and subjective appraisals of burden are probably more important in determining the impact of caregiving on their health and wellbeing than the actual, "objective" demands of caregiving or demographic and contextual variables. Review of the quantitative literature indicates that better outcomes are, for instance, associated with carers' perception of benefits of caregiving, as well as better preparation for caregiving and lower difficulty with tasks, a greater sense of meaning and comfort with caregiving tasks; and the feeling of greater role esteem, self-efficacy, and confidence in relation to caregiving (Stajduhar et al. 2010; Li and Loke 2013). "Reframing" coping strategies, including acceptance and redefinition, and positive religious coping also relate to better outcomes (Stajduhar et al. 2010; Li and Loke 2013). Reviews of the qualitative literature also indicates that carers often lack preparation, knowledge, and ability for caregiving and that lack of preparedness is associated with negative psychological outcomes (Funk et al. 2010). This clearly provides pointers for interventions with carers.

6 What Do Carers Say They Need Help with?

Given that carers' own appraisal of their caregiving situation is likely to be of prime importance in determining the impact of caregiving on them, it is crucial to understand how individual

carers appraise their situation, what they struggle to manage, and where they feel they need additional support. To help with this, we investigated what carers normally need support with when looking after someone during palliative or end of life care, in order to help improve individualized carer assessment and support and highlight what areas we may generally need to address to support them. We conducted a large-scale qualitative study involving 75 bereaved carers in focus groups and interviews (Ewing and Grande 2013). Participants were carers of patients who had been referred to one of five hospice home care services across the UK.

Findings showed that carers' support needs fell into two broad groups: carers needed support to enable them to support the patient in their role as a key "co-worker." They also needed support to look after their own wellbeing in their role as a "client" in their own right. Responses indicated that carers felt a deep sense of responsibility for the patient's care and may be more willing to talk about their needs as "co-workers," and more reluctant to talk about their own needs (see Sect. 8). However, we have to recognize that to fully support carers, we must address their support needs both in their roles as co-worker and client. Within each role, carers' needs for support encompassed seven broad domains (see Box 1).

Box 1 Support needs of carers as co-workers or clients during end of life caregiving

Enabling carers to care (co-worker role)	Direct support for carers (client role)
Knowing who to contact when concerned	Own physical health concerns
Understanding the patient's illness	Dealing with their own feelings and worries
Knowing what to expect in the future	Beliefs or spiritual concerns
Managing symptoms and giving medicine	Practical help in the home
Talking to the patient about their illness	Financial, legal, or work issues
Equipment to help care for the patient	Having time for themselves in the day
Providing personal care for the patient	Overnight break from caring

The 14 domains were incorporated into a Carer Support Needs Assessment Tool (CSNAT). To ensure the 14 domains captured, the support needed by carers during palliative and end of life care, we conducted a validation study with 225 carers who were currently supporting a patient who had been referred to one of six UK hospice home care services (Ewing et al. 2013). Carers completed a postal survey indicating if they needed more support with any of the 14 support need domains or with "anything else," and completed standard measures of strain, distress, preparedness, global health, and positive appraisals of caregiving. Survey results showed that all the 14 domains were used by somebody to indicate further need for support. Further, only five of 225 carers wrote that they needed help with "anything else" that was not already fully covered by the existing domains, and what they added was nevertheless very closely related to existing domains, e.g., information on services available in the area. Need for further support with the domains was significantly correlated with increased carer strain and distress, worse global health, and reduced preparedness for caregiving, but not to positive appraisals (Ewing et al. 2013). Further linear regression analysis showed that a need for more support explained the greatest variance in strain (47%), followed by global health (35%), distress (29%), and preparedness (27%), but explained very little variance in positive appraisals (9%) (Grande et al. 2012). In terms of direction of these relationships, it is probably more likely that insufficient support predicts worse carer health and wellbeing, and that a lack of carer preparedness predicts a need for more support, but the nature of these relationships requires further investigation.

The validation study results indicate that the 14 domains were both comprehensive and sufficient in capturing carers' support needs and that they related to important measures of health and wellbeing. This study and subsequent research (Aoun et al. 2015a) show that the main domain carers need more support with are "knowing what to expect in the future," "dealing with your feelings and worries," "having time for

yourself in the day" and "understanding your relative's illness." However, carers' support needs will differ and all the domains will be important to someone.

It is furthermore important to recognize that carers will differ in the individual support needs they have within any given domain and correspondingly the supportive input that they will require to meet those needs (Ewing and Grande 2013). Needing more support with symptom and medication management, for instance, will encompass a range of different support needs. These may include a need to understand the medicine regimen; what side effects to expect; being involved in discussions about symptom control; knowing at what point there is cause for alarm so that further help should be sought; or something else specific to the individual. Each of these scenarios requires different input and only the carer can define what supportive input is helpful in their case. While the 14 domains therefore comprehensively capture the broad areas that need to be considered when supporting carers, it is important that carers have the opportunity to express their individual support needs and to define what input would actually help with these needs.

7 How Well Have We Done in Supporting Carers to Date?

There is limited evidence to date that interventions have been effective in improving carer outcomes. An early systematic review by Lorenz et al. (2008) found that in general there was moderate evidence that palliative, supportive, and end of life care interventions increased carer satisfaction, but only weak evidence that such care actually improved carer outcomes This review did, however, find moderate evidence that interventions for carers of people with dementia were beneficial, but these may not necessarily be relevant to other palliative and end of life carers (e.g., they may focus on dealing with behavior problems or personality change). A Cochrane review (Candy et al. 2011) of supportive interventions, mainly to improve the psychological health of carers of patients in the terminal phase of their illness, found that interventions reduced carer distress short-term, but the effect was small (effect size $d = 0.15$). Further, there were no significant improvements in coping and quality of life. A more recent Cochrane review of home palliative care interventions by Gomes et al. (2013b) concluded that the overall evidence for improvement was nonsignificant, inconclusive, or conflicting with only some individual studies indicating shorter term improvement in burden, sense of reward, or reduced distress.

Part of the problem in assessing the effect of palliative and end of life interventions on carers is the wide range of interventions considered, so that it is difficult to draw clear and consistent conclusions and establish the "active components" of an intervention that may make a difference. Lorenz et al.'s (2008) review included regular palliative care and enhanced palliative care, group interventions and individual interventions. Gomes et al. (2013b) considered both regular and enhanced home palliative care, which again comes in many forms. Candy et al.'s (2011) review was more focused but still encompassed a considerable range of supportive interventions. Another problem is that many of the above interventions were mainly aimed at the patient, e.g., home palliative care, so it is perhaps unsurprising that they did not show a clear impact on carers, although there was a hope that carers would benefit. Further, even when interventions are targeted at carers, there may be a lack of effect because the intervention that is offered does not fit with what carers actually need (Buck et al. 2013; Levesque et al. 2010). Conclusions from Lorenz et al.'s review (2008) were that interventions were more likely to be effective when they were individually targeted and when they had multiple components (not just focused on one aspect).

To achieve meaningful improvements in carer outcomes, we therefore probably need to design interventions that are specifically focused on carers, more responsive to their individual needs and that address the range of needs or problems they may have. This means we need to understand the perspective of carers themselves; look at the whole individual; and let carers define what

they need and let that drive the intervention. This comes back to asking carers themselves what it is they need support with, and sits squarely within the person-centered, holistic approach to support and care which is normally seen as core to palliative and end of life care.

8 Fitting Interventions to Carers' Considerations, Situation, and Individual Needs

There are several challenges that have to be overcome to ensure a fit between intervention (or support offered) and carers: negotiating carers' dual role and ambivalence at receiving help; restraints of location, time, and energy; and ensuring support fits the needs of individual carers.

As we have seen, carers have a dual role as both co-worker and client. Norms and expectations (held by carers themselves, but also sometimes by patients, family, and services) mean that carers often do not see themselves as legitimate care recipients and are ambivalent about receiving help or taking a break from caregiving. Carers may only accept support if they feel this will help them care and does not take resources and attention away from the patient (Harding and Higginson 2001). To provide effective support, we need to recognize these dynamics, help legitimize the expression of need for help and support, and ensure that help is on carers' own terms. This is likely to require a proactive approach as carers themselves are often reluctant to express what they themselves need help with, may not know what aspects of support are available or what it is legitimate to ask for support with. While volunteering that they need help is often difficult for carers, being asked about needs and/or offered help as part of an established, formal process may help overcome barriers. It may also help if this is done in such a way that carers do not have to express their needs in front of the patient (Ewing and Grande 2018).

Any standardized interventions need to be sensitive to the dilemmas and constraints of the carer role. They need to recognize the potential conflict between carers' desire to sustain caregiving and looking after their own needs. Respite may for instance be easier for carers to accept in the form of briefer daytime breaks or overnight sitting, rather than inpatient admission. Help with the patient's personal care may be more acceptable if the carer can still be present and involved. In each case, it is important to know what carers want; some may want a complete break from caregiving, but for others this can be hard to accept, although they need a rest and some support. Interventions that depend on carers leaving the patient, e.g., to attend group activities or therapies, are often also practically difficult for carers, unless formal care for the patient forms part of the intervention, and even then carers need to feel this is an acceptable solution for the patient. Carer interventions that can be delivered at home or during delivery of day care, outpatient or inpatient care for the patient may therefore prove more feasible. Joint patient/carer interventions may provide a solution and be desirable where the aim of the intervention for instance is to foster communication or joint problem solving. However, this may inhibit expression of carers' own needs and concerns. Interventions that to some extent can be tailored are also likely to be of more use to carers who will have limited time and energy. For instance, one can hypothesize that access to bitesize, individualized information is likely to be more helpful than bigger, standardized chunks. Any standard intervention needs to be developed from carers' perspective to ensure they actually fit carers' situation and address what they need. It is therefore essential that we engage carers in the design of general interventions or support services for carers.

If we are to provide more individualized support, however, this normally requires individual assessment of need for support. There are two broad approaches that can be taken to assessing carers' need for support: assessment of adverse effects of caregiving or more direct assessment of the problems that carers need support with.

Assessment of adverse effects of caregiving enables identification of carers that are suffering particularly high impacts from caregiving, which enables us to focus intervention resources on

those most in need of help and most likely to benefit from intervention. Numerous tools exist that may be used for assessment of adverse effects during caregiving (Hudson et al. 2010). The main groups of adverse outcomes that have been considered include psychological morbidity, subjective burden, and quality of life. Measures of psychological morbidity have not been developed specifically for carers, but general measures have successfully been used with the carer population. These include the Hospital Anxiety and Depression Scale (HADS), the Beck Depression Inventory (BDI) (Hudson et al. 2010), and the General Health Questionnaire (GHQ-12) (Grande et al. 2018), all of which are relatively short (12–21 items) with good reliability. The single item Distress Thermometer has also been used as a brief screening tool for anxiety and depression in carers to identify those who may require further follow up (Zwahlen et al. 2008). Measures of subjective burden, or strain, have been specifically developed for carers to capture burdens related to the caregiver situation. These include the Zarit Burden Interview (ZBI), the Caregiver's Burden Scale in End-of-Life Care (CBS-EOLC), and the Caregiver Strain Index (CSI) (Hudson et al. 2010). Again these are relatively short (13–22 items) with good reliability. The Family Appraisal of Caregiving Questionnaire for Palliative Care (FACQ-PC; 25 items) seeks to capture both strain and distress, as well as positive appraisals (Hudson et al. 2010). Questionnaires that have been used to measure carers' quality of life include both generic questionnaires and questionnaires specifically developed or adapted for carers. The former include the SF-36 and the Quality of Life Scale (QOLS) (16 items). The latter include the Quality of Life in Life-Threatening Illness – Family carer version (QOLTTI-F) and the Caregiver Quality of Life Index – Cancer (CQOLC) scale (Hudson et al. 2010) with 16 and 35 items, respectively, all again with good reliability.

These measures can give an indication that a carer is experiencing adverse effects from caregiving likely to need further intervention. However, these measures still require us to then identify the individual areas of difficulty or needs the carer has as well as appropriate courses of action to help ameliorate the psychological morbidity, burden or poor Quality of Life. Appropriate action may for instance be to target carers' psychological appraisals of caregiving burden and improve coping, resilience, and capabilities, or more direct intervention with the day to day problems they experience with caregiving. In any case, actions should involve discussion with carers regarding what may help. Further, one would ideally want to try to intervene before burden, psychological morbidity and deteriorating quality of life reach critical levels, where possible.

Here more direct assessment of the issues that carers need support with or that give rise to distress can help by providing practical pointers for meaningful action or earlier intervention to prevent adverse impacts reaching critical levels. Tools that may help with this include The Needs Assessment Tool – Caregivers (NAT-C), Carer Support Needs Assessment Tool (CSNAT), Carers' Alert Thermometer (CAT), and The Family Inventory of Needs (FIN). The NAT-C (Mitchell et al. 2010) is a 32 item tool developed from the literature and 25 interviews with practitioners and carers. It can be self-completed by carers or together with a practitioner and enables carers to indicate their levels of concern on a range of issues including physical and psychological wellbeing, spiritual, existential, social, financial and legal concerns, and whether they would like to discuss them with their GP or other practitioner. The CSNAT (Ewing and Grande 2013), as previously noted, contains 14 items or domains and was developed from focus groups with 75 bereaved carers. It is intended to be self-completed by carers and enables them to indicate whether they need more support with looking after the patient or with preserving their own wellbeing (Box 1). The Carers' Alert Thermometer (CAT) (Knighting et al. 2016) contains 10 items about the carers' caring situation and their health and wellbeing. It is designed for practitioners to complete to identify any alerts that require further intervention. The Family Inventory of Needs (FIN) (Kristjanson et al. 1995) identifies areas of importance to the carer where services "fall short." Its

20 items represent a range of needs, mainly in relation to information including having questions answered honestly, knowing what treatment the patient is receiving, and what to do for the patient. It enables carers to rate how important each item is to them and indicate the extent to which these are met by practitioners.

However, assessment tools in and of themselves are unlikely to improve carer outcomes. If used as a questionnaire or form without subsequent discussion of, and response to, identified problems, none of these tools are likely to have beneficial impact on carer outcomes. Both the NAT-C and CSNAT are examples of tools that have been designed to be used as part of a defined intervention process, and whose impact has subsequently been tested through trials. In the NAT-C intervention, the completion of the tool by the carer is intended to be followed by a discussion of the NAT-C with their GP or other practitioner. As part of the process, the GP is supported by resource folder outlining potential carer problems and suggested resources and strategies that may help (Mitchell et al. 2010). A randomized controlled trial of this intervention with GPs indicated that for carers with clinical anxiety at baseline, the intervention improved mental wellbeing, and for those with clinical depression at baseline, the intervention slowed the worsening of depression (Mitchell et al. 2013).

The CSNAT is explicitly designed be part of a person-centered process that is led by the carer, although facilitated by practitioners. Early CSNAT feasibility work with practitioners highlighted the important features of this process to ensure it has meaningful impact and represents a truly person-centered comprehensive approach (the CSNAT Approach; Ewing et al. 2015). The CSNAT Approach is encapsulated in five stages, which also have relevance for other assessments: (1) Introduction: It is important to ensure the carer understands that the tool is part of a process of assessment that gives them the opportunity to consider their own support needs as distinct from the patient not just another leaflet or form. (2) Carer consideration of needs: The carer needs time to consider what areas they need support with, in privacy if required. Whatever time they require, carers need to know they will then have opportunity to discuss identified support needs with a practitioner. (3) Assessment conversation: In completing the CSNAT, the carer will have highlighted domains where they need more support and then prioritized those most pressing for them at the moment. The focus of the conversation is on the carers' individual needs within the domain(s) they have prioritized, to establish the particular issue they need help with and what supportive input they feel would help in relation to this. As highlighted earlier, carers will differ in the supportive input that they need within each domain, so it is important not to work from set assumptions by the practitioner as to the problem and its solution. (4) Shared action plan: Supportive input is based on the assessment conversation; it summarizes and documents actions put in place. This can take different forms: actions carers themselves take to access support (self-help or help from family); support directly delivered by practitioners such as "active listening," reassurance, advice giving, provision of information (which may be accomplished within the visit/contact); signposting the carer to other sources of support or referral to other agencies. Not all support needs have to be met by the practitioner or their organization. (5) Shared review: Carers' support needs change and so review of their situation needs to be ongoing. The prompt for a review can come from either the carer or the practitioner. It is important that carers are aware that they may raise their support needs at any time.

Further feasibility studies and trials showed that use of the CSNAT to support carers was seen as valuable both by practitioners and carers. Practitioners felt that use of such an assessment tool opened up different conversations with carers, challenged their assumptions regarding what carers needed help with, and improved expression, visibility and "legitimacy" of support needs (Ewing et al. 2016). The carers themselves felt that this helped them identify and express support needs that would otherwise not be possible; that it enabled necessary reflection, although this could at times be challenging; and that it provided them with validation, reassurance, and empowerment (Aoun et al. 2015b). Cluster

trials of the impact of the CSNAT intervention on carer outcomes found that the intervention group had significantly lower levels of strain during caregiving from baseline to follow up (effect size, d = 0.35) (Aoun et al. 2015a) and that they had significantly lower early grief and better psychological and physical health post-bereavement (Grande et al. 2017).

9 How Do We Implement Carer Support in Practice?

Successful development and trialing of interventions will not be of broader benefit unless evidence-based practice can be implemented and integrated into mainstream care. This normally entails a change in practice, which requires change not only at the level of individual practitioners but also at organization level to provide the structures and processes needed to support implementation and sustain it longer term, beyond a research project or practice initiative. The challenges of implementing change can be overlooked within policy, practice, and research. The MORECare Guidance for palliative care research recommends that implementation should be considered from the outset, within development, piloting and testing stages (Higginson et al. 2013).

In England, the Government's strategy for palliative care has for a long time highlighted that there should be assessment and support for carers as well as patients (DH End of Life Care (EOLC) Strategy 2008; NPEoLP Ambitions for Palliative and End of life Care 2015). Yet within this strategy, there has been no consideration of how this will be implemented in practice for carers. It was largely in response to this gap in the Government's 2008 strategy that the CSNAT was developed. However, our feasibility testing, trial, and implementation work with the CSNAT intervention helped us begin to identify the factors that need to be in place for successful implementation of change in practice in general and the assessment and support for carers in particular.

These lessons were consolidated and extended in a UK project to develop key recommendations for implementation of comprehensive, person-centered carer assessment, and support in end of life care. The project involved research review and stakeholder consultation through three interlinked stages: (1) secondary analysis of rich data from pragmatic implementation of person-centered carer assessment and support within 36 palliative care services using the CSNAT intervention; (2) new focus groups with hospice practitioners/leads, and (3) wide consultation with stakeholders from hospice, hospital, community, policy, and academia as well as carer groups to confirm and validate the set of recommendations. Box 2 lists the resulting ten recommendations, all of which were identified as key issues for implementation of carer assessment and support in practice and not consistently met by current provision in end of life care. Broadly, the first four recommendations indicate what needs to be

Box 2 Ten recommendations for achieving organizational change to enable provision of comprehensive, person-centered assessment and support for family carers towards the end of life

1. Consistent identification of carers within the care setting.
2. Demographic and contextual data on who the carer is and their situation.
3. A protocol for assessing carers and responding to the assessment.
4. A recording system for carer information, separate from patient data.
5. A process for training practitioners about carer assessment and support.
6. Available time/workload capacity for carer assessment and support.
7. Support from senior managers for carer assessment and support.
8. Role models/champions for carer assessment and support.
9. Pathways for communication about carer assessment and support.
10. Procedures for monitoring/auditing processes and outcomes of carer assessment and support.

embedded in organizations to provide person-centered support for carers and the remaining six are the structures and processes needed to successfully implement and sustain this approach in practice. Together they illustrate the whole-systems approach that need to be taken to implementation (Ewing and Grande 2018).

While developed for carer assessment and support, these principles are likely to have general applicability for implementation of interventions to support carers. The context for each recommendation is described in more detail below.

Underpinning any carer interventions is the need to know who the patient's main carer or carers are. Current practice of carer identification can be quite ad hoc, allowing many carers to slip through the net. A more systematic and proactive approach is necessary for **Consistent identification of carers within the care setting** as many carers do not self-identify and can miss out on much needed support. This is particularly the case where they see themselves in relationship terms, as a wife/husband or son/daughter of the patient and do not recognize themselves as a "carer." In these circumstances, a questions such as "who provides the patient with most support" (who is not a healthcare professional) can be helpful in carer identification.

Closely linked to carer identification is the recommendation for **Demographic and contextual data on who the carer is and their situation**, to aid communication with carers and awareness of their circumstances. Even where carers are known to palliative care services, there can be a lack of documentation about them. Our project found this was particularly the case in hospital settings where the primary focus is on the patient but was also true in hospices. There was a lack of basic information such as number of carers known to the organization, and even for identified carers contact information and basic details about their situation or needs were often not recorded. This again makes it difficult to sustain meaningful intervention.

The project's third recommendation – **A protocol for assessing carers and responding to the assessment** is a principle that translates to implementation in general, in that there has to be a clear protocol for how any new intervention is to be delivered in practice. In terms of delivering consistent carer assessment and support, this normally represents a considerable practice change: identification of carers' needs may currently be missed altogether, and when it does take place, is often an informal, practitioner-led approach conducted as part of the patient assessment or takes the form of "doorstep conversations" (Ewing et al. 2015) when carers don't want to talk in front of the patient. Further, solutions are often based on practitioners' assumptions rather than identified by carers. A clear protocol is a prerequisite for implementing consistent, comprehensive, person-centered carer assessment and support. This puts carers on a more equal footing to patients and helps legitimize their support in palliative and end of life care.

A recording system for carer information, separate from patient data, is to ensure that information on carers is recorded in a defined location for record keeping and future reference. This is an issue linked to consistent carer identification and data gathering. If this information cannot be easily accessed and utilized, it is unlikely to aid effective interventions. Current health record systems focus on patients: any information that is recorded about carers is usually done within the patient record, often under family support. However, a systems change in recording processes is needed if carers are to be consistently identified and supported. Flexibility to develop separate carer records will vary across settings with particular challenges for hospital-based palliative care teams, but many hospices are already developing separate carer record systems.

Fundamental to achieving consistency in practice with carers is putting in place **a process for training practitioners about carer assessment and support**. Training is core to ensure everyone is on board with the purpose and procedures of the

intervention and how it is different from existing practice, otherwise what may be a beneficial intervention at conception, may change to become ineffective or even detrimental in its implementation (Neuberger et al. 2013). It is, for instance, important to identify the differences between a comprehensive, person-centered approach and current practice for those already working to support carers in everyday practice. Training about carer assessment and support also has resonance across all settings and at all stages: from broader carer awareness raising early in nurse education to understand the key role of carers in end of life care; to assist more junior frontline staff who are unfamiliar with identifying carer needs; through to more experienced practitioners who feel they "already do" carer assessment and support, providing an opportunity to "up their game."

Available time/workload capacity for carer assessment and support: For implementation of any intervention, organizations need to consider how to make sufficient time to plan, implement, and sustain a change in practice. For carer assessment and support the leadership in organizations needs to decide whether this is part of their "core" business, rather than an "add-on" to patient care, only when time allows. If core, organizations need to consider how to make sufficient time for meaningful implementation. Investment of time on carers in the short-term can achieve longer-term gains in averting crises. However achieving capacity at practitioner level for this new way of working not only requires a mind-shift away from a focus solely on patients but also time and resources for its practical implementation by frontline staff.

Support from senior managers for carer assessment and support: This is crucial to provide a wider strategic overview and the authority for implementation of new interventions across all settings. This includes (1) initiating the change from current practice and (2) driving forward the new way of working through facilitating training and ensuring workforce capacity for implementation. Input from senior managers is vital to sustaining the change to comprehensive, person-centered assessment and support in the longer term, through review, improving processes and providing evidence to commissioners to support palliative care delivery for carers, not just patients.

Role models/champions for carer assessment and support: This highlights the need for organizational support at several levels for implementation. Rather than managers, champions need to be credible practitioners committed to the new intervention and able to promote its implementation in practice. Champions provide essential facilitation through creating a positive culture around the new way of working, cascading training and support to practitioners working with carers as well as acting as a source of advice. Organizational investment in the role is crucial to ensure champions are supported and have the necessary resources but also that the role continues even if the original post-holder moved on.

Pathways for communication about carer assessment and support: Different communication processes are important to embed and sustain new ways of working. This needs to operate both between and within different organizational levels. Two-way processes are required: (top down) from service leads and champions to communicate what is expected of practitioners and to provide help and advice, but also (bottom up) feedback by practitioners who are implementing a new intervention about what is helping or hindering its use in practice. Putting in place peer discussions for problem solving and sharing of good practice provides further opportunities to support a different way of working.

Procedures for monitoring/auditing processes and outcomes of carer assessment and support: This is not always well done within palliative care services; yet these are key organizational activities for internal purposes to measure progress towards targets and review work done by the services in supporting carers. Crucially, these processes can communicate impact of service delivery on carer outcomes, demonstrating achievements in carer assessment and support to external agencies such as commissioners of palliative care services and other funding bodies.

Overall, achieving comprehensive, person-centered assessment and support for carers is not without challenges for palliative care delivery. The first main challenge is that this way of working with carers is not commonplace: It represents a substantial change in practice for end of life care, not just for practitioners directly supporting carers but for organizations in terms of the structures and process that need to be in place. The ten recommendations identify the building blocks to achieving the necessary organizational changes. There is, however, a second and perhaps more difficult challenge of addressing the question of where carers "fit" within palliative care provision. Since its beginnings, palliative care has had an ethos of services being there for the carer and family, not just the patient. While this is a strong philosophy, its translation into practice is hindered by the many issues underpinning the ten recommendations. If carers are to be identified, assessed, and supported in end of life care, the fundamental question of whether or not they are to be viewed as true clients of services (and therefore their care and support can become legitimized through commissioning and funding processes) has to be addressed.

10 Conclusion and Summary

This chapter has shown that family carers provide vital support for patients towards the end of life. Formal services clearly have an essential part to play, but resource constraints mean that the time and support they can provide will always remain limited. Family carers therefore undertake the main bulk of patient care and support and make care at home viable. Our dependence on carers is likely to increase in light of a projected increase in the older population and number of deaths.

Carers suffer adverse consequences from caregiving, particularly in terms of their mental health. The prevalence of clinically significant psychological morbidity among carers during end of life care may indeed be so high that it can be deemed a public health problem. However, there is considerable individual variation in who is most affected. While the patient's disease burden and hours of caregiving have some impact on carers' health, impact also depends on carers' demographic characteristics and context, and in particular on carers' own subjective appraisals and preparedness for caregiving. This indicates that there is considerable scope for intervention.

In terms of what may help, carers support needs fall into two broad areas: firstly, they need support to enable them to support the patient, in their role as "co-workers"; secondly, they need support to look after their own health and wellbeing, as "clients" in their own right. Both areas need to be addressed if we are to fully support carers. It is important to realize that the type of supportive input carers need in each case varies greatly from individual to individual, and that "one size does not fit all." This implies that it is important to take an individualized approach to carer support and to ensure that the assessment of carers' support needs and identification of what supportive input would help, is carer-led.

Reviews indicate that interventions to support carers so far have had fairly limited success. Part of the problem may be that interventions have not been specifically designed to support carers or that what is provided has not matched what carers actually need. Again more individualized interventions that encompass a broader range of needs appear to be more successful. Further, any intervention should be designed with carers' situation and concerns in mind and include meaningful carer involvement in its development.

Individualized, tailored intervention is difficult to achieve without some form of assessment of need. This may be in the form of assessing which carers are suffering critically high levels of adverse impact on their health and wellbeing and focusing efforts on these carers. However, this still requires identification of what intervention is appropriate. Assessment may also be in the form of directly assessing what carers say they need more support with, to enable more direct and potentially more preventative interventions with carers. However, assessment in itself is not likely to be beneficial without subsequent discussion and follow up.

If we are to implement carer support within mainstream palliative care practice, this is likely to require a considerable change in practice which entails a whole-systems approach to implementation. Such a whole-system implementation would need to encompass organizational procedures for identifying carers and recording carer information, as well as protocols for how to support carers. To implement and sustain such a change, wider organizational support is also required in terms of leadership, staff training, champions for driving change forward, protected time for supporting carers, communication pathways, and procedures for auditing and monitoring change.

However, the fundamental, underlying question that needs to be addressed if we are to provide consistent, meaningful carer support within palliative care is where carers fit within palliative care provision. We have to decide whether supporting carers is simply an add-on which only is covered on a more intermittent basis or whether it is part of "core" business which is consequently funded and has protected time.

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Volunteers in Palliative Care

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_120

Abstract

Volunteers are key members of the hospice and palliative care team. In some countries, they are the only source of care provision for a person at a palliative stage of a disease. This chapter highlights both the importance of volunteers in these settings and the impact their contribution makes to care. The chapter covers the definitions of volunteering, the historical development of volunteering in hospice and palliative care, as well as research evaluation to document volunteer practice, an understanding of their distinct role in patient and family care, and assessment of their impact on patients and their families experience. The chapter also provides five case studies from volunteers across the world on their experiences in volunteering.

1 Introduction and Aim of the Chapter

Like the concepts of hospice and palliative care, volunteering can be described variously. For volunteering what is distinctive and important in these settings is that volunteering is inextricably linked to the development of the modern hospice and palliative care movement. Volunteering is also distinctive and important in hospice and palliative care because of the breadth and depth of volunteer involvement not only in directly supporting the provision of care but in leading some services, in administrative roles, in fundraising, and in influencing organization and the care it provides. Volunteers may also have a special and unique role in direct patient and family care. This has been described as "being there," which may involve a social or quiet presence, and a link between the patient and their family and health professionals. Reliance in hospice and palliative care on the work of volunteers is likely to increase with the aging global population and increased recognition of the need to provide access to hospice and palliative care to all irrespective of disease.

Research evaluation in hospice and palliative care is needed to both evaluate what interventions work and what work best and where. Evaluation is also needed to help understand how an intervention may work. Such research evaluation includes the contribution of volunteers. With finite resources in hospice and palliative care and a growing demand for these services, it is important to know how best to involve and support volunteers, to recognize their distinct contribution, and to sustain the large contribution they make in these settings.

The aim of this chapter is to provide an overview of both the importance of and evidence on understanding the role and impact of the contribution of volunteers in hospice and palliative care.

2 What Do We Mean by Volunteering in Hospice and Palliative Care?

Before focusing on volunteering in hospice and palliative care, it is worth considering volunteering more generally in order to gain an

understanding of its breadth, diversity, and complexity. Volunteering means many things to many people. For some, it can be seen as a force for good in making a difference, yet for others it can be a reminder of difficult times, for example, under some communist regimes, where volunteering was compulsory for children and adults. As a result, volunteering is often less prevalent in former communist countries. The word "volunteering" in reality encapsulates a diverse range of people of all ages, motivations, skills, activities, and contexts. We will, therefore, explore a number of volunteering constructs before narrowing these down to be clear about what we mean by volunteering in hospice and palliative care in this chapter. The United Nations (UN) describes volunteering as happening at all levels: individual, community, national, and global (United Nations 2015). They consider that volunteering encompasses "traditional forms of mutual aid and self-help, as well as formal service delivery" in addition to "enabling and promoting participation and engaging through advocacy, campaigning and or activism" (p. xiv). The UN defines volunteering as "activities ... undertaken of free will, for the general public good and where monetary reward is not the principal motivating factor" (United Nations 2015, p. xiv). In seeking to apply more generic volunteering definitions to hospice and palliative care, the European Association of Palliative Care (EAPC) Task Force on Volunteering in Hospice and Palliative Care arrived at a specific definition following consultation across a number of countries. They propose the following definition in their EAPC White Paper "...the time freely given by individuals, with no expectation of financial gain, within some form of organised structure other than the already existing social relations or familial ties, with the intention of improving the quality of life of adults and children with life-limiting conditions and those close to them (family and others)" (Goossensen et al. 2016).

Within such a broad definition, there are necessarily many different volunteering models and structures ranging from informal to formal. Informal volunteering may be defined as individuals giving help without payment to others outwith their family (Rochester et al. 2016). This type of volunteering often operates outwith any recognized organization and often within local communities (United Nations 2015). One example of this might be the person motivated by the plight of refugees who travels overseas to provide help as an independent individual, unrelated to any organization. In contrast, Rochester et al. (2010) describe formal volunteering as help for which no remuneration is given, which benefits people or the environment and is undertaken through organizations (Rochester et al. 2016). An example of this would be the person who offers specific help regularly on a voluntary basis within an statutory, not-for-profit, or private organization.

Volunteering in hospice and palliative care is often only understood solely in terms of formal volunteering traditionally seen in many well-resourced countries, and that is provided within a dedicated hospice, at home, or in specialist units within a general hospital. This is typified by a hierarchical structure within which volunteers are managed by paid staff, work regularly in specified roles within limited and boundaried activities. This structure, however, does not include all possible ways of volunteering in hospice and palliative care in different countries. For instance, the community (and volunteer) led approach to volunteering in hospice and palliative care as seen in countries such as India or Africa and the "almost-at-home-houses" well established within the Netherlands (Kiange 2018) in addition to those within the UK such as Hospice Neighbours and Compassionate Neighbours. In reality, therefore, within hospice and palliative care volunteering in the same way as in the wider context of volunteering, there is a spectrum of volunteering.

What we mean by volunteering in this chapter, therefore, draws upon the definition from the EAPC Task Force on Volunteering White Paper, recognizing that hospice and palliative care volunteering encompasses a broad spectrum of activities and structures ranging from more informal volunteer-led approaches to formal service delivery models (Goossensen et al. 2016). Having arrived at a working definition, the next section

will now go on to consider some of the origins of hospice and palliative care volunteering.

3 History of Hospice and Palliative Care Volunteering

Hospice and palliative care has evolved in diverse ways in different countries, often influenced by culture, society, and available resources (Morris et al. 2013). This can also be seen in the development of volunteering. It is beyond the scope of this chapter to consider this in detail, and so this section will give a brief overview giving examples from a number of countries.

In many countries throughout the world, volunteering is inextricably linked to the development of hospice and palliative care services and the support that the services offer to patients and families. Scott (2015) suggests that volunteers were instrumental in establishing many palliative care services particularly hospices (Scott 2015), while Radbruch and Payne (2010) describe the development of hospice care in general as "a civil rights movement based on volunteering" (Radbruch and Payne 2010) (p. 26). The work of Dame Cicely Saunders, considered by many to be the founder of the modern hospice movement, has been influential in the development of palliative care in many countries. Having worked as a volunteer herself, she was committed to the involvement of volunteers as a fundamental part of St Christopher's Hospice in London, UK, from its inception in 1967 (Howlett and Scott 2018).

A Volunteer in Australia Describes Her Experiences

My journey volunteering began in 2013 when I decided to apply to Concord Palliative Care Unit. I went to the orientation with no idea of what was actually involved but just knew that I wanted to "put back" something into the community. I was excited to be part of the team in palliative care that could make just the smallest amount of difference at a time when both the patients and family were under duress. For 12 months, I did the weekend "jolly trolley," taking around an array of sweets and beverages. It was almost like the naughty trolley and many of the patients loved the fact that even though they were desperately ill, they could sort of cheat a bit and eat and drink things perceived "not allowed." Many times they just loved to chat and pass some time before loved ones arrived. Others shared intimate life experiences and confided their most inner thoughts and frailties. I felt so privileged to not only get a firsthand account of their lives but also to feel like I was in the inner circle. To them they reached out to a stranger and for just a small amount of time felt connected to the outside world, not the new world they had become accustomed to, and had some sort of normality. In turn, each week I would walk away knowing that in some shape or form I had given them just a little respite from their stresses and made them feel like they were important and valued. Many did not have family and friends, and even though it saddened me to think that they were going it alone, they weren't totally alone, because as a volunteer I was there to ensure that they had a helping hand and I was there to listen and also support them in the little time they had. I felt like I was part of one of the most important, intimate part of a patients' life, and it humbled me.

In Austria and Poland, it was volunteers in conjunction with catholic and protestant churches who were influential in establishing hospice and palliative care services (Krakowiak and Pawłowski 2018; Pelttari and Pissarek 2018). In Poland, it is interesting to note that this development took place in the face of significant political opposition (Krakowiak and Pawłowski 2018). In Germany, hospice and palliative care volunteering developed "in parallel" with palliative medicine. Hesse and Radbruch (2018)

describe this as a "citizen's movement" motivated by poor societal attitudes to death and dying (Hesse and Radbruch 2018) (ibid.). Volunteering emerged somewhat differently in Australia where UK hospice models (involving dedicated hospice units within the community) were less common with palliative care considered as a clinical rather than community issue (Huntir 2018). Volunteers, therefore, became involved in hospitals and community health centers or separate not-for-profit organizations with close links to hospital networks (ibid.). In the Netherlands, having considered the UK hospice model, there was a move toward more community-led hospice care (Goossensen and Somsen 2018). While in many countries hospice and palliative care development was a reaction to poor care of the dying, in Africa, the involvement of volunteers was in response to the overwhelming challenge of communicable diseases such as HIV and TB (Kiange 2018).

So far the focus has been on adult services, and it is worth taking a moment to consider what is known about volunteers within pediatric hospice and palliative care. Children's services developed at a later date than adult, when the first children's hospice, Helen House opened in Oxford in the UK in 1982. In the UK, however, the children's hospice and palliative care sector was slower to embrace volunteering than their adult equivalents. Burbeck et al. (2013) suggest this may be due to stakeholder anxiety about the complexity of the children's conditions and the number of professionals already involved in the lives of families caring for a child with a life-threatening and life-limiting condition and issues involved in safeguarding children and young people (Burbeck et al. 2013). Volunteering in this sector has evolved to a stage where currently in the UK most not-for-profit children's hospices and some voluntary and statutory community pediatric palliative care teams now involve volunteers. Likewise in Austria, volunteers often take care of siblings, and there is a special curriculum for volunteers in pediatric hospice and palliative care.

What seems to emerge from this history is the strong influence that people from local communities can have in responding to the palliative and end of life care needs of others.

4 Influences of and on Volunteering in Palliative Care

As we have seen in the last section, volunteers made a significant contribution to the development of hospice and palliative care in many countries. The involvement of volunteers, however, necessarily has significant influence on organizations. As members of the local community offering their time and skills with no expectation of financial reward, volunteers bring a wide range of skills, individual values, and perspectives that affects organizational culture and values. Indeed Scott (2013) identifies a number of key organizational areas which are influenced by volunteers including (1) diversification of available skills, such as professionals providing their skills as volunteers, and service quality, (2) leadership and governance, (3) financial sustainability, and (4) support of local communities and general public (Scott 2013).

This section, therefore, focuses briefly on the role of volunteers (discussed in more depth in further sections) in order to explore how different volunteering activities influence both the care of patients and families and the organization more widely. It is important to recognize that volunteering in turn is also affected by a range of external factors, and this section also explores the ways in which volunteering can be affected by societal and demographic factors.

In considering the diversity of volunteering roles in hospice and palliative care, the EAPC Task Force in Volunteering White paper, as earlier mentioned groups these under three distinct headings: (1) volunteers from local communities who provide direct practical or social support to patients and their families, or who provide other skills to the organization which may include fundraising, administration, catering, and gardening; (2) governance volunteers, trustees, and board members of hospices and other not-for-profit services; and (3) professionals using their professional skills in a voluntary capacity, for example, doctors, nurses, and chaplains (Goossensen et al. 2016). These roles may take place in many different settings including inpatient hospices, day hospices, in the

community in patients' homes, hospitals, specialized units and elsewhere, and care homes (Goossensen et al. 2016).

Volunteers enable hospice and palliative care services to increase the range and enhance the quality of services offered (Scott 2015). A brief scoping of the research literature indicates that volunteers can have a beneficial influence on the care of patients and families; this includes that they can help to make care more person centered and less medicalized (Morris et al. 2015; Claxton-Oldfield 2015a; Block et al. 2010; Wilson et al. 2005; Pesut et al. 2014), while Luijkx and Schols (2009) highlight that volunteers make life less stressful for families caring for a loved one at end of life (Luijkx and Schols 2009). Indeed Herbst-Damm and Kulik's (2005) study found that volunteer support can extend survival time in terminally ill patients (Herbst-Damm and Kulik 2005). A more in-depth discussion of the research evidence on the impact of volunteers in hospice and palliative care can be found in Sect. 6 of this chapter.

The role of volunteers in the leadership and governance of not-for-profit organizations is often little recognized. As trustees (or non-executive board directors), these volunteers carry strategic and legal accountability for ensuring that organizations in particular hospices are effectively run and meet regulatory requirements. Volunteer trustees, therefore, have significant influence on the culture, leadership, and future direction of hospice and palliative care services. It is somewhat perplexing, however, that this voluntary strategic leadership is often responsible for the restrictions and boundaries imposed on other volunteering roles, influencing the activities that volunteers can and cannot undertake.

Morris et al. (2015) suggest that volunteers play a key role in bringing the local community into hospices and in extending the reach of the hospice and palliative care services in supporting patients and families at home (Morris et al. 2015). McKee et al. (2010) suggest that volunteers "inhabit a unique third culture of care" (p. 103) and play a vital role within community networks that enable high-quality hospice and palliative care (McKee et al. 2010). These themes are further explored in Sect. 5.3.

The influence of volunteers extends as already documented beyond patient care, and in some countries, volunteers are also involved in raising awareness of hospice and palliative care and in generating income to support the delivery of services (Scott 2015). Wilson et al. (2005), while recognizing a lack of evidence, suggest that volunteers may be important to the viability of organizations (Wilson et al. 2005). A later research study by Scott (2015) in the UK supports this hypothesis and found that volunteers were essential to the sustainability of not-for-profit hospices, with a number of respondents indicating that without volunteer support, their services would close (Scott 2015).

It is possible, however, that the influence of volunteers may be felt beyond hospice and palliative care organizations. Scott (2015) highlights the role of volunteers in educating the public about hospice and palliative care and including to "dispel myths and taboos" (p. 81) (Scott 2015). For example, in Austria, in common with a number of other countries, this includes hospice and palliative care volunteers going in to schools to talk to children about death, dying, and hospice and palliative care. The Council of Europe (2003) suggests that the role of volunteers in hospice and palliative care "is often underestimated" and contends that volunteers help to normalize dying and contextualize death as a societal rather than solely a medical issue (Council of Europe 2003) (ibid. p. 67).

While volunteering may influence a number of aspects of hospice and palliative care, there are a number of external influences which can impact on volunteering itself including culture, society, politics, legislation, or regulation. Culture affects not only how volunteering is perceived but can also encourage or inhibit the development of volunteering. As noted earlier, the level of volunteering may be affected by political influences, but this is not always the case. Globisch (2005) suggests that there is little tradition in Denmark of volunteering in healthcare settings (Globisch 2005). The reasons cited are the high level of female employment (who at least traditionally volunteered more than their male

counterparts) and resistance from staff in the hospice and palliative care sector (ibid.).

Changes in volunteering are also evident in a number of countries as a result of societal changes. Howlett and Scott (2018) highlight that volunteers in many countries today have less time available and want their time to be utilized wisely (Howlett and Scott 2018). Today's hospice and palliative care volunteers may demand more from their experience than earlier generations. They may be motivated by personal and professional development, seeking responsibility and meaningful activities (ibid.). This poses challenges for hospice and other palliative care organizations which may see the increased involvement of the community as volunteers as key in helping to address the current and future growing demand as populations age.

In the light of these changes in and effects on volunteering, there is perhaps one further influence that is worth considering before leaving this section. The EAPC launched "Voice for Volunteering," the EAPC Madrid Charter on Volunteering in Hospice and Palliative Care in May 2017 (European Association of Palliative Care 2017). The purpose of this Charter is to emphasize the importance of and embed volunteering within hospice and palliative care. The aims of the Charter are:

- Promote the successful development of volunteering for the benefit of patients, families and the wider hospice and palliative care community.
- Recognise volunteering as a third resource alongside professional care and family care, with its own identity, position and value.
- Promote research and best practice models in the recruitment, management, support, integration, training and resourcing of volunteers. (ibid.)

The Charter calls for organizations to recognize the role of volunteers in direct patient care as one of "being there" which is described as focusing on the "human connection on 'being with' the person, that is the basis for sensing what kind of support the volunteer can provide to this particular person at this particular time." Actions outlined in the Charter are targeted at individual, organizational, local, and national levels and encompass areas such as recognizing the role of volunteers, effective management, training, and support, and identify volunteering as a key area for evaluation and research (ibid.).

5 Using Research to Understanding the Volunteers Role in Hospice and Palliative Care

5.1 Why Use Research to Understand the Volunteers Role in Hospice and Palliative Care?

The previous sections have highlighted many aspects of the volunteering in the context of hospice and palliative care such as definitions and the development of the modern hospice movement. They have also raised discussions about the complexity of the volunteering role and the many influences which mold this role, both on a personal (e.g., expectations) and on a wider societal and organizational level. At the same time, little is currently known from a population viewpoint about how volunteers deliver care in hospice and palliative care, in particular the level of activities provided within hospice and palliative care and in what settings do these activities occur? What are volunteers' own experiences? Are they overall good or bad? How do volunteers perceive their role and do they feel adequately prepared to perform it?

It is obviously important to understand these issues. Volunteers are as already stated often a vital resource in the delivery of care. To ensure that they continue to play an active role and do not suffer from burnt-out, research is needed to inform best practice. Although volunteers work has historically been linked closely to the development of the hospice movement (Goossensen et al. 2016), it is important to ensure that volunteers help provide good quality care, especially in an age where there is a growing emphasis on accountability. Within this context and to help plan services for the future at a population, it is necessary to quantify the types of care delivered

by volunteers and in what settings. To help answer these questions robustly, research provides a range of tools.

Firstly, to recap what is research? It is the systematic and rigorous progress of inquiry that aims to describe processes and develop explanatory concepts in order to contribute to the scientific body of knowledge. Conducting good quality research facilitates the production of reliable and valid data from which effective and acceptable decisions can be applied to the broadest set of phenomena. This chapter section explores the research looking at volunteers in patient- and family-facing roles in hospice and palliative care to:

1. Quantify the activities of volunteers
2. Explore the role of volunteers
3. Discuss limitations in current research and to explore potential ways forward in future research

There are, as discussed earlier in this chapter, Sect. 2, different types of roles and settings that volunteers may work in within hospice and palliative care. These differences can be grouped in various ways: (1) community volunteering both in direct patient and family care-facing contact and in indirect facilitative roles, (2) voluntary board membership, and (3) professionals working within their discipline without receiving payment (Goossensen et al. 2016). The focus in this chapter section (and subsequent sections on research) is on research evidence in regard to patient- and family care-facing volunteers in hospice and palliative care settings. This focus is chosen as it is important to understand in what way volunteers have a direct impact on patient and family experience. At the same time, volunteers have unique concerns and challenges that exist in the role of providing care to patients and family in these settings. These include involvement in caring for very vulnerable patients of persons with non-professional training. Research evaluating their role in such care could also help combat any element of resistance and difficulty volunteers may suffer in establishing a link with some paid staff within the palliative care sector. The focus on research in this area is also needed as the number of volunteers is likely to increase greatly due to insufficient numbers of available professional staff to care for the growing demand for hospice and palliative care. Moreover there is now increasingly global interest in understanding the extent and best practice of volunteer involvement in providing this support (Morris et al. 2013) as demonstrated by the EAPC charter for volunteering in hospice and palliative care (see Sect. 4).

It is important to highlight that the focus of this section and subsequent research sections in this chapter aims to provide an international context to research looking at volunteers in hospice and palliative care. However, we acknowledge that most of the studies conducted in these settings have been conducted in Europe, North America, and Australia and may not be relevant to all volunteer hospice and palliative care services in other areas of the world.

5.2 What Activities Do Volunteers in Hospice and Palliative Care Engage in?

Previous studies have grouped the main roles of volunteers in hospice and palliative care in patient- and family-facing roles into five areas: emotional, social, practical, informational, and spiritual (Wilson et al. 2005; Claxton-Oldfield 2015b). Large surveys, e.g., national or international, are important tools in helping to illuminate the broader picture and quantify the breadth and depth of the role of volunteer involvement in patient- and family-facing care, as they illustrate both the settings where volunteers work within hospice and palliative care and the types of activities they engage in within these settings. Several large national surveys have been conducted across different European countries such as the UK, Poland, and Belgium or the various countries involved in the recent EAPC Taskforce initiative on volunteers. These surveys have both confirmed and quantified that most volunteers are involved in a wide range of patient-facing roles, meeting and greeting patients (Burbeck et al. 2014a),

providing emotional support/psychosocial care to patients (Burbeck et al. 2013, 2014a; Pabst et al. 2017; Pawłowski et al. 2016; Vanderstichelen et al. 2017) and bereavement support, feeding patients or cleaning rooms (Burbeck et al. 2013; Pawłowski et al. 2016), and providing a range of complementary and diversional therapies, pastoral/faith-based services, and beauty/hairdressing (Burbeck et al. 2014a).

Two published surveys have looked at where volunteers work by care setting. One within the Flemish healthcare system found that volunteers based in palliative care units were more likely to be involved in direct patient care compared with those based in medical oncology unit. These volunteers were also more likely to be providing psychological, spiritual, and existential care (Vanderstichelen et al. 2017). The other, a UK-based survey of volunteers in adult hospice and palliative care services, found that volunteers were more likely to be involved in day care, bereavement services, and with in-patients, but less likely to be involved in home care (Burbeck et al. 2014a). In looking at volunteer involvement in patient and family-facing care delivery, those working in the voluntary sector (when compared to those working in the statutory sector) were more likely to be involved in the range of specific activities such as creative/diversional therapies, complementary/alternative therapies, counseling, pastoral/faith-based activities, and hair dressing/beauty, and where in many cases, volunteers were entirely responsible for the running of these services (Burbeck et al. 2014a).

A Volunteer in India Describes His Experiences

I head the creative wing to improve the ambience of Institute of Palliative Medicine. Late one evening, while walking to my room passing by the patients' wards, I saw her sitting by the window waving at me with a bright smile. Rishna was suffering from brain tumor. A bright chirpy 12-year-old girl with a sparkle in her eyes who was interested in Art. I had told Rishna that I'd get her art supplies the last time she was here. Now that she was back. I had the art supplies in my room and planned to give it to her on the way back. Something came up and it was too late to visit her. So I kept the supplies in my bag and decided to visit her first thing in the morning.

Next morning I went by her room but she was sleeping. Little did I know that her condition was bad and she was on heavy medication. I went by her room later that afternoon, she was still sleeping. My heart sank a little, but I hoped that next morning she would be better and I would be able to keep my word. Things just got from bad to worse and soon she was terminal. A few days later, she deteriorated progressively never recovering to her former state. I knew that with her condition, there was no coming back, but I never thought, the day I walked past her room would be the last time I would see her smile – her death posed a lot of questions to me – why didn't I give her the art supplies at the moment itself? Why did I put it off? How granted did I take that moment, thinking I would get a chance the next day – that incident taught me the value of a moment – the moment I had lost. It was a learning lesson for me to cherish every moment then on. In our daily life, there are those little moments we take for granted but only realize the value of that moment once it's gone. Later that week I got a call from my friend saying another girl has been admitted in the same room as Rishna was and she is interested in coloring. I went back with coloring supplies!

Most surveys have investigated the involvement of volunteers in adult services, but it is important not to forget the role of the volunteer in hospice and palliative pediatric care where additional potential ethical issues exist in how volunteers are involved given the relatively young age of the population and societal attitudes to caring for this group. Moreover, there are often

general structural differences between children's and adult hospice and palliative care services. For example, in the UK, this care may be delivered to an individual child over a number of years, which in many cases may additionally involve the provision of education and play. Despite the complexities of providing pediatric palliative care, surveys in this area though are extremely limited, with only one study looking specifically at the involvement of volunteers in the delivery of pediatric palliative care (Burbeck et al. 2013). Although this study was conducted in the UK, some limited comparisons can be made with countries which have a similar service provision. In comparing the activities of volunteers between adult and children services, there were common aspects in their roles. In both cases, volunteers' most common activities included greeting visitors to the service, serving meals and drinks in the hospice, and assisting with social activities. In both settings, many of their services provided by the hospices, such as complementary therapies and pastoral care services, were dependent on volunteers running these services. Nevertheless, clear differences existed between volunteers in both settings. The number of volunteers in this UK survey in pediatric services (median 25 volunteers per service such as a dedicated hospice) is small compared to a UK survey in adult services (median 85 volunteers per service) (Burbeck et al. 2014a). Volunteers in pediatric hospice and palliative care were also found to be less likely to have direct patient care contact with children, but more likely to be involved in music and arts-based activities, befriending, and complementary therapies provision for the whole family. They were also not involved in any aspect of home care (Burbeck et al. 2013). In addition to structural differences with adult service, these findings may reflect that pediatric hospice and palliative care is compared to adult care a relatively recent development with potentially few beds available and a volunteer's role which is less well-defined. However, it should be noted that this survey in pediatric services was undertaken over 5 years ago and services have evolved since then. For instance, some community teams in the UK now involve volunteers.

There are difficulties underlying the current published literature in this area. There are as demonstrated few published surveys. The focus of the research questions of some of these surveys do not specifically address the role of volunteers per se but have their focus on topics such as specific training issues for volunteers (Pawłowski et al. 2016) or the role of motivation in volunteers (Pabst et al. 2017). Some surveys are "in progress," published in abstract only thereby lack sufficient detail (Vanderstichelen et al. 2017). Another difficulty, in generalizing these findings on how volunteers deliver patient-facing care in hospice and palliative care, is that different countries have different structural systems and cultural values in how they run their hospice and palliative care services and what is permissible for volunteers to do. It is also important to highlight that the focus in this section is on surveys published in peer-reviewed journals. There will be other surveys documented elsewhere such as "in-house" yearly service surveys. Only surveys published in peer-reviewed journals were discussed in this section because such papers are in general (across all types of research) likely to be of higher quality or reliability than non-peer reviewed as they are published based on approval of a board of professional experts. There may also be other surveys not noted in this section published in peer-reviewed journals, this is as they were not published in English. These restrictions may have limited the findings in this section.

5.3 What Volunteers in Patient- and Family-Facing Roles Within Hospice and Palliative Care Settings Understand About Their Role

The previous section explored the role of volunteers in the context of the activities that they performed in different settings within hospice and palliative care. It is equally important to understand how volunteers see their role. In this section, the perspectives of volunteers in patient- and family-facing roles in hospice and palliative care are explored using the findings of qualitative

designed studies. Although we acknowledge that quantitative designed studies (those that predominantly provide numerical data), particularly large surveys, may be useful in identifying general trends, qualitative research are more valuable in exploring a phenomenon from the perspective of the individuals experiencing it, in this case what volunteers understand about their role, and there are now numerous qualitative studies available exploring this.

In the first part of this current section, the review of qualitative studies by Burbeck et al. (2014b) is critiqued and presented on how volunteers perceive their role and also how other key stakeholders (such as patient and their families and professional staff) perceive the role of the volunteer in hospice and palliative care. In the second part, the results of this review are compared with qualitative studies published since the review.

The Burbeck et al. review uses a qualitative evidence synthesis approach in its interpretation of how volunteers understand their role. The synthesis explores the qualitative analysis from all known qualitative studies (Burbeck et al. 2014b). It takes a thematic approach in the synthesis of the individual studies analysis; in doing so it considers connections, similarities, and differences between the findings of each study. This may identify "higher-order" key themes not identified in any study but only apparent in the pooling of their findings. This can produce a deeper and potentially new understanding of what the volunteers may understand of their role. This review identified 12 studies, mainly from North America (7/12) or Europe (4/12), but with 1 study originating from Uganda. The total sample comprises of 294 participants who were mostly volunteers but also other stakeholders relevant to understanding the role of the volunteer including a patient and their family and hospice and palliative care staff. Most participants were female.

The review identified three theme clusters in the studies. Theme 1 highlights the *distinctness of the volunteers' role*, in which the volunteer saw their role as having an identity separate from paid staff. This distinct role was often described in terms of recognized work boundaries. Volunteers felt they were not restricted in either the tasks or the time they could offer to patients or families in the same way that paid staff were. Volunteers saw their roles characterized by two factors: independence in that the task that they would perform would not be done by a paid member of staff and surrogacy which was possible due to the blurred relationship between volunteers and patients. Within these role characterizations, volunteers act either as "go-between" between the patients and their family and members of staff or as advocates for patients and families in representing the interests of these people. These roles highlight the surrogate nature of the volunteer role, where volunteers potentially become an "additional" members of the family due the person time at the hospice.

Theme 2: characteristics of the role. This theme highlights *the social nature of the volunteer role*, as opposed to being task-orientated. This aspect of the volunteers' role is further illustrated by the value that volunteers feel that they provide patients and family in terms of social support, notably in providing emotional support and "being there" for them. The perceived social aspect was seen as a motivating factor for volunteering in a hospice setting.

Theme 3: volunteers experience of the role, defined in terms of its ambiguity, flexibility, and informality and their relationship with paid members of staff. The synthesis identified *ambiguity in how volunteers understood the role*. Volunteers viewed the flexibility and informality of their role positively, but at the same time, they found it stressful when there was uncertainty around the tasks that they should be doing. The relationship between volunteers and paid staff was central in shaping the volunteers' experience of their role, in particular the way that staff controlled their role by restricting the availability of patient information or treating volunteers as subordinates. The synthesis highlighted tensions between the perceptions of informality of the volunteers' role with the growing formalization of their roles, through the need to be increasingly professionalized, often due to the increased need to work within a legal framework.

This review provides a distinct understanding of how volunteers perceive their role in patient and family-facing settings. It also highlights many issues that planners and managers of hospice and palliative care services may need to be aware of to facilitate the best of volunteers' contributions, namely, that it can be perceived as social in nature and it may also be about dealing with the ambiguous nature of the volunteers' role. This review by including 12 studies of different populations of volunteers, as well as some other key stakeholders such as family members, enabled the role of the volunteer to be constructed from a range of different perspectives. The studies reviewed came from a variety of North American and European countries, which increased the generalizability of the findings to a wide range of healthcare settings. Furthermore, the review explored differences in care settings, with volunteers working in inpatients services adopting a quasi-professional approach to their role while those volunteering in home-based care tended to act more as surrogate family members. Nevertheless, there are some methodological issues that need to be considered when interpreting the findings from this review, in particular the range of questions asked by the researchers from the 12 studies in collecting their primary data where not all directly asking about the role of the volunteer.

Since the publication of the Burbeck et al. (2014) review (Burbeck et al. 2014b), four relevant qualitative studies on volunteers perspectives in hospice and palliative care have been published (Brighton et al. 2017; Dean and Willis 2017; Gale 2015; Söderhamn et al. 2017). The studies are European, three from the UK and one from Norway. Unlike the studies analyzed in the Burbeck review where the volunteers were all from dedicated hospices and palliative care units, the volunteers from two of these studies came from community palliative care (Gale 2015; Söderhamn et al. 2017). These studies have explored the volunteer experience to varying degrees. One study focused on the impact of how working with patients near the end of life influenced volunteers own experience and attitudes toward death and dying (Gale 2015). The second looks at how the experience of volunteers are affected by the training and support provided by a palliative care coordinator (Söderhamn et al. 2017). The remaining two have used the volunteer experience as a means of identifying how to improve training for volunteers working with people with palliative care needs (Brighton et al. 2017; Dean and Willis 2017).

The main findings from these studies chime closely with the three themes identified from the Burbeck et al. review. These include dilemmas around the development of close relationships, friendships, between volunteers and patients (Gale 2015; Söderhamn et al. 2017) and doing tasks not performed by health care professionals (Brighton et al. 2017), "being there" (Söderhamn et al. 2017), and providing emotional and social support to family members (Söderhamn et al. 2017). Nevertheless, the theme of increasingly professionalism and regulation (Gale 2015; Söderhamn et al. 2017) is reflected in the later studies, particularly the importance of volunteers having a clarified role and provided with sufficient knowledge to carry out the task (Söderhamn et al. 2017). Likewise, it is equally important for health professionals to be aware of the volunteers' role (Söderhamn et al. 2017).

A Volunteer in Canada Describes Her Experiences

On a practical level, I have, over the years, been involved with fundraising, for example, the Christmas "Angel's Remembered" campaign, the annual "Hike for Hospice," and giving presentations in the community to bring awareness to the topic and services available. I also teach the "communication with the dying and their loved ones" component of the volunteer training program for a local hospice organization once every year or so. However, mostly I have offered emotional, social, and practical support to patients/clients, for example, accompanying people to medical appointments, taking them for drives, and walking them around

(*continued*)

hospital grounds or their own gardens or homes. I have given hand massages and sometimes used a relaxation technique known as Reiki when requested. I have spent time with the dying person's loved ones listening and talking and listening again to their stories, fears, and concerns for their loved ones and sometimes their concerns for their own future when thinking about their inevitable and impending aloneness. And, last but not least and, by far what I mostly enjoy is the countless hours I have spent just sitting with or at the bedside of the dying person – many of those hours were spent in silence as they lay sleeping or were semicomatose/comatose due to the disease (or more often, due to the drugs used for symptom control of the disease). On these occasions, I will often just touch a hand or a shoulder periodically to remind them that they are not alone. If it is expected to be a long stretch of time with someone who is unconscious, I will take a book with me and during breaks from reading I often find myself watching the breathing patterns and will imagine the person in their life before they entered the final stages. Since we don't currently have any freestanding hospices in our area, I visit people in their homes and the hospitals.

My role as a hospice palliative care volunteer over the last 25 plus years has offered me the opportunity to meet some wonderful people that I likely otherwise would not have met, at a time in their life when they were often the most vulnerable – whether they were the patient/client or the loved one (s). Front-line volunteering has, at times, offered me experiences that have stretched me out of my comfort zone whether through dealing with uncomfortable situations due to stressful family dynamics or because sometimes witnessing the suffering of an individual is just simply almost too much to bare. Then there have been the times when I have felt a bit like a fraud because I've been sure that I have been getting more out of the relationship than I was giving. No matter the situation, every person I have met has taught me something about myself and about life. It has always been a great privilege to be involved – as cliché as that sounds, it's the truth, as anyone who has journeyed with a dying person will tell you. Volunteering in this field has had a profound impact in shaping my life – for the better!

In palliative care, feeling unprepared to perform certain tasks related to their role is a challenge facing many volunteers in direct contact with patients and their families; this includes dealing with imminently dying patients or subsequent bereavement issues with family members (Dean and Willis 2017). Likewise, similar challenges also apply to volunteers working in hospital settings, who, through their roles of acting as hospital guides, chaplain volunteers, and ward visitors and assisting with patient discharge to home, work with patients with palliative and end of life care needs, involving difficult and emotionally intensive encounters (Brighton et al. 2017). These studies emphasize the importance of providing good support to its volunteers (Gale 2015), potentially through a mentor (Söderhamn et al. 2017). There is recognition that tailor-made training is an important element to support volunteers carry out their role (Brighton et al. 2017; Dean and Willis 2017).

5.4 Limitations of Research on the Volunteers' Role in Patient and Family-Facing Support in Hospice and Palliative Care

Studies in this area confirm the broad range of activities that volunteers are involved in and have provided a greater understanding of how volunteers understand their role and how they experience it. Nevertheless, current studies, particularly

looking at the volunteer experience, are limited. The majority of studies have originated from North America, Australia, or Europe (mainly the UK or the Scandinavian countries), with the main findings limited in their generalizability. More studies need to be conducted and published from other European countries and from countries outside North America and Europe. The samples used in these studies have mainly been volunteers, apart from three studies from the Burbeck et al. (2014) review (Burbeck et al. 2014b) which identified three studies exploring either the patient or family members' perspectives of the volunteer role. Although these studies provide a relevant basis to understanding the experience of volunteers, it is equally important to understand the perspectives of all stakeholders, including those who receive care from these volunteers, namely, the patients or their family members as well as those who work closely with volunteers such as nurses. More studies are needed to explore the perspectives of these groups as findings from these groups will enable us to see how they compare with those from volunteer only studies and so build up a wider picture about the role of volunteers in hospice and palliative care. Such an approach has been used in a qualitative study looking at the collaboration between volunteers and staff in a pediatric palliative care unit, which identified communication, particularly good information flow as a key factor in successful collaboration between volunteers and staff (Meyer et al. 2018).

The qualitative studies identified have all used interviews or focus groups to collect their data. While these methods can allow a wide range of topics to be discussed, there are several limitations. Although the interviewees have some flexibility in responding to interviewers' questions, the interviewers/researchers exert control in determining what topics are covered during the interviews or focus groups and how they are discussed. There is also an assumption in conducting interviews and focus groups that what participants say is what they actually do, but this may not be the case in many situations. Interviews and focus groups, by their very nature, do not look at the interaction between how participants interact with their social environment. Within the field of volunteer research, other alternative methods may be more appropriate in teasing out the social interactions between volunteers and other potential stakeholders such as patients, family members, and health professionals working in hospice and palliative care institutions. One such method is ethnography, where the researcher participates openly in the field they are studying and immerses themselves in that social environment, observing the interactions of the topic being explored and recording detailed field notes. This methodology is useful in examining health beliefs and the organization of health care. Although time-consuming, such studies would provide a deeper and richer understanding of how volunteers in hospice and palliative care interact with other agencies.

6 Using Research to Understand the Impact of Patient- and Family-Facing Volunteers in Hospice and Palliative Care

In this section, the focus is on research to assess the impact of patient- and family-facing volunteers in hospice and palliative care settings. The section opens with a discussion on what is the value of evaluating volunteers' involvement in patient care within hospice and palliative care settings. By this, what is meant is on whether the contribution of the volunteer has an influence on the patient or their family, such as in their well-being or care satisfaction. This is followed with an outline on how we may evaluate impact. Presentation and a critique are then made of the findings of studies that have evaluated the impact of patient- and family-facing volunteers in hospice and palliative care. Considering the limitations in this evidence base, the next subsection highlights the challenges in evaluation. The section concludes with discussion on the way forward in assessing impact.

A Volunteer in Austria Describes Her Experiences

Here we are, sitting in a small cafe in the 16th district of Vienna. Mrs. M. sits in her wheelchair, drinks a black coffee, and smokes a cigarette. She starts talking about her uncle's suicide. "You know, he had colon cancer, just like I do. He couldn't bear the pain, the physical limitations and the fear anymore. He had two children and he was Catholic, very religious. I don't know how he could possibly. . .". Tears are flooding her eyes. It's been a year now that I am with her and her family, and it's the first time this strong, brave, and self-reflective woman is crying in my presence. When saying goodbye this day, she shakes my hand longer and more firmly than she usually does. "Thank you," she says, looking deeply into my eyes. This moment makes me realize that I am where I'm supposed to be, doing what matters to me.

During my work as a hospice volunteer, I am honored to experience many situations like this. I feel blessed how much trust, openness, and gratefulness I receive and that I can be there for someone, simply by listening with an open mind and heart. These intimate encounters also allow me to experience myself in a unique way: Being fully present and compassionate, I feel very connected to others, and my experiences and relationships seem more meaningful.

Some other day, I am sitting with Mrs. M. and her husband in their living room. They hardly ever talk about her illness and the impact it has on their lives. During the conversation, Mr. M. looks at me and speaks about how he admires his wife and her strength, what a loving mother she is and how proud he is to be her husband. Mrs. M. sits right next to him and tries to establish eye contact with him. He doesn't react and keeps looking at me, as if he couldn't look at her while saying those words. It feels like magic and I wonder if my presence made this possible. And I am overwhelmingly grateful to witness it.

6.1 Do We Need to Evaluate the Impact of Patient- and Family-Facing Hospice and Palliative Care Volunteers?

In answer to the question on why do we need to evaluate the impact of hospice and palliative care volunteers, let us first take this as a health or social care intervention that involves the contribution of volunteers. If we look broadly at health and social care evaluations, we find that many, be they drug treatments, non-drug, or services, in hospice and palliative care and elsewhere have been implemented without rigorous research to assess their impact. This includes the exploration on the barriers and facilitators to the best implementation in practice of an intervention. In other words, there are interventions that lack sufficient evidence to either recommend or not recommend. In hospice and palliative care because of historic underfunding in research, and because of the complexities in undertaking research in these settings, under-evaluation may be more extensive than in many other areas of healthcare. On the other hand, it may seem intuitive that many healthcare, palliative or otherwise, interventions help and indeed for some evaluation are unnecessary, inappropriate, or even unethical. Many of the most effective treatments have not been the subject of evaluation by controlled trial, including external defibrillation, which is used to start a stopped heart (Howick 2011). In hospice and palliative care, there are clear ethical issues to consider in conducting research that involves withholding from a proportion of the study participants (those in the control or comparison arm of a trial) additional care, which while not of established benefit may be unlikely to cause harm (Casarett 2009). However, without rigorous evaluation, the impact

of interventions on important outcomes is not fully known nor is it known what is the better approach to care. This is not to challenge the value of clinical experience in the provision of good quality healthcare. In the evaluation of care interventions though, clinical judgment does not provide an adequate basis for detecting at population level modest beneficial or adverse effects (Howick 2011). For instance, a review of all published trials on a particular drug or of a new supportive therapy or service perhaps involving a volunteer or a nurse may find a higher rate of adverse events in patients taking the drug or having the supportive therapy compared to those receiving usual care. Unaided by comparative studies, a clinician (who is likely to have seen fewer patients needing the drug or supportive therapy than those participating in trial evaluations) will be less likely to detect this.

The provision of hospice and palliative care varies across countries as does, as demonstrated earlier in this chapter, the role of the volunteer. However, what is consistent is the extensive depth and breadth of volunteer involvement in these settings particularly in the community, in home care, and in dedicated hospice and palliative care facilities. In many countries, the volunteers' contribution was critical to the development and to the sustainability of hospice and palliative care services. In other countries, volunteering is the workforce providing hospice and palliative care. Moreover, alongside the growing global number of older people, there is growing demand for hospice and palliative care. There are insufficient numbers of professional staff to respond to this need, and there may need to be an even greater reliance in many countries on volunteers to help provide care and support. In recognition of this, some governments have endorsed policies that may directly or indirectly promote informal caregivers like volunteers to assume a greater share of care provision at the end of life (Alcock 2010). In parallel, a recent development within hospice and palliative care has been called to adopt the principles of public health to further promote community volunteering to fill the growing gaps in professional support services (Abel and Kellehear 2016). Thereby to identify and accelerate best practice, there has never been a more pressing time for the need to have robust and relevant evaluation of the impact of volunteers in hospice and palliative care.

6.2 How Do We Evaluate the Impact of Patient- and Family-Facing Volunteers in Hospice and Palliative Care?

In answer to the how do we evaluate, firstly we should consider what we should evaluate. A starting point is to consider why patient- and family-facing volunteers are needed in hospice and palliative care. The reasons include as noted earlier, but are not limited to, to enable services to be provided, to allow finite resources to go further, to involve the community, and to provide more holistic care. It is also worth considering to whom patient- and family-facing volunteers make a difference. This could be as already noted the difference made to patients and their families experience. It could also be the difference made to volunteers, the difference made to the local community, and difference made to the organization (e.g., organizational capacity, staff able to focus on specialist roles, reaching more people, and in providing a wider range of services). Exploring all these points though is beyond the scope of this chapter. They are noted here to highlight some of the broad scope of what could be evaluated.

There are various study designs that can be used to measure volunteers' impact on patient and family experience. Randomized controlled trials (RCTs) are considered the gold standard to evaluate the effects of an intervention. This study design more than any other reduces the risk of biased results. However, for various reasons including ethical, there are limited numbers of RCTs in hospice and palliative care. These reasons will be discussed further later in this section. There are though other designed studies that allow, although to a lesser extent, the evaluation of the impact of an intervention to be measured. This is by comparing, like a RCT, one group that experienced the intervention of interest, here

volunteers, with another group who do not experience the "volunteer intervention." These include a range of different designed studies such as quasi-randomized controlled trials, controlled before-and-after studies, and interrupted time series.

The work of Methods Of Researching End of life Care (MORECARE) project aimed to provide evidence-based guidance on research methods in end of life and palliative care (Higginson et al. 2013). One of their recommendations, it is important to note here, is for the use of research exploring patient and family experience in intervention development. These experiences can be gathered via qualitative research methods which are extremely useful in understanding the mechanisms behind what any intervention may achieve.

6.3 Differences Made to Patients and Families in Hospice and Palliative Care: Choice of Outcomes

Comparative studies, such as trials, can tell us a lot about a whether a treatment works, whether it is cost-effective, and whether it causes no serious harm. What such a study can tell is dependent on the outcomes selected. The impact assessment of many care interventions in hospice and palliative settings is characterized as involving a range of different measures. For instance, in a Cochrane systematic review on the effectiveness of home palliative care services, there were eight items of interest in regard to whether the service made a difference to the patient and their family. These items were satisfaction with care, symptom controlled, physical functioning, quality of life, time spent at home, death at home, and caregiver pre- and post-bereavement outcomes (Gomes et al. 2009). Multiple outcome assessments may be undertaken in a study in part as it may be unclear what outcomes an intervention may impact on. It is also because in hospice and palliative care, the impact of many interventions is known to be broad, and one outcome measure is insufficient to assess this. Take, for instance, how palliative care is defined by the World Health Organization (WHO). This is as an "approach that improves the quality of life (QOL) of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual" (World Health Organization 2018). Since it is a goal of palliative care, it would seem appropriate that a key outcome to evaluate the impact of the involvement of patient- and family-facing volunteer is patient and family QOL. But assessment may also include other measures to assess prevention and relief of suffering on varied domains (e.g., pain, other symptoms, emotional, social, and spiritual). This broadness, though, is not the only thing that is not straightforward in hospice and palliative care research. Outcome assessments are complex because of the changing nature of the patients' condition and its impact on symptoms and physical, emotional, social, and spiritual needs. Moreover, in hospice and palliative care where a person's health is deteriorating, in regard to the assessment of QOL, for example, you may not necessarily be focusing in measuring whether the intervention leads to an improvement or not. Evaluation of an intervention may be on measuring whether it limits decline or halts decline in QOL.

The role of a patient and family-facing volunteer can be considered, as discussed in Sect. 5, as distinct from those of healthcare professionals and families role in caring and support. If we follow an overarching theme in the qualitative literature of "being there," then perhaps we have another way we should evaluate the impact of volunteers, namely, on outcomes relating to the social nature of the role of the volunteer. Another complementary way to identify relevant outcomes to assess what the benefit of patient- and family-facing volunteers in hospice and palliative care is what patients and families value in the involvement of volunteers? However, there a few qualitative studies specifically exploring the experiences of patients and their families on receiving support from a volunteer. One qualitative study conducted individual interviews with ten bereaved women

(Weeks et al. 2008). The overarching theme that emerged in their analysis was that volunteers had a unique social role in care:

> And I think, for [my husband], the fact of having somebody from outside, not just staff, is important. I think the staff that deal with you all the time, there is some humiliation in your situation that staff has to deal with at another level, his physical needs, so this is strictly someone to talk and be there, a friendly face, a kind face. (Bereaved wife Weeks et al. 2008)

6.4 What Is the Best Evidence on the Impact of Volunteers in Hospice and Palliative Care?

There are few comparative studies that have evaluated the impact of patient- and family-facing volunteers in hospice and palliative care (Candy et al. 2015). Of these, there is only one known RCT (Walshe et al. 2016). Other comparative studies include retrospective studies of datasets (Block et al. 2010; Herbst-Damm and Kulik 2005). In two of these three studies, the volunteers who delivered the intervention provided weekly social home visits, of up to 3 h (Block et al. 2010; Walshe et al. 2016). In the other, it is not reported what volunteers did or how often they provided support (Herbst-Damm and Kulik 2005).

The ELSA study was a UK-based pragmatic RCT, a prospective wait-list trial that assessed the impact of volunteer-delivered support services at the end of life (Walshe et al. 2016). The intervention involved volunteers providing tailored face-to-face support to people who were anticipated to be in their last year of life. Support was deemed to be supplementary to usual forms of health and social care. It commonly involved befriending weekly visits of between 1 and 3 h, but it could also involve signposting the recipient to relevant services. The setting was in the community, most commonly this was the patient's home. The intervention was compared to usual care. The primary outcome of interest was the impact on change in QOL at 4 weeks after the start of the intervention. Other outcomes assessed were whether the intervention reduced loneliness, affected the perception of social support, or impacted on the use of health and social care services. The study enrolled 196 patients. It was found that there was no statistically significant difference in impact on change in QOL between volunteer-provided support and those in the treatment as usual trial arm. Overall the trial authors noted that "there were trends in the data in favour of the intervention, but the effect is small, and related to reducing the rate of decline rather than improving outcomes." However, the study was underpowered, and the authors had questions about their choice of outcome measures, in that the one they used may not have addressed QOL appropriately within the context of end of life. Therefore, they concluded the effectiveness of these volunteer services remains unknown.

The Herbst-Damm and Kilik (2005) comparative study undertook secondary analysis of a dataset of survival rates of 290 US hospice patients comparing those who received volunteer home visits with those who did not. Volunteers who provided the home visits were trained to listen, to provide conversation, and to provide if requested personal grooming needs such as trimming nails or combing hair. They found that those who received volunteers' visits ($n = 94$) lived longer than those who did not, on average of an 80-day increase in survival. Specifically, and controlling in their survival analysis for patients' physical status (Karnofsky score at study entry), they demonstrated (using Cox's proportional Hazard Model) that neither marital status nor gender independently predicted survival, but the survival rate for those receiving visits was almost three times that of those who were not visited by a volunteer (likelihood ratio, 2.9; p value <0.001).

The third comparative study was by Block and colleagues. It compared satisfaction with care of (United Nations 2015) families whose relative received care from hospices that involved greater volunteer involvement in direct care with (Goossensen et al. 2016) those who received care in hospices with less volunteer involvement (Block et al. 2010). The study using the US National Hospice and Palliative Care Organization National Data Set (NDS) undertook a secondary analysis of hospice programs using the number of direct patient care volunteer hours.

These programs provide support in the home, freestanding hospices, hospitals, nursing homes, and other long-term facilities. The data did not provide detail on what the volunteer involvement in care entailed. Obtained using information from 57,353 individuals from 32% ($n = 305$) of hospice organizations that provided data for the NDS were families' perception of the quality of care. They analyzed "excellent" ratings of care by the number of volunteer hours reported by hospices using a multivariate analysis model that adjusted for hospice characteristics, such as the number of care staff (full-time equivalents) and patient characteristics (diagnosis and hospice length of stay). They found statistically significantly more relatives rated care as "excellent" in those hospices reporting the highest number of volunteer hours per patient week (3.3 h), compared with those reporting the lowest number of hours (0.245 h); coefficient, 6%; and 95% confidence interval, 4–9%.

In conclusion while the RCT found limited evidence of benefit, the other two studies of weaker design report statistically significant positive outcomes in the involvement of patient- and family-facing volunteers in hospice and palliative care. There are limited conclusions to be drawn as the evidence base to date is of low quality. This is as the studies were few, the studies differed in setting and evaluation, and for two the research design was at a higher risk of biased results. While there remains as there is for volunteer-delivered service elsewhere limited evidence on their efficacy (Jenkinson et al. 2013), there are some relevant comparative studies underway. This includes, for instance, in Ireland a pilot randomized trial of a volunteer-led community social and practical support intervention for adults with life-limiting illness.

6.5 Challenges and Way Forward in Evaluation of the Impact of Volunteers in Hospice and Palliative Care

There is a paucity of well-designed evaluations on the impact of hospice and palliative care, not just in services involving volunteers in these settings. There are many methodological and ethical challenges in evaluation in hospice and palliative care (Krouse et al. 2004). The ethical issues, while not unique to these settings, may be more compounded in these settings. The population is vulnerable, and for which inviting and seeking consent to be part of research is complicated because of emotional distress, potential decline in mental capacity, invasiveness of treatment, and physical and mental burden of taking part in an evaluation. In trials, there is also the issue of the "no treatment arm." This is the risk that those allocated to this arm of the trial will receive suboptimal support and care. Although one could argue the other way around, those in the intervention may receive suboptimal support and care. There are other methodological issues that while may not be unique to hospice and palliative care, they may be more extensive in these settings. This includes heterogeneity in population; patients may be dying from a broad range of diseases which have different rates of progression. This if not considered in planning and analysis may lead to bias results. In a trial, for example, this is when in one arm there are a higher proportion of the participants despite randomization have a disease with a shorter prognosis (Hoerger 2017). Results are also at a risk of biases as in these settings as there are often high attrition rates due to declining physical or mental incapacity or death. Other issues include the need for surrogate respondents and difficulty as already noted in selection of outcomes.

This is not to suggest there are no trials. For instance, although disappointingly, a recent systematic review on the association of palliative care and patient and family caregiver outcomes was unable to draw strong conclusions on impact even though it included many trials (Kavalieratos et al. 2016). It included several combined analyses (meta-analyses) of data from up to 13 RCTs. Its conclusion was limited because of issues in the trial evidence including heterogeneity of outcome measures and poorly conducted trials.

So are these challenges insurmountable for research on impact of patient- and family-facing volunteers in hospice and palliative care? It is

worth remembering that hospice and palliative care research is a relatively new endeavor, but at the same time, there is a growing body of researchers and hospice and palliative care research groups around the world who are successful in attracting competitive research funding (Johnson et al. 2017). While there is a need for more focused research attention to better understand how to maximize their contribution while providing better support for volunteers' (Pesut et al. 2014), there are groups exploring how to improve research methods in palliative care (Higginson et al. 2013). This includes the authors of the one RCT of a volunteer intervention in palliative care, they highlight the use of wait-list controls to overcome issues of withholding a potentially beneficial intervention to people who have shorten lives, and they also recommend to enhance completion and reduce attrition and ease of ethical approval short and easy to complete measures (Walshe et al. 2016).

7 Training of Volunteers in Hospice Palliative Care

This section focuses on the training of volunteers in hospice and palliative care. It begins with a discursive section which poses questions on the need to train volunteers. This is followed by a brief exploration of the tensions that exist between training volunteers to be effective in their roles while nurturing the humanity and freedom that characterizes volunteering. This section concludes by examining the limited evidence base on volunteer training in hospice and palliative care and considers the way forward.

7.1 Why Do We Need to Train Volunteers in Hospice and Palliative Care?

There is limited research evidence in the field of hospice and palliative care on the effectiveness and value of volunteer training (Dean and Willis 2017; Horey et al. 2015). Despite this, it is accepted in many countries that training volunteers in hospice and palliative care is good practice, and it is likely that there are few instances where volunteers receive no preparation or training whatsoever. At a minimum, volunteers are likely to receive an introduction to the organization and guidance on the boundaries of their role (Brighton et al. 2017; Dean and Willis 2017). So why is it that training volunteers seems to be so embedded in practice? Is it to enable volunteers to be effective and have confidence in their role; to enable paid staff, patients, and families to trust that volunteers have the right skills; or to satisfy legislative or regulatory requirements? Does the training take a theoretical approach or is the focus on helping volunteers to reflect on and develop their natural skills in responding to the needs those they support? In taking a theoretical approach, do we risk volunteers becoming more like professionals and losing their unique role as community "friend" or "neighbor"; what is the role that we need them to play?

In reality, it may be a mixture of some or all of these reasons and approaches to training depending on the volunteer activity, the organizational philosophy and wider influences as outlined in Sect. 4. The Council of Europe (2003) states that volunteers in hospice and palliative care must receive appropriate training and that "willingness to help not enough" (Council of Europe 2003) (p. 67). Radbruch and Payne (2010) take this a step further stating that such volunteers should receive "an accredited instruction course" and receive ongoing training along with supervision and support (Radbruch and Payne 2010). As highlighted in Sect. 5, training has an important role to play in supporting volunteers to carry out their role (Brighton et al. 2017; Dean and Willis 2017), in which effective training programs are important in mitigating stress for volunteers (Claxton-Oldfield 2015b). Volunteers sought flexibility in deciding what topics they wanted to be trained on, according to their interest and need at the time. Volunteers wanted to be taught by highly respected staff working in the field, which was particularly important for those volunteers working in acute hospitals (Brighton et al. 2017). Volunteers did not think online teaching would be suitable as part of their training (Brighton

et al. 2017; Dean and Willis 2017). As part of their training package, volunteers benefitted from shadowing "experienced" volunteers (Dean and Willis 2017) or being followed up by a highly skilled mentor on a regular basis, who would be able to monitor the volunteer's progress or clarify their role (Söderhamn et al. 2017).

The EAPC Madrid Charter on Volunteering in Hospice and Palliative Care considers that the aim of training is to prepare volunteers for the hospice and palliative care environment and to help them to develop their own natural human ability to reach out others (European Association of Palliative Care 2017).

Before moving on to explore volunteer training in different countries, there remains a question about training for the volunteer professional who offers their skill as a doctor, nurse, chaplain, or complementary therapist without payment. What training do these volunteers require? Are there limits to their role enforced either by their professional body legislation/regulation or by the organization? Does the professional need to learn to become a volunteer?

7.2 What Is Happening Across Countries?

In considering some of these questions, it is helpful to explore what is happening in different countries. A study undertaken in Belgium found that 91% of hospice and palliative care volunteers received training, with only 33% of organizations providing mandatory training (Vanderstichelen et al. 2017). Austria, the Netherlands, and Germany have national curricula for volunteering. In Austria, for example, the required basic volunteer training is 120 h, comprising 80 h of theory and 40 h of practice (Pelttari and Pissarek 2018). All volunteers must undertake the basic training with additional training of 80 h (40 theory and 40 practice) for children's palliative care volunteers. Bereavement volunteers must undertake a separate training of 110 h or may add an additional 80 h to the basic training. In the Netherlands, volunteer training is provided over seven sessions and includes online learning (ibid) (Goossensen and Somsen 2018). In Germany, 100–120 h of training is proposed, and funding for volunteer coordinator roles is dependent on volunteers being trained (Hesse and Radbruch 2018).

Canada has a national volunteer training program of approximately 30 h available to hospice and palliative services. Claxton-Oldfield suggests that a typical hospice volunteer training program would include an overview of hospice palliative care, the roles of the multidisciplinary team, volunteer roles, multicultural faith and spiritual perspectives, clinical care, death, dying and bereavement, and communication and coping skills in addition to volunteer policies and procedures (Claxton-Oldfield 2015b).

A Volunteer in Scotland Describes Her Experiences

I have been a volunteer massage therapist within a Marie Curie Hospice for 3 years now. In an earlier life, I was a career civil servant working for the Scottish Government. At age 54, I was given the opportunity of early retirement and that is when my second, and more satisfying, working life began. A few years previously, I had studied in my spare time for a Diploma in Swedish Massage so I decided to build on this by qualifying in sports and remedial massage therapy. I was fortunate to be offered two part-time jobs, one in a private swimming club and the other in a health clinic which is where I gained real experience and honed my skills. For reasons I will explain, I had wanted to be able to offer treatments to patients coping with a cancer diagnosis, and, when I felt I had sufficient basic skills, I was lucky enough to study massage for people living with cancer. I now volunteer 1 day a week at the Edinburgh hospice and treat inpatients, day patients, outpatients, and also carers and bereaved carers.

The first time I had personal experience of the beneficial effects of massage was, sadly, 20 years ago when my late husband

(*continued*)

was receiving palliative care in hospital. His back was often uncomfortable and I used to climb up behind him in his hospital bed and, with no training – and questionable skills! – would knead his muscles and stroke his back to give him relief. In the latter stages of his illness, he loved me gently massaging his feet. When you are in despair and would do anything to help ease your loved one's pain, being able to do even these small personal things for him helped me cope too. I think, even then, I had made up my mind that this was something I'd like to do for others although it was many years before I felt emotionally able to do so. Although my husband had no hospice care, members of my family and two close friends did, and I had seen firsthand how wonderfully caring the whole environment is and, particularly, how special the staff are who work there. When I got the opportunity to join them, I was delighted. I had not expected it to be easy, but, initially, I struggled quite badly with my sadness for both the patients and their loved ones and my mind and dreams were full of some of these people for days after my weekly session and sometimes longer. Fortunately, I was well supported by both staff within Marie Curie and fellow therapists and began to realize that these were common emotions and that being able to discuss coping mechanisms with others was invaluable. As time passed, while still very moved by particular people and their situations, I found myself able to put my emotions in perspective and just feeling glad that I can help in some small way. Being invited into patients' lives at this poignant stage and knowing that the gentle touch massage gives some pleasure and relief from pain and discomfort in their final days feels such a privilege.

I have also found that my role extends beyond that of massage therapist particularly when treating carers and people who have been bereaved. It may be the safe, warm, and welcoming environment in which we see people or just that they feel able to talk freely to someone outwith their family, but I find that a significant part of my job is listening to their troubles and fears and empathizing and supporting them where I can. I love working with the patients at Marie Curie. There are some tears but lots of laughter and lightheartedness too, and I gain so much more from being there than I give.

Without a national volunteer education program in the UK, it falls to individual hospice and palliative care organizations develop their own training courses for volunteers. However, anecdotal evidence suggests that training topics are common to many organizations and are very similar to those delivered in Canada as outlined above. In addition organizations may require volunteers to undertake some core mandatory training relevant to their role such as infection control, health and safety, moving and handling, and food safety. Resources have recently been launched for community children's palliative care volunteering in the UK entitled "Together We Can"; these online materials from Together for Short Lives include a six-module training program of approximately 21–24 h.

Australia offers a Palliative Care Training Resource Kit in addition to a handbook for Palliative Care Volunteers. The length of training is determined by the needs of the service and varies from 2 to 8 days in length (Huntir 2018). The context in the USA is somewhat different as volunteers are a mandatory part of hospice and palliative care for any hospice that receives payment from Medicare (Brock and Herndon 2017). Under this provision, the training of volunteers is required but not prescribed. However, a 16 h training program is suggested by the National Hospice and Palliative Care Organization. They suggest that this should include hospice ethos, services and aims, confidentiality, protecting the rights of patients and families,

family dynamics, understanding the impact of dying, death and bereavement, and coping strategies. In addition, volunteers should be clear about their role, accountability and reporting structure.

It might be considered, therefore, that the training is firmly embedded within the concept of hospice and palliative care volunteering. It is interesting to note that this extends to community-driven hospice and palliative care services. For example in Neighbourhood Network in Palliative Care in Kerala in India those interested in helping receive 16 h of training (Kumar and Numpeli 2005).

7.3 What Do We Know About the Impact of Training

A review published in 2005 sought to describe the dominant topics in research literature on volunteering in hospice and palliative care. The review focused on publication years 1988–2004 (Wilson et al. 2005). Of the three overarching themes identified in the literature, one was on descriptions of volunteer training programs and training needs. Ten years later, a Cochrane systematic review sought to evaluate the effect of training programs for volunteers in patient- and family-facing roles in hospice and palliative care (Horey et al. 2015). This review focused on comparative prospective studies, such as RCTs. They sought evaluations of training programs according to any stated or implied purpose: of whether the program was intended to build skills for the volunteer's role, to enhance volunteers coping, or to maintain service standards. No relevant well-designed studies were identified. In their conclusions, they highlight that they excluded some comparative prospective trials on volunteer training in this setting (this is because of limitations in the trial design prevented meaningful comparison between those who received volunteer training and those who did not). This they suggest indicates that rigorous research in this area is possible. Although since this publication to our knowledge there have been no new trials published.

8 Conclusion

This chapter has explored volunteering from both practice and research perspectives in both adult and children's hospice and palliative care. While countries and cultures may approach hospice and palliative care differently, there is a surprising similarity in the roles and involvement of volunteers. Research suggests that their roles are distinct from those of paid staff; they are perceived by volunteers as less task oriented and more social in nature. Their activities are diverse, and volunteer presence in hospice and palliative care spans many different contexts in which care is delivered. Volunteering is not without its challenges, however. Research shows that volunteers themselves sometimes feel unprepared for what they face highlighting the importance of good support and training. There is much anecdotal evidence but a paucity of empirical evidence on the impact of volunteering in hospice and palliative care and of the content and effectiveness of training. This chapter has also explored the ethical and research challenges of identifying and measuring outcomes for volunteering and concluded that these are not insurmountable.

Clearly embedded in the history and development of hospice and palliative care across many countries, volunteering plays an essential role in contributing to leadership, fundraising and governance, patient and family experience, and public education. Volunteers, as community members, play an important part in helping to normalize death and dying as a social issue. If we are serious about delivering truly holistic hospice and palliative care to patients and families, we need to recognize and address the vital role played by volunteers.

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Part V

Palliative Care in Specific Disease Groups

Palliative Care and Cancer

57

Koen Pardon and Gaëlle Vanbutsele

Contents

Abstract

There is a growing trend in oncology, both in research and in clinical practice, toward the early integration of palliative care into regular oncology treatment, from diagnosis of advanced cancer onward. This new care approach has been developed to tackle two major problems insufficiently addressed by traditional methods which seriously affect the quality of life of advanced cancer patients – the undertreatment of symptoms

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_56

and the overtreatment of the cancer itself. Although these problems can also be observed in other life-threatening diseases such as heart failure and dementia, the early integration of palliative care is gaining ground particularly in oncology, as the specific, more recognizable symptoms of advanced cancer and the relative predictability of time of death make it more suitable for early palliative care.

Recently, several models of the early integration of palliative care into regular oncological health services have been developed. In some of these models, the oncologists themselves are responsible for the palliative care of the patient during the illness trajectory, and in others specialist palliative care teams are integrated into regular oncology care. There is accumulating evidence that supports the value of early integration of specialist palliative care teams both in outpatient and inpatient settings. However, despite this evidence, palliative care is still largely seen, and applied, only in the later stages. In this chapter, several barriers to the early integration of palliative care related to healthcare professionals, to patients and family, and to the healthcare system itself are identified and discussed.

1 Introduction

There is a growing trend in oncology, both in research and in clinical practice, toward the early integration of palliative care into regular oncology treatment, from diagnosis of advanced cancer onward. This trend is in accordance with the 2002 definition of palliative care by the World Health Organization (WHO) which clearly states that palliative care is applicable early in the course of a life-threatening illness, in conjunction with disease-modifying and life-prolonging therapies, and is not limited to end of life or terminal care when death is likely to occur within a few days or weeks (WHO 2002). According to the WHO, the goals of palliative care, such as improving quality of life through comprehensive symptom management and patient and family support, are ideally applied throughout the trajectory of a serious illness like an advanced cancer. More recently, in 2016, on the basis of accumulating evidence, the American Society of Clinical Oncology (ASCO) issued an official guideline stating that inpatients and outpatients with advanced cancer should receive dedicated palliative care services, early in the disease course, concurrent with active treatment (Ferrell et al. 2017). With this, an important step has been taken toward actual integration into clinical practice.

Figure 1 describes the new model of early integrated palliative care; this differs from the old but still much used model in which palliative care is seen as an attachment to the curative and life-extending phase. This figure is an adaptation of the figure that was developed by Lynne and Adamson in 2003 (with permission of RAND Health) (Lynn and Adamson 2003). In the old model, palliative care is only initiated when there are no options left. In the new model, palliative care starts at diagnosis by evaluating whether the patient has palliative care needs. As the disease progresses, palliative care becomes increasingly important, though in a varying way, according to the patient's needs; additionally, it also focuses on those close to the person who is dying, both before and after death.

This chapter discusses (1) which problems in traditional oncology care have led to the development of this new approach, (2) what models of early integration of palliative care in oncology are being developed and proposed, (3) why the integration of palliative care is gaining ground particularly in oncology rather than in other diseases such as heart disease and dementia, (4) what the research evidence says about the early integration of palliative care into oncology, and (5) what the current state of affairs is with regard to the actual integration of palliative care into clinical practice and which barriers have to be overcome in order to improve it.

2 Problems Insufficiently Addressed by Traditional Oncology Care

There are several problems that seriously affect the quality of life of people with advanced cancer which are insufficiently addressed by traditional

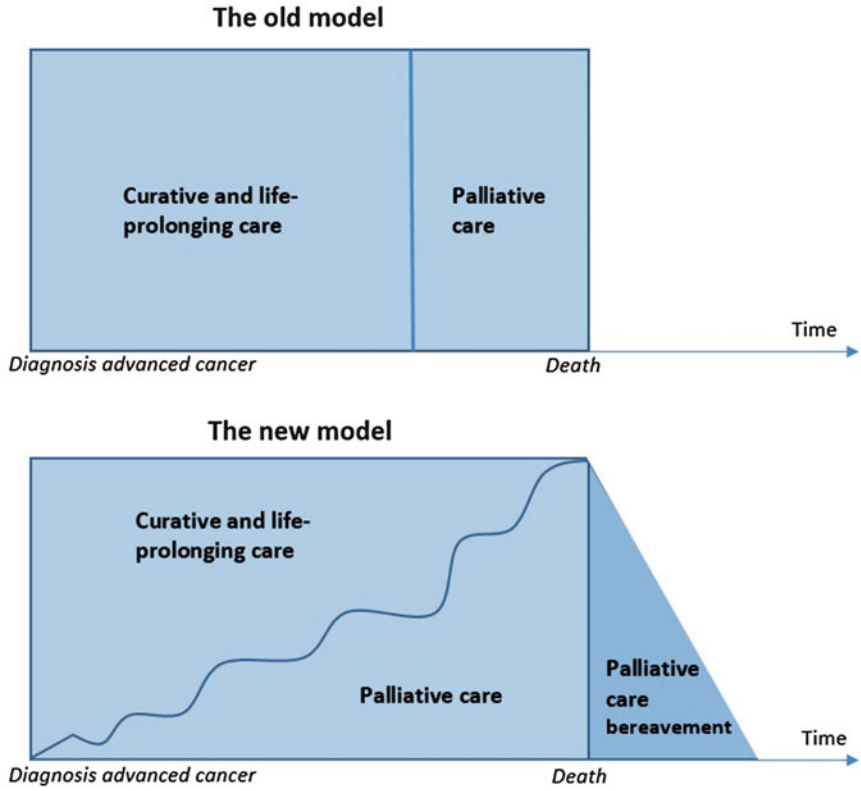

Fig. 1 The old and new model of early integrated palliative care in oncology care

oncology care, a situation that has led to the development of the new approach of early integration of palliative care into oncology care. Perhaps the most obvious of these is that people with advanced cancer with limited life expectancy often suffer from multiple symptoms – on the physical, psychological, social, and existential levels – that appear to be undertreated. A recent study of pain from the USA, one of the most frequent and debilitating of symptoms, shows that of 3123 ambulatory patients with invasive breast, gastrointestinal, or lung cancer, 33% of those who were suffering from pain were receiving inadequate analgesic prescribing, a problem that persisted even after a 1-month follow-up (Fisch et al. 2012). A study in a teaching hospital in Australia examined the treatment of nausea in hospitalized cancer patients and concluded that nausea is often inadequately treated, with more than one third of nauseated patients either not being prescribed an antiemetic or not having taken prescribed medication (Greaves et al. 2009). Studies with regard to other common symptoms in advanced cancer, such as dyspnea, constipation, loss of appetite, and depression, show similar results.

One of the reasons for undertreatment of symptoms is their underdiagnosis; according to a European multicenter study, healthcare providers underestimate symptom intensity in one out of ten patients, with variations between cancer diagnoses (Laugsand et al. 2010). Other related reasons include the strong orientation of healthcare providers toward cure or life prolongation rather than quality of life, a lack of expert knowledge of symptom management, and limited time to spend with patients.

A second problem is that people with advanced and incurable cancer run the risk of overtreatment, of receiving continued burdensome treatment with only marginal positive effect, if any, but with many adverse effects. This has been

demonstrated in several studies; a population-based retrospective study in Ontario, Canada, for instance, used administrative data to examine aggressiveness of end-of-life cancer care. The care was deemed aggressive if there was at least one of the following indicators: the last dose of chemotherapy received within 14 days of death, more than one emergency department visit within 30 days of death, more than one hospitalization within 30 days of death, or at least one intensive care unit admission within 30 days of death. It was observed that almost 25% of patients experienced at least one occurrence of potentially aggressive end-of-life care, and this was most likely in breast, lung, or hematological malignancies (Ho et al. 2011). The researchers also remarked that chemotherapy and intensive care unit utilization was higher in the USA than in Ontario.

This tendency to overtreat can be ascribed to oncologists whose orientation is naturally toward cure and life prolongation, but it might also be related to the wishes of the person who is dying, who may prefer to receive aggressive treatment for as long as possible. However, research shows that the treatment approach has often not been thoroughly discussed with the patient and thus does not always correspond with their fully informed preferences. There is ample empirical evidence that most patients with serious life-threatening illness prefer to avoid hospitalizations and aggressive care when their illness is advanced.

Both problems, the undertreatment of the symptoms and the overtreatment of the cancer, can be tackled by the early integration of palliative care into regular oncological care. The WHO defines palliative care as an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual (WHO 2002). In palliative care the expertise exists to diagnose and treat the many symptoms that advanced cancer patients experience. The focus of palliative care on the quality rather than quantity of life acts as a good counterbalance to the use of possibly futile aggressive treatments. The integration of the two care systems, i.e., oncology with its focus on disease-oriented treatment and palliative care with its focus on symptom reduction and quality of life, can ensure that people who are dying and those close to them receive the best possible care, tailored to their wishes and their needs.

3 Early Palliative Care Is Gaining Ground More in Oncology than in Other Medical Specialties

The early integration of the palliative care model is gaining ground in oncology more than in other medical specialties. This is unexpected because the problems of cancer patients that, as described above, originally led to integrated palliative care do not only affect oncology patients but also others with life-limiting diseases such as heart failure and dementia. Considering heart failure, for instance, a US study compared the symptom burden, depression, and lack of existential well-being of heart failure patients with that of advanced cancer patients and found that both groups had a similar number of physical symptoms, depression scores, and scores for spiritual well-being, after adjustment for age, gender, marital status, education, and income. The authors concluded that heart failure patients, particularly those with more severe heart failure, need the option of palliative care just as much as advanced cancer patients do (Bekelman et al. 2009). Another study in Belgium, Europe, interviewed people with cancer, chronic obstructive lung disease, heart failure, or dementia at different phases of the illness trajectory. They were asked how they experienced the care needs related to their disease from diagnosis onward. The results revealed that various problems and care needs, i.e., physical, practical, psychological, social, existential, and financial, as well as needs for information and communication, were present in every disease group (Beernaert et al. 2016). The needs occurred both in the earlier phases, from diagnosis onward, and in the later phases in the illness trajectory of every disease group.

One explanation for the leading role of oncology in the early integration of palliative care can be found in the specific disease pathway of cancer

compared with other diseases such as heart failure and dementia (Lynn and Adamson 2003). The cancer pathway is characterized by the presence of various symptoms that are highly recognizable and by a relatively predictable time of death. As a result, the match with palliative care is possibly much greater than it is with other diseases. Heart failure usually results in a slow deterioration of the state of health, interspersed with more acute phases of deterioration. Any of these acute phases can result in a more or less "sudden" death. In such patients, there is much less clarity about the imminence of death. The third pathway, dementia, is characterized by a steady period of decline in functional and mental capacity; death itself is usually the result of the occurrence of an acute infection.

The different pathways of cancer, heart failure, and dementia are described in Fig. 2 (with

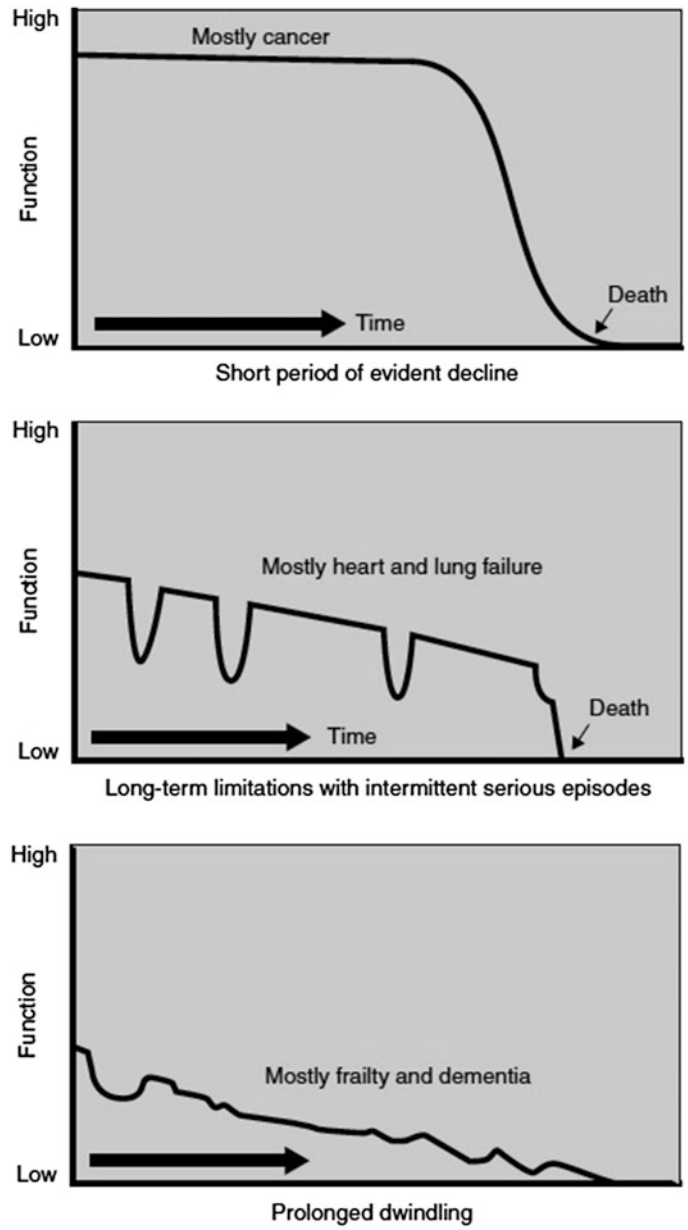

Fig. 2 The typical disease pathway of cancer, heart failure, and dementia

permission of RAND Health). It has to be noted that these disease pathways describe an overall trajectory that is not always applicable to individual patients. This means that even in cancer patients the disease trajectory cannot always be predicted, even with the best prognostic tools and skills. The predictability of the disease trajectory can also depend on the specific cancer diagnosis. The pathway of hematological cancer, for example, is characterized by acute exacerbations and a rapid dying trajectory, resulting in difficulties for hematologists in assessing the right time to refer to palliative care. For some cancer types such as breast and colorectal cancers, there is an evolution toward chronic disease, and the differences with nonmalignant disease have become less. Moreover, the development of new immunotherapies that are effective for some people can add years to a life, further complicating the prognostic estimations of physicians. However, the limited predictability of life-threatening diseases, whether cancer or other conditions, does not need to be a barrier to the early integration of palliative care. Palliative care is in its essence a holistic approach that is focused on the person and not on the disease. This means that it is important in palliative care to evaluate every person separately to assess whether they have palliative care needs and to offer palliative care if indicated, rather than to start from a specific diagnosis.

4 Models of Early Integration of Palliative Care into Oncological Care

Models of early integration of palliative care within regular oncological health services have only recently begun to be developed. Bruera et al., for instance, described three possible models and levels of integration of palliative care services within oncology care: a solo practice model, a congress practice model, and a fully integrated palliative care model (Bruera and Hui 2012). The first, the solo practice model, requires the oncologist to manage all aspects of cancer care, i.e., the treatment of the cancer as well as supportive and palliative care. To be able to achieve this, the oncologist has to fully integrate palliative care knowledge and skills into their daily practice. The second, the "congress" practice model, is one in which the oncologist does not provide palliative care but refers patients to multiple consultants for the management of pain, distress, fatigue, and other symptoms. This requires some knowledge and skills in palliative care by the oncologist as it is important to be able to diagnose the palliative care symptoms of the patient and to assess the need for professional help with these symptoms. The third, the fully integrated palliative care model, is one in which the oncologist focuses on cancer-specific treatments while the palliative care team systematically attends to the patient's physical symptoms and psychosocial concerns. In this model, the oncologist and palliative care physicians comanage care in a complementary manner, thereby reducing the need for the extensive use of outside consultants.

These three models each have their advantages and disadvantages. The solo practice model, for example, has the advantage that both medical disease-oriented care and palliative care are provided by one person, requiring fewer visits for the patient and less coordination between specialists. The disadvantage is that oncologists are often not trained in palliative care and may not always have the time to take on this task. The congress practice model has the advantage that the oncologist can refer to experts and does not need to have all the expertise, but the disadvantage is that there is often limited communication and coordination of care. On the other hand, good coordination and close cooperation are possible in the fully integrated care model, but this coordination can only be effective if good care pathways or protocols are established and followed.

Bruera's three models, however, conceal something that is often mentioned in the literature – the distinction between general and specialist palliative care (Quill and Abernethy 2013). General palliative care is care that is provided by regular healthcare professionals who have basic palliative care knowledge and skills.

In concrete terms, general palliative care would mean that the oncologist engages in systematic basic symptom assessment and management, in discussions about prognosis and goals of care, in shared decision-making, and in timely care planning.

Specialist palliative care involves the separate discipline of palliative care as provided by multidisciplinary teams in hospitals, in outpatient clinics, and in palliative home care. In this case, the palliative care is provided by physicians, nurses, and other specialists who have received special training and whose main activity is to provide palliative care. This form of palliative care is what most people understand as palliative care. Specialized palliative care has become increasingly available in recent years. Researchers at the University of Lancaster, UK, for instance, have identified the existence of 16,000 hospices and/or palliative care units worldwide – standalone units or those attached to a hospital – that treat patients in the final phase of life through the provision of adequate symptom relief (Lynch et al. 2013). The countries in the top category for such provision are Austria, Australia, Belgium, Canada, France, Germany, Hong Kong, Iceland, Ireland, Italy, Japan, Norway, Poland, Romania, Singapore, Uganda, and the UK. According to this WHO-recognized classification, these countries have developed a critical mass in the field of palliative care, spread across various locations within the country. This means there is a complete range of various forms of palliative care from multiple service providers. In these countries both professional caregivers and society and government as a whole are aware of the need and importance of palliative care; there is widespread though heavily regulated availability of morphine and other analgesics. In addition, the specialist healthcare providers are organized into one or more palliative care associations (WPCA and WHO 2014). Unfortunately, there is still a large group of countries, 75 in total, where no center for palliative care exists. These are mainly countries with a low gross national income.

The question arises of which model of early integration of palliative care into oncology is preferable. Much research has been undertaken looking at the third model of full and early integration of specialist palliative care in oncology care, and strong evidence for the effectiveness of this model has been found. However, one clear disadvantage of this model is that it is time intensive and expensive, which raises the question of whether the full integration of specialist palliative care is actually feasible in times of increased aging and increased numbers of chronically ill people. For this reason it has been suggested and argued that the support of a fully integrated model throughout the disease course is not necessary but is only required when the patient develops complex palliative care needs. At other times general palliative care, i.e., that provided by an oncologist who has had a basic training in palliative care, will suffice. In other words, in this scenario the best overall model would be one in which integrated specialist palliative care is being interchanged with general palliative care provided by the oncologist, depending on the complexity and the severity of the palliative care needs of the patient.

5 Research Evidence for the Value of Early Integration of Palliative Care into Oncology

There is accumulating scientific evidence that demonstrates the added value of models of early integration of specialist palliative care provided by an interdisciplinary palliative care team both in outpatient and inpatient settings. Other models of early palliative care in oncology, such as the model of general palliative care in oncology, have not been studied thoroughly, and therefore no definitive statements can be made regarding their effectiveness.

The randomized controlled trial (RCT) studies that have tested the early and fully integrated specialist palliative care model are discussed below. These trials were strongly based on others that studied palliative care in the home or hospital setting but have the specific feature that the palliative care was provided early in the disease trajectory to maximize the beneficial effects on quality of life and symptom burden of the person who is dying and those close to them.

5.1 Temel et al. (USA): Study 1

Temel et al. undertook an RCT with 151 outpatients with metastatic non-small cell lung cancer (NSCLC) who were treated in the thoracic oncology clinic of Massachusetts General Hospital in the USA (Temel et al. 2010). They compared early specialist palliative care integrated into standard oncology care versus standard oncology care alone with no palliative care provision or care provided only late in the disease course. The researchers chose to study newly diagnosed metastatic lung cancer patients because they have a median life expectancy of less than 1 year and experience a high symptom burden.

The early palliative care intervention consisted of consultations with the patient by a member of the hospital palliative care team shortly after diagnosis and at least monthly thereafter. The palliative care team of the hospital consisted of six palliative care physicians and an advanced practice nurse. The consultations were guided by newly developed palliative care guidelines that differed from the existing guidelines for standard palliative care in that the clinicians were specifically encouraged to assess physical and psychosocial symptoms throughout the disease trajectory, to establish goals of care and to assist with treatment decision-making and coordination of care. Table 1 gives an overview of the early palliative care guidelines.

Table 1 Ambulatory palliative care guidelines in the study of Temel et al.

1. Illness understanding/education
Inquire about illness and prognostic understanding
Offer clarification of treatment goals
2. Symptom management – inquire about uncontrolled symptoms with a focus on:
Pain
Pulmonary symptoms (cough, dyspnea)
Fatigue and sleep disturbance
Mood (depression and anxiety)
Gastrointestinal (anorexia and weight loss, nausea and vomiting, constipation)
3. Decision-making
Inquire about mode of decision-making
Assist with treatment decision-making, if necessary
4. Coping with life-threatening illness
Patient
Family/family caregivers
5. Referrals/prescriptions
Identify care plan for future appointments
Indicate referrals to other care providers
Note new medications prescribed

The researchers found that the people in the early palliative care group had a significantly higher quality of life compared with those in the standard care group alone at 12 weeks after baseline. The percentage of patients with depression at 12 weeks was significantly lower in the palliative care group than in the standard care group, but there was no difference between groups in scores for symptoms of anxiety. With regard to end-of-life care, 33% of those who were assigned to early palliative care compared with 54% of the standard oncology group had received aggressive end-of-life care. Another important finding that drew the attention of the medical community was that patients receiving early palliative care had a longer median survival rate than those in the standard care group (11.6 versus 8.9 months since diagnosis). It is not yet clear what precisely causes the increased survival time in the early palliative care group. The researchers concluded that early integration of palliative care for patients with metastatic non-small cell lung cancer is a clinically meaningful and feasible care model that has effects on quality of life and survival that are similar to the effects of first-line chemotherapy.

5.2 Temel et al. (USA): Study 2

Temel et al. then conducted a further RCT with 350 patients with newly diagnosed incurable lung cancer (NSCLC, small cell, or mesothelioma) or non-colorectal gastrointestinal cancer (pancreatic, esophageal, gastric, or hepatobiliary) recruited from the Massachusetts General Hospital (Temel et al. 2017). Patients were randomly assigned to the intervention group providing at least monthly consultations with a palliative care clinician plus usual care or the control group providing usual care alone.

There was no significant improvement in quality of life in the early integration group at

12 weeks after baseline, but there was at the 24-week time point. People in the intervention group also had lower depression at week 24, controlling for baseline scores. At 24 weeks there were also significantly more in the intervention group who had discussed their end-of-life wishes with their oncologist than in the control group. Exploratory analyses of the study outcomes by cancer type revealed important differences in both cancer groups. Lung cancer patients in the intervention group improved in quality of life from baseline to 12 weeks, while those lung cancer patients in the control group reported worsened quality of life. On the other hand, the non-colorectal gastrointestinal cancer patients improved in quality of life in both groups with no differences between groups. Thus, there seems to be a difference in the effect of the intervention depending on cancer type.

5.3 Bakitas et al. (USA): Study 1

Bakitas et al. studied 322 patients with different types of newly diagnosed advanced cancer in a rural comprehensive cancer center, affiliated outreach clinics, and a Veterans Affairs Medical Center (USA). In this study, people were randomly assigned to early palliative care and usual care (intervention group) versus usual care alone (control group) (Bakitas et al. 2009). The intervention consisted of a multicomponent psycho-educational intervention (the ENABLE study: Educate, Nurture, Advise, Before Life Ends) that was given shortly after diagnosis of advanced or recurrent cancer. Trained palliative care advanced practice nurses undertook four weekly educational sessions with the patient and monthly telephone sessions thereafter for follow-up. The sessions focused on patient activation, empowerment, and self-management; patients learned important palliative care principles and crisis prevention through the practice of problem solving, symptom management, communication, and advance care planning. The nurses also had a referring role to other healthcare professionals when this was indicated in order to improve quality of life. Patient-reported outcomes were measured on baseline, at 1 month and every 3 months until death or study completion.

Patients in the palliative care group had significant higher quality of life scores compared with control group patients, better mood, a trend toward lower symptom intensity, but no different resource use (i.e., days in hospital, days in intensive care unit, number of emergency department visits). The survival time in the intervention group was not significantly higher compared with the control group.

5.4 Bakitas et al. (USA): Study 2

Bakitas et al. conducted another RCT later on in the same centers with a similar intervention to determine at what time in the illness trajectory it is best to begin early palliative care; they compared two early palliative care groups, one in which palliative care was begun after enrollment, within 30–60 days (early palliative oncology care), and one in which palliative care was started 3 months after enrollment (still early but delayed palliative oncology care compared with the other group) (Bakitas et al. 2015). The researchers found no significant differences in the patient-reported outcomes of quality of life and symptom impact at 3, 6, and 12 months after enrollment. However at 1 year, a 15% survival advantage was found in the early palliative oncology care group. The precise mechanism of the prolonged survival is not clear yet and can have many possible causes according to the researchers.

5.5 Zimmerman et al. (Canada)

Zimmerman et al. undertook a cluster RCT in the Princess Margaret Cancer Centre in Toronto, Canada, in which 24 medical oncology clinics were randomized to early palliative care integrated in standard cancer care or standard cancer care alone (Zimmermann et al. 2014). A total of 461 advanced cancer patients with solid tumors with a clinical prognosis of 6–24 months participated. The core intervention of early palliative care comprised a consultation and follow-up in

Table 2 Components of the intervention of early palliative care in the study of Zimmerman et al.

1. Within 1 month of recruitment: a multidisciplinary assessment of symptoms, psychological distress, and social support. The duration of this consultation was approximately 60–90 min
2. One week after the first consultation and thereafter as needed: routine telephone contact from a palliative care nurse
3. On a monthly basis: outpatient palliative care follow-up. The duration of these follow-up consultations was 20–50 min
4. 24/7: an on-call service for telephone management of urgent issues

the oncology palliative care clinic by a palliative care physician and nurse. The components of the intervention are described in more detail in Table 2.

The results of the study showed that there was no significant improvement in the early palliative care group compared with the control group at 3 months after enrollment, but there was at 4 months. Their satisfaction with care was significantly better both at 3 and 4 months, and the symptom scores were significantly better at 4 months. There were no significant differences in the specific problems of patients in their interactions with nurses and doctors. Looking at the effects of early palliative care on the caregivers, a significant improvement in their satisfaction with care was observed, while the results regarding their quality of life were inconclusive (McDonald et al. 2017).

5.6 Maltoni et al. (Italy)

Maltoni et al. conducted a multicenter RCT study in Italy of 207 outpatients with metastatic or locally advanced inoperable pancreatic cancer (Maltoni et al. 2016b). The goal was to compare the impact of standard cancer care with systematic early palliative care on the one hand with that of standard cancer care with on-demand palliative care on the other hand. The difference between the two groups was that in the first group all participants received palliative care as a standard, whereas in the second group it was only provided if there was an explicit request from a doctor or patient.

The intervention and trial were very similar to Temel's study. Patients in the intervention arm were given an appointment with a palliative care specialist who used a checklist of topics that were the same as those used by Temel. They were seen every 2–4 weeks until death by a member of the palliative care team. Palliative care appointments and interventions initiated by the palliative care specialist were shared with the oncologist.

Systematic early palliative care significantly improved quality of life 3 months after baseline compared with on-demand palliative care. There were fewer people with depression and anxiety in the intervention group, but the difference was not significant. There was no difference in overall survival between the two groups. With regard to the aggressiveness of end-of-life care, there were differences in favor of the intervention group on some indicators, in particular the use of hospice services and chemotherapy provided in the last 30 days of life (Maltoni et al. 2016a).

5.7 Overall Assessment of Research

When we compare the six trials, there are a number of similarities and differences. Looking at the intervention that was being evaluated, in all studies it involved early integration of specialist palliative care into standard oncological care and consisted of at least monthly patient consultations by a member of the specialist palliative care team. In the studies of Bakitas et al., the first consultations were highly educational, which was not the case in the other studies, and the subsequent monthly consultations were conducted by telephone because of the rural setting in which the study took place. The palliative care guidelines on which the consultations were based were most clearly described in Temel and Maltoni's study. According to these guidelines, the following topics were required to be discussed in the consultations with the person and those close to them: illness perception, symptom management, medical decision-making, coping with the illness, and referral to other healthcare professionals. In the study of Zimmerman et al., the description of the intervention explicitly mentioned – besides the

monthly consultations – the possibility of telephone contact with a palliative care nurse if needed and 24/7 on-call service for the telephone management of urgent issues.

Different patient populations were studied in the six studies. The first study of Temel and the study of Maltoni examined one type of cancer, i.e., non-small cell lung cancer and pancreatic cancer, respectively, both being very deadly cancers with a high symptom burden. In the second study of Temel, two types of cancers were studied, incurable lung cancer and non-colorectal gastrointestinal cancer. In the studies of Zimmerman and Bakitas, a heterogeneous group of patients with different types of advanced cancer were studied. In all studies, quality of life was the primary factor investigated, and an effect was found in all studies. However, this effect was not observed in Temel's second study and in Zimmerman's study at the intended 3 months after baseline, but only at 6 and 4 months after baseline, respectively. It seems that the palliative care intervention may require longer than 3 months before having a noticeable effect on quality of life. The other outcomes that were often investigated in the studies were depression, anxiety, symptom burden, use of resources, and survival time. These outcome measures were sometimes significantly improved in the intervention group compared with the control group, and sometimes they were not, depending on the study. Increased survival time in the intervention group was only significant in the first study of Temel and in the second study of Bakitas.

6 Actual Integration into Clinical Practice: Barriers to Overcome

Despite the established principle of early integration of palliative care in oncology and evidence of its benefits, research evaluating the use and timing of both general and specialist palliative care shows that, overall, it is still both seen and applied as terminal care (Quill and Abernethy 2013; Beernaert et al. 2013; Van den Block et al. 2008). A survey to determine the availability and degree of integration of palliative care services in the USA showed that the median duration from referral to specialist palliative care was 90 days before death for outpatient clinics, 7 days for inpatient consultation teams, and 7 days for palliative care units (Hui et al. 2010). A study on referral practices of oncologists to specialized palliative care conducted in Canada also showed that referral was late in the disease trajectory for patients with uncontrolled symptoms (Wentlandt et al. 2012). In Belgium, about 60% of patients who did not die suddenly of cancer were referred to a palliative care service, and for about half of those, this was less than 20 days before death (Beernaert et al. 2013).

Using specialist palliative care does not, of course, necessarily reflect whether or not palliative care was being provided, as regular care could also have been aimed at improving the quality of life of patients and those close to them by addressing their palliative care needs. There are however several studies that indicate that this is not the case. Mortality follow-back studies in Belgium, for instance, have looked at the type of care delivered in the final 3 months of life and demonstrated that, in a majority of cases, the aim of care shifted to comfort or palliation only in the final weeks of life (Beernaert et al. 2013; Van den Block et al. 2008).

Several studies have been done to examine why palliative care is often offered only very late in the disease trajectory when death is imminent, if at all. Three types of barriers have been identified that play a role in the lack of early integration of palliative care in oncology – barriers related to the healthcare professionals, barriers related to the person who is dying and those close to them, and barriers related to the healthcare system.

6.1 Barriers Relating to Healthcare Providers

At the level of healthcare providers, one of the main barriers is the fact that many oncologists still have the idea that palliative care equals terminal care and that palliative care thus only needs to be initiated at the end of life. In order to address this barrier, it is important that healthcare providers become well-informed about the benefits of early

palliative care, both through scientific literature and textbooks such as this one and through their own professional organizations. A good and important step was taken by the American Society of Clinical Oncology (ASCO), which established a provisional clinical opinion in 2012 based on the first RCT study of Temel stating that patients with metastatic NSCLC should be offered concurrent palliative care and standard oncologic care at initial diagnosis (Smith et al. 2012). By 2016, ASCO updated this provisional clinical opinion reflecting changes in evidence since the Temel study and recommending that all patients with advanced cancer should receive palliative care early in the disease course, concurrent with active treatment (Ferrell et al. 2017).

Even if oncologists are convinced of the benefits of early palliative care, they are still sometimes hesitant to discuss and initiate it because of fear that the use of the term palliative care will take away hope from their patient. Research has indeed shown that oncologists tend to avoid discussing more difficult topics such as prognosis, life expectancy, and palliative care, even if the patient wants this information (Pardon et al. 2011). Some investigators have suggested using the term supportive care instead of palliative care, in order to address this problem. There are studies that have demonstrated that renaming palliative care as supportive care effectively led to more referrals to palliative care. A study by the MD Anderson Cancer Center in Texas, for example, observed a 41% increase in palliative care consultations and a quicker referral to palliative care after a name change (Dalal et al. 2011).

Another barrier at the level of oncologists is that very often they have not received any training at all in palliative care and thus lack basic palliative care knowledge, skills, and attitudes (Aldridge et al. 2016). A basic training in palliative care is fundamental in enabling oncologists and other regular health professionals to recognize palliative care needs. It would also facilitate oncologists in providing general palliative care themselves whenever necessary and in referring to and working with specialist palliative care teams in the case of complex problems. Training in palliative care is also important because it may contribute to the elimination of other barriers such as the idea that it is the duty of the oncologist to provide palliative care themselves or the negative image of palliative care they may have as a result of negative experiences in their clinical practice. For the integration of palliative care in oncology, it is additionally important that oncologists have specific knowledge of how palliative care is organized in their country, to what degree palliative care services are accessible and available, and what the legal and financial framework is for the cooperation between oncology and palliative care.

Besides barriers at the level of the oncologist, there are also barriers at the level of palliative care professionals. One barrier is that early integration of palliative care into oncology leads to a greater workload for palliative care specialists, who are already underrepresented and often overburdened (Kain and Eisenhauer 2016). Another barrier for successful integration might be that the palliative care experts are insufficiently informed about the therapies the patient is receiving from diagnosis on, the side effects of these therapies, and the overall expertise and modus operandi of oncologists in relation to their patients.

6.2 Barriers Relating to the Person Who Is Dying and Those Close to Them

One barrier relating to the person who is dying and those close to them is that they often think of palliative care as terminal care, as many regular healthcare professionals do, although terminal care is only part of what palliative care provides. Patients who participated in the RCT of Zimmerman were asked after the study how they had viewed palliative care before the study had started (CAPC 2015; Zimmermann et al. 2016). In their answers it became clear that most patients associated palliative care with death, dependence, and end-of-life comfort care in inpatient settings. This perception changed for those who received the intervention of early palliative care, even though they still thought that the term itself was very much associated with stigma and that it needed to be better explained by healthcare

professionals. An important step toward eliminating this barrier is to educate the public about palliative care through awareness campaigns and through more accurate information provision by healthcare professionals. Another way is to change the name as discussed above.

6.3 Barriers Relating to the Healthcare System

The early integration of palliative care into oncology is challenging because it questions the adequacy and efficacy of the current structure and organization of the healthcare system as it exists in many countries. The current healthcare system is primarily organization-centered, with limited communication and cooperation between the different specialties that are involved in care and between the different healthcare settings (hospital, nursing home, home). The aim of the integration of services however is to enhance cooperation and communication and organize healthcare around the person who is dying and his or her needs. To be able to let healthcare services cooperate more and to make the patient central is another way of working that is not financially and structurally endorsed in the current system. In many countries, for instance, the financing of healthcare is such that technical performance may be rewarded, while the quality of care and the time spent on communication and coordination is less highly regarded.

The current system thus needs to a certain extent to be changed from an organization-centered to a patient-centered system, and one way of doing this is to develop pathways or protocols (Kaasa et al. 2017). These are structured, multidisciplinary care plans that clearly identify who is responsible for care in the various disciplines and how communication will be achieved. Care pathways also make clear what resources are needed to make optimal integrated care possible during the disease trajectory. Researchers have stressed the importance of such care pathways and have clarified that they should reflect different needs, different goals, and different forms of expertise and that therefore different pathways need to be developed for different subgroups of patients. Information and communication technology (ICT) can be very helpful in developing integrated palliative care models. ICT can, for example, facilitate communication between healthcare providers, carers, and the patient through shared digital medical records, interdisciplinary meetings using video communication, and digital educational or informational programs for the patient, helping them to understand and to cope with their condition. ICT can also be used to enable systematic and automatic monitoring of symptoms, allowing professional and informal carers and the patient to respond rapidly to clinical changes, symptoms, and other care needs in a population where time is of the essence. However in order for care pathways and ICT to be successful, the input and support of all stakeholders – e.g., healthcare professionals, patients, hospital administrators, and health policymakers – in the development, evaluation, and implementation of these tools is of crucial importance.

The WHO captures the use of protocols, care pathways, and ICT to improve the care of patients with chronic or life-threatening disease under the heading "Health Technology" which it defines as "the application of organized knowledge and skills in the form of devices, medicines/vaccines, procedures and systems developed to solve a health problem and improve quality of lives" (WHO 2007). Although health technology is a fast-moving field that offers huge possibilities, it has yet to be developed and evaluated thoroughly in the domain of the early integration of palliative care in oncology.

Another barrier on the level of the healthcare system that hinders the widespread integration of palliative care in oncology is that of costs. Palliative care services in most countries are too understaffed to be able to take on the extra workload of the early integration of palliative care and thus require new investment and incentives. In the USA, for instance, a study found that there is only one palliative medicine physician for every 1200 people with a life-threatening disease. In comparison, for every 141 newly diagnosed cancer patients, there is one oncologist (CAPC 2015). Several studies point out that investing in

palliative care has a cost neutral or even a cost-saving effect. Palliative care interventions, for instance, limit the number of hospitalizations at the end of life, and such hospitalizations make up 5% of the healthcare costs of a dying patient. Two studies in US hospitals revealed that the implementation of specific palliative care consultation programs helped to bring down overall healthcare costs in the last months of life (Ciemins et al. 2007; Penrod et al. 2006). The early integration of palliative care might typically involve the withholding and withdrawal of expensive surgery as well as of life-prolonging therapies such as chemotherapy, hormone therapy, or radiotherapy, which can compensate for the costs of the new palliative care interventions.

7 Conclusion and Summary

The severity and multiplicity of symptoms of advanced cancer warrant a comprehensive care approach, integrating adequate oncology treatment with general and specialist palliative care options. Evidence for the benefits of the early integration of palliative care into oncological care is very promising but has not yet been widely translated into implementation in clinical practice. For this to happen in the future, it will be necessary to disseminate information about the beneficial effects of the early integration of palliative care into oncology and confront the misapprehension that palliative care is only terminal care. Moreover, organizational and structural changes in healthcare systems will be necessary in order to support the efforts of healthcare professionals to collaborate intensively and effectively with each other and with the person who is dying and those close to them, for the benefit of all involved.

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Palliative Care and Neurodegenerative Diseases

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David Oliver and Simone Veronese

Contents

Abstract

Neurological disease is a major cause of disability and death across the world. There is increasing evidence that palliative care is effective in managing symptoms, maintaining and improving quality of life, and helping patients

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_58

and families cope with the deterioration. As the disease progression varies, both between diseases and for individuals, palliative care may be involved for varying periods of time, and may need to be involved episodically throughout the disease progression. Careful assessment of all the issues – physical, psychosocial, and spiritual – will allow appropriate management and support for patients and families. Carer support is very important as families face all the issues of coping with a progressive disease. Recognition of the later stages of life is helpful in enabling patients, families, and professionals to be able to prepare for the dying phase and manage all the issues appropriately.

1 Introduction

1.1 Extent of the Problem

Neurological disease is a major cause of ill health, disability, and death across the world. In 2015 it was estimated that 12% of all deaths worldwide were due to neurological disease – this included progressive disease, stroke (10% of all deaths), and infections (WHO 2006). These disease groups vary greatly, and there is individuality for each patient – as the symptoms, progression, and prognosis can vary from person to person.

The commonest causes of death from neurological disease are cerebrovascular disease (10.2%), dementias (0.81%), epilepsy (0.21%), Parkinson's disease (PD) (0.20%), and multiple sclerosis (MS) (0.03%) (OFNS 2012). Infections are common – with tetanus and meningitis causing 0.4% of deaths worldwide. The distribution varies greatly across the world, and neurological disease accounts for a higher percentage of deaths (16.8%) in lower middle-income countries, compared to 13.2% in high-income and 8.2% in low-income countries (WHO 2006). There is the expectation that these figures will increase over the coming decades, as the majority of neurological diseases develop with increasing age, and by 2030 it has been estimated that 12.22% of all deaths will be due to neurological disease (WHO 2006).

Palliative care may be appropriate for many of these disease groups. In some instances, there may be a sudden deterioration and death may be unexpected – such as in epilepsy or cerebrovascular disease. The principles of holistic care within palliative care may be appropriate for all these people as they face a sudden deterioration in their functional state and quality of life. However with many progressive diseases, there is a slow and gradual progression, and there is no curative treatment, with the best that treatment can offer being the slowing of progression or the management of symptoms.

Although progressive neurological diseases are relatively rare individually, as a group they do cause both morbidity and mortality. The common progressive diseases are motor neurone disease/amyotrophic lateral sclerosis (MND/ALS) with a prevalence of 7/100,000, Parkinson's disease (PD) 180/100,000 but with a prevalence of 1750/100,000 for people over 80 years, dementias 700/100,000, multiple systems atrophy 5/100,000, progressive supranuclear palsy 7/100,000, Huntington's disease 6/100,000, and multiple sclerosis 80–140/100,000 but with higher rates in higher-income and northerly areas compared to lower-income or lower-latitude countries (WHO 2006; OFNS 2012; Alzheimer's Society 2015).

Thus neurological disease does lead to morbidity, disability, and death, and with the aging of the population on many countries, there will be increasing numbers of people affected and increasing palliative care needs.

2 Role of Palliative Care

Palliative care may be seen as appropriate for many neurological diseases which have no curative treatment and progress over time – such as MND/ALS, PD, MS, MSA, PSP, HD – and the World Health Organization definition of palliative care defines palliative care as helpful for "life-threatening illness" (WHO 2002). Moreover for other diseases which may have a more sudden onset, such as cerebrovascular disease (stroke), there may be an uncertainty of the prognosis and future progression with many people left with

severe disability and/or the risk of further deterioration and death.

Even for the progressive diseases, the prognosis and progression can be very variable, and patients have to cope with uncertainty of the future – both in terms of quality of life and prognosis. The prognosis of MND/ALS is usually 2–3 years from diagnosis, which may only be made after a year of symptoms, but 25% of people are alive at 5 years from diagnosis and 5–10% at 10 years (Shaw et al. 2014). PD has an average prognosis of 14 years but many people live 20–30 years, and as they are elderly there may be only a small reduction in life expectancy.

Palliative care has been increasingly recommended for neurological disease, and a consensus document from the European Association for Palliative Care (EAPC) and the European Academy of Neurology (EAN) has recommended that "palliative care should be considered early in the disease trajectory, depending on the underlying prognosis" (Oliver et al. 2016). Moreover there have been many guidelines recommending palliative care for different diseases, such as MND/ALS (Andersen et al. 2012) and PD (NICE 2006), and for neurology in general (Boersma et al. 2014).

However it is often considered that palliative care is only appropriate at the end of life, and referral for care may be very late in the disease progression. Within cancer there has been increased awareness of the effectiveness of early palliative care involvement, and a study of lung cancer patients showed that not only did early palliative care involvement improve quality of life and reduce depressive symptoms, but the prognosis was extended from 8.9 months to 11.6 months (Temel et al. 2010). Other studies have suggested early integration of palliative care within oncological services, so that patients' problems can be identified and managed appropriately (Gaertner et al. 2011).

As the prognosis of progressive neurological diseases varies – average prognoses are MND/ALS 2–3 years, PD 14 years, MSA 9 years, PSP 7 years, MS 30 years, and Alzheimer's disease 8–10 years – the involvement of early palliative care can be complex. However earlier involvement, according to the person's particular needs, can be very helpful in improving quality of life and managing symptoms, and also establishing a relationship with a multidisciplinary team so that the care can be easily accessed and accepted as the disease progresses (Oliver 2014). This approach, considering all aspects of care – physical, psychosocial, and spiritual – and considering family as well as patient, is the basis of palliative care. Although this approach may be helpful over a long period of time, the involvement of palliative care may be episodic, responding to particular issues (Bede et al. 2009). For instance, for a person with ALS, there may be particular concerns and issues at diagnosis, consideration of a gastrostomy, development of respiratory problems, and consideration of ventilatory support as the person deteriorates at the end of life (Oliver 2014).

3 Palliative Care in Neurological Disease: Evidence of Effectiveness

From the WHO definition of palliative care, it is clear that the measurement of the effectiveness of palliative care should be focused on the improvement of the individual quality of life (IQoL) of both patients and families and on the other physical, psychosocial, and spiritual issues that can be caused by the advanced disease.

Effectiveness can also be gauged by the evaluation of the complex services provided by palliative care, considering the wide range of these facilities. These vary in different countries and health services, and palliative care can be considered as a "simple approach" adopted by any health-care provider to severely ill patients or provided by primary medicine operators for patients with a low burden of palliative care needs (often known as generalist palliative care) or the specialist palliative care, provided by multidisciplinary services, with training and ongoing involvement in the care of people with complex needs in specific settings like hospice inpatient facilities, home specialist palliative care, or hospital teams.

The role of palliative care services in terms of impact of care, outcome measurement, and effectiveness has been increasingly studied. In 2003 the first study reporting the positive impact of palliative care was released (Higginson et al. 2003). A later review showed that the evidence for benefit from specialized palliative care is sparse and limited by methodological shortcomings (Zimmermann et al. 2008). More recently other researchers highlighted how palliative care can have a moderate positive effect on the main palliative care outcome (IQoL) (Catania et al. 2015), the integration of early palliative care can improve QoL and mood (Bakitas et al. 2009), and, even though not being a primary outcome, survival increased in patients with advanced lung cancer (Temel et al. 2010). Palliative care has been shown to have cost savings (Smith and Wasner 2014).

In patients affected by long-term neurodegenerative conditions, palliative care provision and integration with neurological services remains heterogeneous. There is a need for an improved model of integration that should be rigorously tested for effectiveness. Nevertheless the impact of palliative care services on the specific outcomes of patients severely affected by neurological disorders was studied for the first time by the King's College London palliative and supportive group for people with multiple sclerosis (MS) (Higginson et al. 2008). A phase 2 randomized controlled study was performed comparing a fast track group of patients who received immediately the palliative care service versus a control group who had a waiting list of 3 months before being cared for. This study showed how the involvement with the palliative care service appeared to positively affect some key symptoms and reduced informal caregiver burden and is cost effective (Higginson et al. 2009; Edmonds et al. 2010).

Using the same methodology, a similar RCT was repeated widening the service to a mix of neurological disorders (ALS, MS, PD, and related disorders). Fifty patients were randomized to receive immediate specialist palliative care (SPC) versus standard care (SC). This study showed how patients who received SPC input reported a significant clinical and statistical improvement in IQoL and in important physical symptoms like pain, dyspnea, quality of sleep, and bowel symptoms versus those who had SC (Veronese et al. 2015). Patients in the fast track group received home care multidisciplinary visits and were seen by palliative care physicians, nurses, physiotherapist, and psychologist if required. The team was in contact with the neurological service if specific issues emerged. On average, patients received weekly visits for all the duration of the study (16 weeks), and the service was not discontinued at the end of the follow-up.

An Italian multicenter, phase 3 RCT studied the impact of a home based palliative care approach (HPA) on the needs of patients with severe MS and their informal carers (Solari et al. 2015). The preliminary findings indicate that HPA reduced symptom burden, but there was no evidence of HPA efficacy on patient QoL or secondary patient and carer outcomes. The difference in the intensity of the service provision may explain the lack of effectiveness as the team were less experienced, and it may show that a specialist palliative care approach is necessary to really affect patient experience.

This available evidence shows that there is strong interest in elucidating the appropriate role of palliative care for people with neurological conditions. At present there is data showing a positive impact of palliative care on patients and their carers, even though the intensity of care or specific service that is ideal for such a heterogeneous group of disorders is not exactly clear. The model suggested by Bede (Bede et al. 2009) and adopted in a NHS document in the UK (NELCP 2010) represents the optimal option for the challenge of providing the correct amount of care at the right times during the disease trajectory. This approach creates useful links with the specialist palliative care services for significant moments where palliative care issues emerge and to better identify the end-of-life phase which is obviously inherent to palliative care.

4 Physical Symptom Management

Patients affected by advanced neurological conditions suffer a high burden of physical symptoms, often not adequately assessed and treated (Veronese et al. 2017). In the consensus review on the development of palliative care for patients with chronic and progressive neurological disease (Oliver et al. 2016), three recommendations focus on the importance of assessing and treating physical symptoms:

- Proactive assessment of physical and psychosocial issues is recommended to reduce the intensity, frequency, and need for crisis intervention.
- Physical symptoms require thorough differential diagnosis, pharmacological and non-pharmacological management, and regular review.
- The principles of symptom management, as part of the wider palliative care assessment, should be applied to neurological care.

Studies showed that many symptoms in people severely affected by multiple sclerosis (MS) are as highly prevalent and severe as those experienced by patients with advanced cancer and that increased disability is associated with increased severity for some symptoms (Higginson et al. 2006). Patients with late-stage PD, MSA, and PSP experience a complex mix of non-motor and motor symptoms. In a 1-year follow-up, symptoms are not resolved and half of the patients deteriorate. Palliative problems are predictive of future symptoms, suggesting that an early palliative assessment might help screen for those in need of earlier intervention (van Vliet et al. 2016). In ALS the impact of unmet physical issues is also very high (O'Brien et al. 1992), and the fear of choking to death, related to the shortness of breath, can be a leading cause for requests of hastening death (Veldink et al. 2002).

4.1 Motor Symptoms

In general, advanced neurological conditions cause motor complications and physical disability that impact deeply in the IQoL of patients and cause high burden of care to the informal carers (Veronese et al. 2015). Clinically, motor impairment can appear as muscular flaccidity, typical when the second motor neurone is involved such as in traumatic paralysis, in some forms of ALS, or in spinal cord metastasis. In other conditions, the patient can suffer from muscular rigidity or spasticity, like in stroke, MS, movement disorders, and ALS forms with prevalent first motor neurone involvement. Other muscular symptoms can be spasms, cramps, fasciculation, or myoclonus.

Some of these symptoms can be treated by modulating the specific drugs for the primary disorder; for example, in IPD rigidity can be improved by increasing L-DOPA or dopaminergic drugs. Since most of these conditions do not respond to specific treatments, in the advanced stages motor symptoms are treated with a symptomatic approach. A combination of physical therapy and muscle relaxant and muscle relaxant drugs can be used for stiffness and rigidity, for example, in advanced MS or ALS. Even in the very advanced stages, when the patient is restricted to a wheelchair or bedbound, adequate stretching programs can be adopted and useful to control the pain related to stiffness, maintain joint elasticity, and prevent bedsores. Occupational therapists play a role in prescribing aids to compensate for the disability and can be useful for transferring, writing, and other activities of daily living. The use of medications like baclofen, tizanidine, or dantrolene can be effective as muscle relaxant, but doses must be individually titrated and re-evaluated on regular bases. Benzodiazepines have also a role in treating stiffness, taking into account the possible central side effects. Botulinum toxin injections are used for those patients whose rigidity does not respond to symptomatic treatments. This option can help in hygienic procedures like allowing the movement of thighs in MS of very rigid patients and facilitating personal care. In specific cases advanced treatments can be effective for motor symptoms and complications. Intrathecal continuous injection of baclofen is used in advanced MS for general rigidity, using a

pump often positioned in the patients' abdomen (Otero-Romero et al. 2016). In IPD, selected patients' motor symptoms can be approached with specific options like apomorphine subcutaneous infusion, deep brain stimulation, and continuous intrajejunal infusion of levodopa-carbidopa intestinal gel (Worth 2013).

In most cases, however, motor complications cannot be effectively resolved, and patients and carers are exposed to the restless progression of disability. A role of palliative care is to help their assisted patient to accept the condition trying to enhance resilience and adaptation strategies. Disability is challenging, but feeling abandoned can be worse. One of the most touching quotes from the founder of modern palliative care, Dame Cicely Saunders, says: "You matter because you are you, and you matter to the end of your life. We will do all we can not only to help you die peacefully, but also to live until you die." According to this mandate, palliative care must face patients even when they cannot solve their problems, but continue providing help and promoting the residual quality of life.

Pain is a common and often unrecognized symptom in patients affected by neurodegenerative conditions (see Table 1).

Table 1 Prevalence of pain in neurologic conditions

Neurological disorder	Prevalence of pain	References
Parkinson's disease	40–86%	(Simuni and Sethi 2008)
Multisystem atrophy – MSA	88%	(Higginson 2012)
Progressive supranuclear palsy – PSP	60%	(Higginson 2012)
Multiple sclerosis	50–86%	(O'Connor et al. 2008; Bermejo et al. 2010)
ALS/MND	40–73%	(Miller et al. 1999)
Alzheimer's disease	57%	(Pautex et al. 2006)
Post stroke	14–85%	(Kumar et al. 2009; (Klit et al. 2009)
Spinal cord injury	64.9%	(Modirian et al. 2010)
Guillain-Barré syndrome	89%	(Moulin et al. 1997)

Chronic pain in patients with neurologic disorders has some challenging features to be considered. Chronic pain causes significant changes in function, anatomy, and chemistry of the brain (Borsook 2012); these changes are "brain-wide" including areas like the cerebellum, not normally involved in the pain system (Moulton et al. 2010). For many diseases the pathophysiology of pain remains unclear, but patients can suffer more than one pain at a time, and the symptom can be related or not related to the underlying disorder, in the latter case being due to comorbidity, but always painful (Lee et al. 2007). Finally the association of pain with depression and mood disorders is very common. This dangerous loop can worsen the intensity and the impact of both symptoms and makes difficult to understand and treat both. Furthermore, it is known how depression, hopelessness, and pain can drive the request for hastened death (Breitbart et al. 2000).

There are peculiar painful syndromes in different neurological conditions that should be tackled with specific approaches. In PDs and related disorders, pain can be musculoskeletal 70%, dystonic 40%, radicular neuropathic 20%, or central neuropathic 10% (Lee et al. 2007; Borsook 2012). Pain can increase and decrease with dopaminergic fluctuations or may be related to a central dopaminergic deficit and in both cases can be alleviated by adjusting L-DOPA medications (dystonic and central pain). Botulinum toxin may help involuntary muscular contractions related to dystonia, and neuropathic pain can benefit from anticonvulsants and other drugs used for this type of pain. NSAIDs may reduce local irritation and work on musculoskeletal pains, and opioids modulate pain pathways and can be useful in all pain syndromes.

4.2 Respiratory Symptoms

Patients affected by advanced neurodegenerative disorders frequently experience respiratory distress including dyspnea, weak cough, trouble in management of secretions, respiratory infections, neurogenic pulmonary edema, and noisy secretions at the end of life (death rattle).

Respiratory complications represent a frequent cause of death in advanced neurological patients since the muscular impairment can lead to dysfunction like choking, ineffective cough, and susceptibility to atelectasis and aspiration pneumonia (Aboussouan 2005).

In neuromuscular disorders, the main cause of respiratory symptoms is the muscular impairment directly caused by the neurological disease. In ALS respiratory impairment is caused by the lack of innervation, caused by the death of the motor neurones, and the following development of respiratory insufficiency with hypoventilation on the basis of diaphragmatic and intercostal muscle weakness (Mangera et al. 2012). In MS the nervous denervation and spasticity above all of the expiratory muscles can lead to the development of voluntary or autonomic respiration, diaphragmatic paralysis, paroxysmal hyperventilation, apneustic breathing, and neurogenic edema; the pattern depends on the location of the lesions in the brain, which follows both axonal and neuronal death. Muscular weakness and lack of coordination, worsening with the course of the disease, are involved in PD. In other disorders like HD or Alzheimer's disease, a combination of neurologic damage in the brain is responsible for the respiratory impairment and consequent symptoms.

Shortness of breath (dyspnea) is a personal unpleasant experience that can cause the fear of choking to death. It has been defined as "a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity." This experience is the combined effect of multiple physiological, psychological, social, and environmental factors and can itself induce both physiological and behavioral reactions. It can be associated to an objective respiratory insufficiency or just being a subjective feeling. It is strongly related to anxiety and often it creates a dangerous loop in which both symptoms are enhanced and worsened. The prevalence of breathlessness and respiratory distress varies with the disease: Dementia 12–52%, PD 22–35%, ALS 81–88%, and MS 26% (Moens 2014; Lee et al. 2007).

Symptoms of respiratory insufficiency in ALS include dyspnea on exertion, supine dyspnea, marked fatigue, disturbed sleep (frequent nocturnal awakenings, excessive daytime sleepiness), cough, and morning headaches (Miller et al. 2009). Weak coughing may be tolerable for patients who have an intact swallowing mechanism and minimal airway secretions, but the onset of complications like acute bronchitis or bulbar dysfunction may precipitate a life-threatening crisis.

Patients with neurological disorders should be monitored in the course of the disease for the possible onset of respiratory problems. In ALS specific guidelines provide indications on the timing and the clinical decisions to be undertaken. In other conditions, however, the pulmonary function should be assessed since its earlier detection can lead to the improvement of patients' outcome (Aboussouan 2005).

Treatment of respiratory symptoms should start from the recognition and treatment of possible underlying causes (e.g., respiratory infections), toward a more palliative approach when there is not a treatable cause. In the latter case, both pharmacological and non-pharmacological options can be effective, often combined. Physical therapy can help in correct positioning of the patients, and help in clearing secretions with techniques including manually assisted coughing, and others such as oscillation or percussion use of aids such as the assisted cough machine. Speech and language therapy can help when there are problems of coordination or vocal cord adduction. Noninvasive ventilation (NIV) via external mask is often effective for the support of inspiratory muscle function (Aboussouan 2005), though it may be contraindicated in some patients such as ALS with bulbar impairment or patients with cognitive decline or agitation. It can improve QoL of patients and data suggest an increase in survival in ALS (Radunovic 2013).

Invasive ventilation (IV) via tracheostomy remains a debated issue. There are differences in the adoption of this treatment in different countries. Although IV may increase survival, the disease continues to progress to the extent that the person becomes "locked in," with no form of communication, or it becomes a burdensome therapy. There are also ethical issues as it is an expensive treatment and may lead to the request of withdrawal from the ventilator, which will usually

lead to the person's death within a short time. There is strong consensus that NIV should be preferred to IV for many reasons, including ease of administration, less strain on caregivers, lower cost, greater portability, fewer infections, the virtual elimination of airway complications, and reduced need for hospitalization (Radunovic 2013). The impact on survival of ALS patients is not very clear since the literature shows a range of life protraction from less than 1 year to more than 40 months after tracheostomy. The role of family carers is very important in the constant care (24 h/7 days) required by patients in need of frequent tracheal aspiration. There are studies showing that the carers' QoL can be seriously affected by these tasks (Kaub-Wittemer et al. 2003).

Palliative and hospice care represent an alternative choice which can effectively impact on respiratory symptoms (Veronese et al. 2015), through the accurate use of drugs, like opioids, found useful in respiratory distress (Jennings et al. 2001) and recommended in specific guidelines and consensus reviews (Andersen et al. 2012; Miller et al. 2009).

4.3 Dysphagia and Swallowing Problems

Difficulties in coordination of the processes of contraction and relaxation of the various muscles involved in mastication, deglutition, and the progression of the bolus toward the stomach are common in neurodegenerative disorders causing difficulty with swallowing food, liquid, or saliva. The characteristics of the swallowing disorder can vary according to the neurological condition, the severity of the neurological disease, and other comorbidities. Dysphagia is considered as a general indicator of decline in any neurological disorder having a negative impact on survival above all if associated to weight loss (Thomas and Armstrong Wilson 2016). In late-stage PD, it occurs in up to 95% of patients and is associated with aspiration pneumonia. It is also very common in Parkinson's plus syndromes, and studies show that its onset has a negative prognostic meaning (Walshe 2014).

In advanced MS dysphagia affects 33% to 50% of patients, possibly because of uncoordinated respiration during swallowing.

Many people with ALS will experience problems with dysphagia (swallowing problems), which can make eating and drinking difficult. Dysphagia is reported to be prevalent in 30–100% of individuals depending on the type of ALS and the stage of disease affecting all individuals in the later stages of the disease. This can cause anxiety for people with ALS and their carers/family, who may have concerns about choking on food and liquids.

Dysphagia in advanced stages of dementia is associated with malnutrition and aspiration pneumonia which is a significant cause of death in this population. It is also prevalent in Huntington's disease and Prion diseases.

Managing swallowing issues can be really challenging for both patients and carers. Food and liquids are essential for living and are often associated to ethical and existential aspects. Help can be provided by an accurate assessment of the cause of dysphagia, treatment of underlying secondary causes, and advice on dietary modifications. Intervention can be focused on compensatory (changes in posture, modification of food and/or fluid, and adaptation of methods of eating and drinking) or rehabilitation techniques depending on the specific disorder.

Some treatments showed benefits for dysphagia in selected populations. Electrical stimulation and botulinum toxin treatment have been shown to be helpful in reducing the swallowing impairment in MS. In PD, speech and language therapy and dopaminergic drug adjustment are suggested to improve deglutition. Rotigotine patches can play a role in advanced PD when swallowing is impaired, but deep brain stimulation (DBS) did not show positive effects on dysphagia.

When swallowing becomes very difficult, distressing, very slow, or impossible, the tube feeding option can be considered. This is very often offered to ALS patients, even earlier stages, when first signs of swallowing impairment appear. This is due to the positive impact on QoL with improved dietary intake, and the patient may be able to continue to eat and taste his or her favorite food in

small amounts. Furthermore, PEG placement should be done before a decrease in pulmonary function becomes clinically significant, to avoid surgical and postsurgical risks of respiratory complication. In terminal dementia or in other neurological diseases with significant cognitive impairment, there is no evidence of positive effect of tube feeding in terms of QoL, survival, or other patients' outcomes, and the placement and later care may cause distress and even mortality (Sampson et al. 2009).

Even when clinically appropriate, patients can refuse tube feeding for many personal reasons – for instance, they may not want any further treatment to prolong their life. In this case the decision should be respected, and the involvement of palliative and end-of-life care becomes very important. Advance care planning should involve these decisions that are to be reassessed frequently, because as problems progress, they may change their mind.

5 Psychosocial/Spiritual Care

Facing a neurological disease may lead to many psychological and emotional issues. These may depend on the physical issues that affect the person; for instance, a person with PD who has severe mobility issues may become more anxious and concerned about how they cope with day-to-day activities and become disturbed. The response will also be affected by the previous experiences and issues faced by the person and their family – for instance, if there have been difficulties within a relationship, these may be heightened when there are stresses associated with a progressive disabling illness. Moreover changes in cognition and communication may also affect the person's coping mechanisms and lead to increased distress.

There are many psychological issues that may be faced:

- Concerns about the diagnosis – this may be a disease which is unknown to the person, or they may have experience, such as someone with HD who often has memories and experiences from a family member who has suffered and died of HD.
- Concerns about increasing disability and dependency.
- Feelings of depression or anxiety as they face the various symptoms and disability due to the disease progression.
- Fears of the process of dying. Many neurological diseases are associated with a distressing death, which may have been highlighted in discussions and debates about dying or assisted dying. For instance, people with MND/ALS have talked publically of their fears when discussing and advocating assisted dying, talking of choking to death and their fears of distress.
- Fears of losing control, especially as they may fear losing mobility, communication, and cognition. These are possibilities for many neurological diseases and needed to be discussed and ways of minimizing the effects on the person and their family considered (Goldstein 2014).

There may be no easy answers for these fears and concerns, but it is important to allow patients and their families to discuss and express their feelings. An openness of professional carers allows this, and this again emphasizes the need for longer-term involvement with teams, so that trust is engendered and discussions can more easily occur.

Most people are part of a wider family or caring network and those close to them may have similar issues. They may have the same fears about deterioration, dependency, disability, dying, and death, and depending on the previous relationship, they may or may not be able to discuss these openly with the person. If communication and discussion is limited, this may in turn lead to more difficulties as trust is lost, and the issues increase for both parties if there is not the opportunity to discuss and resolve these issues. Moreover if the spouse or carers are elderly, they may be facing their own illnesses and comorbidities, including psychological or cognitive change, and they will thus find the issues very difficult to cope with (Smith and Wasner 2014). If the person has cognitive change or dementia, there may be great stresses within a household, and it may become increasingly difficult to cope at home,

or extra care may be needed that further disrupts the previous normality.

There may be very practical issues faced by someone with a neurological disease as they become more disabled that may lead to fear, anxiety, and family conflicts – the roles within a family may become disrupted as the person becomes more disabled and is unable to perform their normal roles within the family and conflicts may arise; care within the housing may become more difficult, and consideration of changing the housing such as the installation of lifts or planning to move to more suitable accommodation may be needed, with ensuing stress and the potential for conflict.

There may also be spiritual issues faced by both the person and family. The experiences, beliefs, and values of any person will affect how they cope and manage with illness and disability. This may be particularly so for a person with a neurological disease who is facing increasing deterioration and dependency and death. These issues may be very important for their family as well. The beliefs may be manifested in a religious belief or practice, and the involvement of others from their religious group, such as a faith leader, may be helpful. However many people do not espouse such belief but still search for meaning and value in their life – their own individual spiritual values. All may find coping with these deeper questions, such as the meaning of life and death, very difficult. These issues may not have any easy answers but should be heard and acknowledged (Lambert 2014).

With all these areas of care, there is the need for listening and awareness of the possibility of concerns by all the professional carers involved. Sharing of concerns and encouraging families to share their concerns together are often helpful. Specialized counselling may be helpful for some, and access to this service is essential if we are to help patients cope with their disease.

6 Communication Issues

The need for careful communication with both the patient and family has been emphasized in the EAPC/EAN consensus document (Oliver et al. 2016) and may be especially important in neurological disease, due to the complexity and variability of the disease progression and the risks of both communication ability and the cognitive ability of the patients as the disease progresses (Oliver et al. 2016). The areas that may need particular attention are the following.

6.1 Diagnosis

The giving of the diagnosis of a progressive neurological disease will set the agenda for future care, and may influence the patient and their family's response and coping with the disease as it progresses. There is evidence from the telling of the diagnosis in cancer that the use of a protocol, such as the SPIKES protocol, allows an open and clear discussion and aids in the telling of bad news (Baile et al. 2000). Such a protocol suggests that consideration is given to **S**etting up the interview, with preparing the setting and ensuring all the information is available; assessing the patient's **P**erception by asking for their thoughts and views; obtaining the patient's **I**nvitation by ascertaining their wishes on the information they would wish; giving **K**nowledge and information, by giving clear information in small chunks and without bluntness or over negative views; addressing the patient's **E**motions with empathic responses; and setting a **S**trategy and **S**ummary at the end of the discussion so that the patient has a clear plan of the next steps to be taken (Baile et al. 2000).

It has been shown that the SPIKES protocol can be helpful in enabling neurologists to tell the diagnosis of MND/ALS. In Australia it was found that 36% of patients were dissatisfied with the telling of the diagnosis and patients were more satisfied if the neurologists spent longer time, responded empathetically, shared information and suggested realistic goals, explored the expectations of patient and family, and made a clear plan with follow-up (Aoun et al. 2015). Moreover 70% of neurologists in this same study found telling the diagnosis somewhat to very difficult, and 65% were stressed and anxious when delivering this news (Aoun et al. 2015, 2016). Families also were concerned when communication was

not satisfactory and commented on long-term emotional stress in these circumstances (Aoun 2017). There is evidence that these skills can be acquired through training in a specific program (Lienard et al. 2010).

Throughout the disease progression, there is the need for good communication and discussion of the disease, its effects, and the future prognosis. This may need to be repeated many times, and patients and families may take this information on board in different ways at different times. Time is needed to ensure that they have the information they wish and to facilitate communication within families, so that they are able to be open together. It has also been suggested that two appointments allow patients and families more time to understand and discuss the news and then ask more questions at the second appointment (Seeber et al. 2016).

However there may be family situations when communication is not open and conflicts arise. The aim should be to allow the patient to discuss what they wish, within their abilities of communication and understanding. Families may need extra support, as they are facing the issues of loss and change in the same way as the patient, but with their own particular concerns and experiences that may color their reactions. This may be compounded when there are communication issues, due to dysarthria or dysphasia and cognitive change – as one family described: "He received a death sentence and it felt like I had received a life sentence."

6.2 Advance Care Planning

As communication and cognition may deteriorate with disease progression, knowing the wishes of the patient while they are able to communicate with them is important. Advance care planning (ACP) is "a voluntary process of discussion and review to help an individual who has capacity to anticipate how their condition may affect them in the future and, if they wish, set on record choices or decisions relating to their care and treatment so that these can be referred to by their carers – whether professional or family – in the event that they lose capacity to decide once their illness progresses" (Chapman 2012). It is a voluntary act, without coercion, and should be offered appropriately and over time and may need to be repeated and reviewed (Chapman 2012).

A person can give their wishes for many aspects of care and treatment including the place of care and death, foods they may like/dislike, how they would like to be cared for, their values, and the treatment options they may wish/may not wish to receive. They may be able, according to the country's legislation, to refuse certain treatments if they define these clearly and show that they realize that these decisions could lead to their death (Chapman 2012).

ACP may be as:

- An advance directive – where the patient defines treatments they do not wish to receive – such as admission to hospital, cardiopulmonary resuscitation, tracheostomy ventilation, antibiotics for a urinary or chest infection.
- Appointment of a proxy to make decisions when they are not able to do so – this proxy would be asked by the professional team for a decision in the same way as they would have asked the patient, if he had been able to make the decision.
- An expression of their general views on care and treatment – in the UK this is known as an advance statement and is not legally binding, but should be taken into consideration in the decision-making.

In the care of neurological patients, ACP has been found to be helpful (Voltz et al. 1998), and it has been shown that patients do wish their ACP to be adhered to (Jox et al. 2008). Moreover patients with MS did want to express their views, and if doctors avoided these discussions, patients felt that they were less empathetic (Buecken et al. 2012).

Thus ACP is helpful and should be considered for patients, particularly when loss of communication or cognition is a possibility. However this may not be easy as patients and families often do not want to consider the future, due to fears of what may happen and concerns that these considerations may precipitate a decline. Professionals may also be reluctant to discuss the issues, as they

find it difficult and stressful and time consuming. Thus careful discussion early in the disease progression may be necessary if the patient is able to express their wishes easily, and ACP may need to be discussed on several occasions – the completion of ACP is "a process" over time, and careful explanation of the benefits for the person and their family needs to be stressed.

6.3 Wish for Hastened Death

There is evidence that people with neurological disease and their families may wish to discuss hastened death – euthanasia and assisted suicide (Stutzki et al. 2014) – even if this is not an option within the specific country. There is a debate as to whether hastened death is part of palliative care, and in Belgium the services often work together (Bernheim and Raus 2017), but the European Association for Palliative Care White Paper on euthanasia has stated clearly that there is a clear separation and palliative care does not include hastened death (Radbruch et al. 2015).

However there is a need to allow patients and their families to discuss these issues. The request may come from the fear of symptoms, and a distressing death, of dependency, or of maintaining control over their life and death. For instance, although many patients with ALS fear a distressing death, there is increasing evidence that with good palliative care, this is unlikely and choking to death, a common fear, is rare (Neudert et al. 2001). These issues should be discussed, and with clear explanation, planning for possible crises, and ACP, the wish may lessen. There will be a number of patients who will still wish to retain control, and in areas without any legislation, there will need to be ongoing support for the patient, their family, and all the professional teams involved (Ganzini et al. 1998).

6.4 Communication Issues

Communication may become complex for people with neurological disease because of loss of speech and/or cognition. Speech may be affected due to bulbar changes (affecting the mouth, tongue, and lips), the respiratory muscles/diaphragm (causing weakness of respiration and reducing the ability to articulate), the central neurological control of speech or damage to the speech centers of the brain. Careful assessment is necessary, involving speech and language therapy, to help patients communicate. This may involve relatively low-tech equipment, such as pad and paper or a communication board, to high-tech computer-based systems, and even systems based on eye gaze or electroencephalograms. Extra time is often necessary to allow the person to communicate, as even the most sophisticated computer communication system is much slower than normal speech. It is essential to allow people to communicate their wishes and allow them to complete the communication (Scott and McPhee 2014).

There may also be a loss of cognition, which may be complex and not immediately obvious. Subtle changes in understanding or language may not be understood by families or carers but cause distress to all as communication becomes confusing and the behavior affected. For instance, frontal lobe changes, which may be found in up to 50% of people with ALS, may affect decision-making, cause subtle language difficulties including word and sentence comprehension and word finding, increase distractibility, lead to impulsivity, and lead to difficulty in planning activities, forgetfulness, difficulty in judging the emotions of others, and loss of empathy (Goldstein 2014). These changes may be subtle but may affect the person's ability to function and carers, both family and professional, need to be aware of the possibility of needing to provide extra support in helping the person with decisions or activities. Reduction of the "cognitive load" when making decisions can be helpful, so that the information provided is limited and the decision is reduced to a small number of options, which may be possible for the person to understand (Goldstein 2014). Awareness of the possibility of cognitive change is essential when communicating with people with neurological disease so that they can be involved in discussions and decisions, within the limits of their abilities.

7 Support of Carers

Family or informal carers are persons who take care of patients affected by chronic illnesses, disability, or other care need, outside a professional or formal employment framework. They are considered as beneficiaries of palliative care according to the WHO definition (WHO 2002), but, above all in a home setting, they are often viewed as a co-worker or even a member of the caring team but as such may not be identified as having care needs in their own right (Grande and Ewing 2009). They are the ones who spend most of their time with patients and, therefore, can provide essential information on minimal changes in needs and health status. Family carers should be educated and trained in medication management and symptom control (Bede et al. 2009).

Early education on the practical, technical, and emotional aspects of providing end-of-life care may be required for those caring for people with nonmalignant disease when the trajectory of dying is more uncertain (Funk et al. 2010). Professionals need to "think family" and consider how support for family carers can affect the care of the patient, above all when they tend to have problems related to aging. Understanding the complexities of end-of-life care in the home and the support needs for family carers can improve services, and among the main areas of need identified by lay carers are social and psychological support, financial concerns, and the need for choice and information (McIlfatrick 2007). Assessment of carers of patients with severe MS has shown a need for qualified personnel and care coordination in day-to-day home care, in particular identifying personal hygiene, a supportive network, and the preservation of patient/carer roles within the family and community (Borreani et al. 2014).

As many family or lay carers have never seen a person deteriorate or die, they can be worried about the future: uncertainty about the disease progression; physical dependency; mental deterioration; and the need to take decisions on behalf of their loved ones can cause anxiety and have a negative impact on their daily life.

Considering informal carers of people affected by neurological disorders, some aspects are to be taken into account:

- Carers, as well as patients, are often very frightened of the dying process and may be more fearful of the process of dying than of death itself.
- Appropriate information on further support is essential as well as opportunities to share their concerns and fears.
- Some carers (e.g., those caring for MS patients) will have been told that their condition is not one people die from and therefore may be unprepared, especially where there has been a slow and severe progression and death occurs suddenly.
- Carers could be the first to recognize and interpret subtle changes in reduced energy, engagement, and mood as the neurological condition worsens. They may experience patients' acute crises that may require hospital admission (infections, trauma, agitation).
- They need information about significant changes in care management, for example, in oral feeding and hydration.
- They may feel they have already "lost" the person and experience episodes of grieving during the care management.
- They may need specialist palliative care for unmet needs requiring psychosocial or spiritual input from the services to prevent severe psychiatric illness and even suicide among carers.
- Cultural and religious differences around the end of life deserve respect.
- Support for carers should continue into bereavement.

The needs of carers should be assessed on a regular basis, and the support of carers – before and after death – is an indispensable part of palliative care, reducing complicated bereavement and improve patients' quality of life (Oliver et al. 2016).

The care needs of carers of patients with neurodegenerative conditions are extensive and when unmet may be related to negative changes in their quality of life. Issues can range from significant

anxiety and insomnia, related to their role, to depression related to caregiver burden and social dysfunction. Family suffering increases when the neurological disorder reaches advanced stages, and also financial problems are to be taken into account (Whetten-Goldstein et al. 2000). As the disease progresses and end of life approaches, the primary caregivers and also the wider family of persons with progressive neurological conditions need more supportive interaction and information.

8 End-of-Life Care

The General Medical Council in the UK defines end of life (EoL) as patients who are "approaching the end of life" when they are likely to die within the next 12 months. This includes those patients whose death is expected within hours or days; those who have advanced, progressive incurable conditions; those with general frailty and coexisting conditions that mean they are expected to die within 12 months; those at risk of dying from a sudden acute crisis in an existing condition; and those with life-threatening acute conditions caused by sudden catastrophic events. The term "approaching the end of life" can also apply to extremely premature neonates whose prospects for survival are known to be very poor, and patients who are diagnosed as being in a persistent vegetative state (PVS) for whom a decision to withdraw treatment and care may lead to their death. The "end stage" of life may be considered as the final period or phase in the course of a progressive disease leading to a patient's death (GMC 2017).

The identification of when someone with an advanced neurological condition may be approaching the EoL phase of their illness is important, because it enables the appropriate action to be taken. The consensus review on the development of palliative care for patients with chronic and progressive neurological disease states that the recognition of deterioration in disease progression near the end of life is essential in enabling the provision of appropriate care and support for patients and their families. Once recognized it must be considered how a regular reassessment is important, with careful continued discussion to enable the changes to be recognized (Oliver et al. 2016).

Unfortunately there are challenges in recognizing EoL in many neurological disorders because of many factors:

- The long duration of disease with the involvement of complex multidisciplinary care (e.g., MS).
- Sudden death (e.g., ALS, MSA).
- The lack of a predictable or fluctuating course (e.g., PD).
- The involvement of specialist treatments (e.g., deep brain stimulation, continuous intrajejunal infusion of levodopa-carbidopa, or continuous apomorphine subcutaneous infusion).
- Neuropsychiatric problems (e.g., behavioral and cognitive changes) can appear throughout the course of the disease creating confusion between terminal delirium and treatable complications.

Rapidly progressive diseases may need palliative care early on in the disease trajectory, in some conditions even from diagnosis (Oliver 2014). The role of comorbidities needs to be considered as many people (in particular the elderly) die with, but not from, their neurological condition. Nevertheless the neurological disease may play a role in the dying process, often causing difficulties in medical decisions and the priorities of care.

Palliative care can play a role at different times in the progression of a neurological disease. Figure 1 shows how this has changed over the decades – in the past palliative care was often only considered at the end of life, and more recently there has been a gradual transition with both neurological and palliative care services collaborating in care. However palliative care may have a role throughout the disease progression and in an episodic way, according to the patient and family's needs. Early involvement will enable a relationship to be developed between the patient and family and the multidisciplinary team which will facilitate care and may also make it easier for professionals to recognize the deterioration at the end of life.

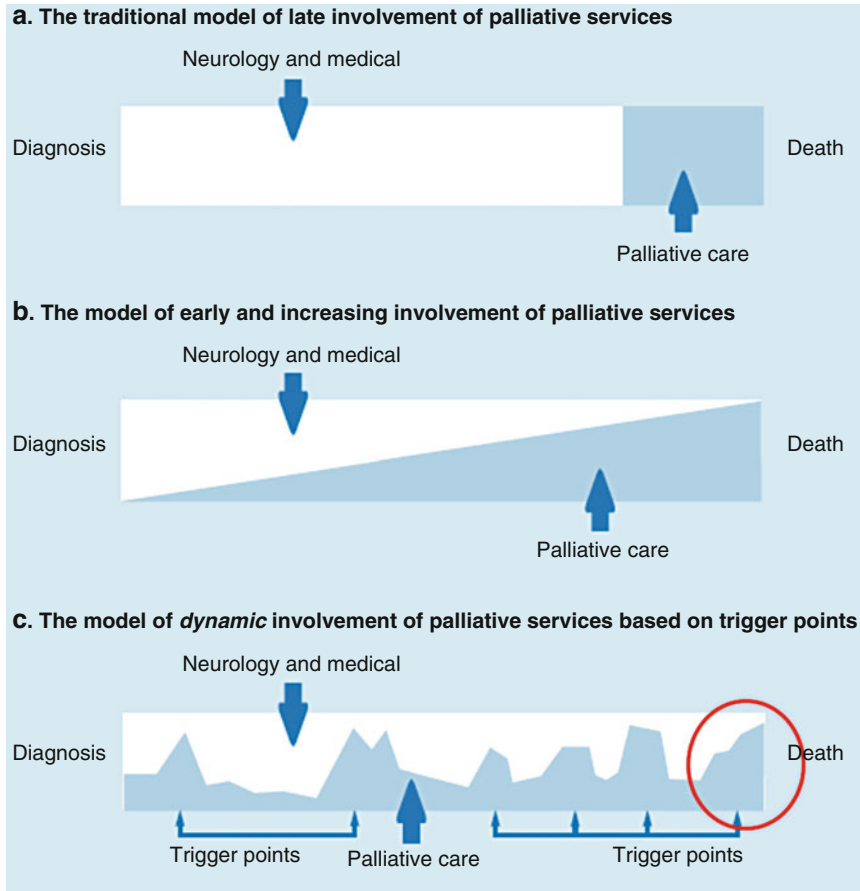

Fig. 1 Possible model of palliative care involvement in neurological disorders (Adapted from Bede et al.)

There are various instruments that can guide the clinician in the process of identification of an EoL trajectory. The Gold Standard Framework provides a multi-step decisional approach to identify patients approaching EoL Proactive Identification Guidance 2016 (GSF 2017). This toolkit is aimed at helping the primary medicine professional to screen the patients that they see and enter into the palliative care register those who are at risk of death and starts from the surprise question: "Would you be surprised if this patient were to die in the next 6–12 months?". If the answer is no, then the patient with advanced disease is further investigated in order to understand the desired choices of care and the presence and intensity of special need of supportive/palliative care. There is also the assessment of specific clinical indicators related to the main diagnosis that can indicate that the disorder is end stage. These indicators are also listed for neurological conditions like ALS, MS, PDs, stroke, and dementia. This approach helps to identify, assess, and plan for living well and dying well.

General triggers for EoL in neurological disorders were found to be rapid physical decline; significant complex symptoms, including pain; infection in combination with cognitive impairment; and risk of aspiration (NEOLCP 2010). Research has shown that the number of triggers increases as death approaches and the terminal phase was recognized for 72.6% of patients (Hussain et al. 2014).

The Supportive & Palliative Care Indicators Tool (SPICT™) is used to help identify people

at risk of deteriorating and dying with one or multiple advanced illnesses for holistic, palliative care needs assessment and care planning (http://www.spict.org.uk/).

In the care planning of patients at the EoL, it is essential to assess important issues:

- The preferred place of care
  Including the desirability and feasibility of care for this person at home.
- The preferred place of death
  The person may feel better in his/her home or may feel more secure better in a more protective environment (such as a hospice or a nursing home).
- The family coping systems to deal with a death in their house
- The presence of other frail people at home who may need some protection – children, other seriously disabled family members, drug abuser, or alcohol addicted

In order to achieve a good quality of death, physical symptoms and psychosocial and spiritual issues are to be accurately addressed and reviewed any time the phase of illness changes, and the care plan has to be adapted.

Patients with ALS fear choking to death, even though there is good evidence that for those receiving good palliative care, most deaths are peaceful (Neudert et al. 2001). However, if they are not addressed, these worries can lead to desperation, and some patients are more likely to wish hastened death (Albert et al. 2005). The provision of appropriate medication "in case of need" may be appropriate – the Breathing Space Programme in the UK suggests the provision of morphine, midazolam, and glycopyrronium bromide injections in case of a sudden deterioration or distressing symptoms (Oliver 1996). For other conditions prevention of possible crises and careful planning of the EoL can be possible. The adopting of the principles of symptom management, as part of the wider palliative care assessment, should be applied to neurological care, allowing open discussion about the dying process and explanation that most patients will die peacefully with appropriate care.

9 Education

There is a need for information for all involved in the care of a person with a neurological disease. The diseases are relatively rare and may not have been encountered at all by patients and families and may be rarely seen by health and social care professionals. Thus there is the need for information to be available if the person is to attain the best quality of life and activity.

9.1 Patient and Family

At the time of diagnosis, patients and families may have limited information about what they face. However with some disease, which has a genetic component, they may be only too aware, having seen family members with the disease, such as in Huntington's disease. All need good and reliable information, but how this is provided is often difficult as some people may want limited information, whereas others feel let down if they develop new problems and feel that they have not been prepared beforehand. There is evidence that patients may seek information in different ways – "active seekers" who look for information, "selective seekers" who often rely on family members or friends to prescreen information and pass it on if they feel it is suitable, and "avoiders" who would rely on others to "buffer" and check any information (O'Brien 2004). Care is needed in allowing these people to receive information in the most effective way for them.

There are also issues if people look for information on the Internet, for although there are many excellent sites, often provided by specialist support societies, there are many misleading and erroneous sites and some which try to extort money for "cures" which are unsubstantiated or completely dishonest.

In the provision of information, awareness of the understanding of those involved is essential – many people may not be able to use written information due to literacy or language issues, and cultural differences may affect how information is perceived. However good information from reliable sources can be very positive, providing

support and understanding and enabling care – for instance, awareness of behavioral changes in ALS when there is cognitive change enables family to understand why the person is acting in different ways and develop ways of coping and minimizing the difficult behavior (Goldstein 2014).

Specialist support groups and associations are very helpful in providing reliable information for people. They are able to provide specialist information for patients/families and professionals. They also help to facilitate general awareness of the issues facing people with the particular illness and help to raise funds for further research.

9.2 Professionals

There is increasing awareness of the need for professionals to be more aware of the needs of both patients with neurological disease and their carers/families. This may be for increased awareness of the role of palliative care for neurological/rehabilitation services and for increased knowledge of neurological disease for palliative care services (Creutzfelt et al. 2016). This is part of the ongoing development of health-care professionals in awareness of holistic care and the need for improved communication skills (Aoun et al. 2016).

10 Conclusions

The care of people with neurological disease can be complex and involves a wide multidisciplinary approach. There is a need for careful assessment and care needs to be individualized for every patient and family. This complexity is a challenge for palliative care services, as there is variable involvement over a variable period of time and collaboration and interaction with other professional teams. However with a careful collaborative approach, much can be done to improve the quality of life of this patient group.

To improve care further, it is hoped that there will be increased awareness of palliative care within neurology – including within guidelines on care. This will enable patients and families to receive the care they need. The numbers will increase over the coming years and decades as the population ages and all professionals will need to become more familiar with the palliative care of this population, who may also have multiple comorbidities.

The education of all professionals in the principles of palliative care will enable the approach to become more usual with a clearer understanding of the aims of management – often to minimize symptoms and allow people to live their lives as effectively as possible. As Dame Cicely Saunders, founder of St Christopher's Hospice where neurological patients were cared for from the opening in 1967, our aim should be "to help people live, live until they die."

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Palliative Care in Dementia

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_113

Abstract

An optimal approach to palliative care for people with dementia has been defined by the European Association for Palliative Care with 11 domains including applicability of palliative care; person-centered care, communication, and shared decision-making; and setting care goals and advance care planning. Not all people with dementia will require specialist palliative care, and all involved in dementia care should be able to provide palliative care focusing on care and treatment which aims to increase the comfort and quality of life of the individual and supporting their family. There are many complications and symptoms which may arise for someone with dementia including increased infections, shortness of breath, swallowing difficulties, and pain which the individual may not be able to clearly express. These complications can lead to difficult decisions which need to be made by not only practitioners but also family caregivers as proxy. There should be a shared decision-making approach to these complications and symptoms, with advance care planning performed where possible. Caring for someone with dementia is one of the most difficult caring roles; support for family caregivers as part of a palliative approach is essential. Each person with dementia is different, and needs should be assessed on an individual basis, adopting a person-centered approach to care.

1 Introduction

With aging populations across the world, the numbers of people with dementia continuing to increase and with no known disease-modifying treatment, the delivery of high-quality palliative care is becoming a high priority for health and social care services. Dementia is often not recognized or understood as a terminal illness which will ultimately lead to death; however, research over the last decade has increased, and attention paid to palliative care for people with dementia continues to be recognized. Through the use of a case study/vignette (Mrs. S) in this chapter, we provide a definition of optimal palliative care for older people with dementia through the domains of the European Association for Palliative Care (EAPC) (van der Steen et al. 2014b). Drawing on a case study, we discuss common issues and symptoms for those with dementia including

symptoms which may be experienced in the dying phase, and their associated treatments, considering the controversy of some of these treatments, such as artificial nutrition. The chapter considers the role of family caregivers in decision-making and the difficult decisions which are often left to them to make as proxy. The importance of family caregivers in dementia palliative care is highlighted including their health and psychological needs. Throughout this chapter we highlight the person-centered approach which should be adopted and needs and support should be considered on an individual basis.

2 Defining Palliative Care for People with Dementia

Palliative care has a great deal to offer for people with dementia. The trajectory of dementia usually involves multiple changes in condition and in the situation of people with dementia. What is needed is a care approach that is highly responsive to such changes, and which therefore explicitly incorporates and anticipates the future, to promote a feeling of being in control in a situation where people often feel loss of control. This does not mean that all people with dementia need specialist palliative care. Rather, with no cure of the disease available, the palliative approach may help as a reminder to focus care and treatment on maintaining or improving quality of life of the patient and supporting the family caregiver in changing and often difficult roles. As the course of the disease is much less predictable than, for example, with cancer, it is more problematic to limit palliative care in dementia to the end of life: when should that be? In order to integrate a palliative approach in dementia care, and for specialist palliative care to appreciate what is specific about dementia, a common understanding of what is needed from palliative care in dementia is needed.

A single sentence to define palliative care in dementia would not suffice. Therefore, in a Delphi study based on evidence and consensus among palliative care and dementia care experts, the European Association for Palliative Care (EAPC) sought to identify the important domains in palliative care in dementia to serve as a framework for development of practice, policy, and research (van der Steen et al. 2014b). This Delphi study focused on older people with dementia, as little is known about the specific issues of young-onset dementia at the end of life. Within each domain, the most important recommendations were provided to optimize palliative care in dementia, backed up by an explanation and evidence where available.

Box 1. Domains of Palliative Care in Older People with Dementia European Association for Palliative Care (EAPC) (van der Steen et al. 2014b)

1. Applicability of palliative care
2. Person-centered care, communication, and shared decision-making
3. Setting care goals and advance care planning
4. Continuity of care
5. Prognostication and timely recognition of dying
6. Avoiding overly aggressive, burdensome, or futile treatment
7. Optimal treatment of symptoms and providing comfort
8. Psychosocial and spiritual support
9. Family care and involvement
10. Education of the health-care team
11. Societal and ethical issues

The first domain is applicability of palliative care, because dementia is not always considered a terminal disease. It does shorten life expectancy (Rait et al. 2010), but perhaps more important is that dementia is a progressive disease and there needs to be continuous assessment of the needs of the individual, whether resulting in death with or from the dementia. Palliative care asserts that knowledge of and acceptance of the course of a disease, with no cure, is essential, even though this may be an emotionally charged area. In dementia there are indications that (on average) people die more comfortably and with better quality care when family and professional caregivers

recognize dementia as a terminal disease before the dying phase (van der Steen et al. 2013). Also physicians perceived that patients suffered more in the final hours of life if their physician felt unprepared with an unexpected death (van der Steen et al. 2017a). Studies of advance care planning also speak to a general benefit of conceptualizing dementia as a terminal disease and preparation for declining health.

The important question then arises when palliative care should begin. In principle, when diagnosed with a terminal illness, one may wish to start and prepare. However, and especially with an early diagnosis, the end of life may still be far away. The exclusive focus on advance dementia seen in research suggests that moderate dementia is not yet a terminal disease (Mitchell et al. 2009). This is, however, difficult to maintain if half of people with dementia die before ever reaching the advanced stage, and after having experiencing a number of complications, with pneumonia and dehydration of cachexia occurring in moderate dementia as well (Hendriks et al. 2016). Moreover, people with advanced dementia may survive for many years (Gill et al. 2010), often referred to as dwindling; with good care, they may even form a selected subgroup of "survivors." The domain of prognostication and timely recognition of dying (Box 1) acknowledges difficulties in prognostication and is therefore typical for palliative care in dementia, where it is not usually a domain in itself in palliative care more generally or for other diseases.

The EAPC work also acknowledges that it is not possible to state a uniform and good starting point for palliative care for all people with dementia. Instead, palliative care is conceptualized as most compatible with two of three major care goals: maintenance of function and maximization of comfort (Fig. 1), which both relate strongly to quality of life. There may be a mixture of care goals, which can shift over time, with progressive dementia. Also, because this is a model, how exactly care goals may shift differs between individuals. In principle, however, palliative care can start at diagnosis (such as with naming of a proxy decision-maker; see advance care planning discussion Sect. 3 in this chapter), even though the care goal that overwhelmingly takes priority at that point may be life prolongation (Fig. 1).

Understanding the applicability and mainstays of palliative care in dementia is not only important for practice but also for policy making, given the benefits and slow uptake in, for example, national dementia strategies where, if included, palliative care is often regarded as care for the dying. Two other domains are relevant especially for policy makers, which are the final two domains (education of the health-care team and societal and ethical issues); however, these are beyond the scope of this chapter and as such not discussed.

The most important of the 11 domains (Box 1) of palliative care in people with dementia according to the experts – and perhaps for all patients with no dementia or palliative care needs – are optimal

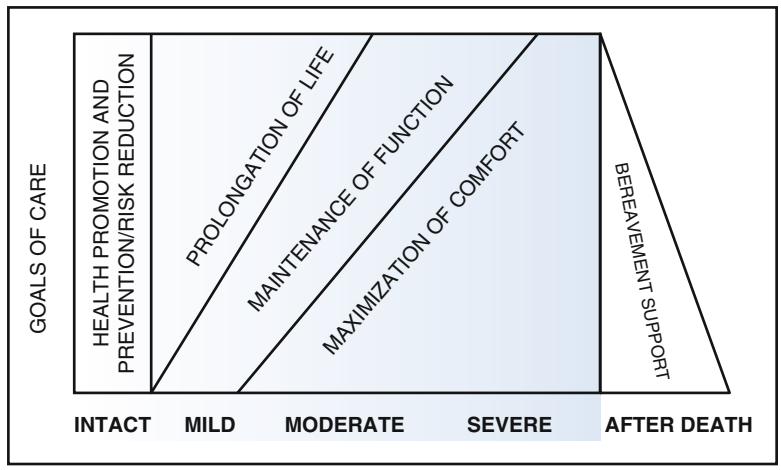

Fig. 1 Dementia progression and suggested prioritizing of care goals. The goals of maintenance of function and maximization of comfort are compatible with palliative care which aims to improve quality of life (van der Steen et al. 2014b. Copyright © 2014 by the Authors. Reprinted by permission of SAGE Publications, Ltd.)

treatment of symptoms and providing comfort and person-centered care, communication, and shared decision-making. Nevertheless, how this is being achieved is different with dementia than with several other terminal diseases; this is discussed in Sects. 4, 6, and 7. Several of the domains listed in Box 1 are emphasized more in palliative care in dementia than with palliative care in other diseases. These are the domains of setting care goals and advance care planning, because of missed opportunities when waiting for the patient to decline in cognitive functioning, and family care and involvement because of the great burden placed on families through both the physical and cognitive decline of the person with dementia. It may be argued that in advanced dementia or at the end of life, continuity of care, avoiding transfer and change or adding of new staff in the last phase, is also of special importance in people with dementia. The same may be true for the two domains that relate to a historical development of palliative care in response to an overly aggressive unilateral medical approach until (almost) dying: avoiding overly aggressive, burdensome, or futile treatment and psychosocial and spiritual support. Explicit attending to needs for spiritual care may fill a gap in dementia care practice, as spiritual care is nearly absent in most dementia guidelines and national dementia strategies (Durepos et al. 2017; Nakanishi et al. 2015).

Palliative care issues, however, may not be raised at all in the absence of a timely diagnosis of dementia which is shown in the case below.

Patient Case/Vignette Part 1 Mrs. S is an 82-year-old lady who lives at home. She has two children, a daughter and a son; her husband died 6 years ago. Her daughter visits her at home as much as possible. Her son lives abroad.

She has a history of a hypertension and has had a hysterectomy. She visits the GP regularly to check her blood pressure. Over the past year, she has visited her GP a few more times due to two urinary tract infections. She calls her daughter and son a couple of times a day and never remembers she has just called. Her daughter often finds moldy food in the fridge, and Mrs. S has got lost on her way home several times.

One day Mrs. S does not answer the phone; her daughter is worried and goes over to her mother. Mrs. S is lying next to the toilet; she does not know how long she has been on the floor. She can't use her right leg because she is in too much pain. Her daughter calls an ambulance, and in the hospital, a hip fracture is diagnosed.

During her stay in the hospital, Mrs. S gets very disoriented and hallucinates and is diagnosed with delirium. The possibility of dementia is mentioned, but at this point, it is not possible to run tests. Mrs. S's daughter agrees that her mother cannot go back home, and they decide to transfer Mrs. S to a rehabilitation unit.

3 Advance Care Planning

As can be seen in the case of Mrs. S, there has been little planning for her future care or treatment as her cognitive decline progresses and as her ability and capacity to make her own health, care, and welfare (including financial) diminishes. This stresses the importance of advance care planning.

3.1 Definition

Advance care planning (ACP) has been defined as "process of discussion that usually takes place in anticipation of a future deterioration of a person's condition, between that person and a care worker" (Henry and Seymour 2007). Advance care planning can include advance statements about wishes to inform subsequent treatment, for example, how one's religious beliefs should be reflected in care, or an advance decision to refuse treatment such as antibiotics to treat an infection. Included in the advance care plan are nonmedical decisions such as decisions about who should manage the individual's finances. An advance decision may sometimes be referred to as a living will, advance directive, advance policy making, or advance physician orders. It is important to highlight that ACP is a process of communication. It does not necessarily lead to a living will or nomination of a proxy decision-maker, it may also simply be conversations which are not documented; however, this is not recommended

and documentation of decisions should be made when possible.

3.2 Why Is ACP Important in Dementia?

A timely diagnosis of dementia can be vital to encourage the process of ACP. As discussed above as cognitive decline progresses, an individual's ability to consider their own health and care needs deteriorates, along with their ability to make informed decisions. At this point many decisions are left to families to make in a shared decision-making process with practitioners, leaving families often unsure about their status and feeling guilty. ACP has demonstrated improved outcomes for both people with dementia and their caregivers (Dixon and Knapp 2018), including reduced depression, stress, and anxiety in family caregivers (Dixon and Knapp 2018). As is in the case of Mrs. S in patient case/vignette part 5, ongoing discussions around the future and complications may have reduced the surprise for the family when she deteriorated. There is little evidence, however, if there are subgroups of people who benefit more or less than others – for example, if there are people who would rather benefit from support in living one day at a time.

Patient Case/Vignette Part 2 Mrs. S in the rehabilitation unit is dependent on nurses' care, and she becomes more disoriented in time and place as her cognitive decline progresses. She has more difficulty finding words to express herself. After a while Mrs. S is diagnosed with dementia of Alzheimer type. Her children and the multidisciplinary team do not think Mrs. S can go back home, and they want to transfer her to a nursing home with a special dementia care unit. Her children feel quite guilty about this even more so since Mrs. S wants to go home.

3.3 What Should They Discuss and the Approaches: Who, How, and When?

The EAPC recommendations on optimal palliative care for people with dementia recognize ACP as a core domain (Box 1, domain 3) (van der Steen et al. 2014b). According to the EAPC, ACP should be considered early in the disease process shortly after diagnosis, continually reviewed as an ongoing process with the patient and family on a regular basis and following any significant change in health condition. As can be seen in Fig. 1, the care goals will change, and priorities may alter over time from life prolongation and maintenance of function in early dementia through to maximizing comfort in the severe/advanced stages of dementia.

However, there is ambiguity about when to start advance care planning. Starting shortly after diagnosis may not be appropriate for everyone and is currently not necessarily a common practice in many countries. In recognition that the optimal timing of initiating the process is highly individual, the EAPC recommends a minimum as to what should be done at diagnosis, which is to name a (future) substitute decision-maker. The health-care team may also just "plant the seed." Introducing planning and decision-making as early as possible is encouraged in many countries. Decisions about when to start ACP should be considered on an individual patient by patient level and should include both the person with dementia and those close to them.

There are many national guidelines across many countries which provide example templates for ACP, including how to begin discussions and what the discussions should include. Initial discussions may include identifying the wishes and preferences of an individual, including preference of where they would like to be cared for (e.g., hospital, nursing home, or at home), but this often depends on the care that is needed and how they may like their religious and spiritual beliefs incorporated in their care. Although an individual with dementia may express their preference of place of care throughout their dementia, for example, in the case of Mrs. S in patient case/vignette part 2. Often people with dementia want to remain at home, being a familiar environment and close to their relatives. Often, like in the case of Mrs. S, people are admitted to a hospital and are

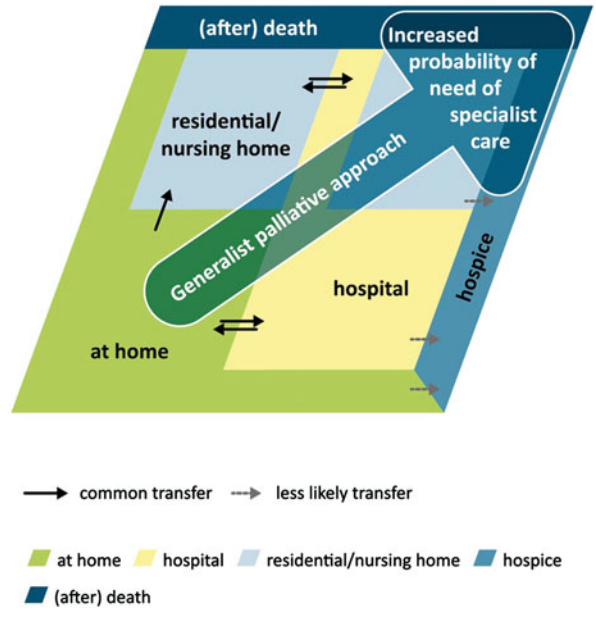

Fig. 2 Possible journey for person with dementia and health-care service transitions (Published with kind permission of © JT van der Steen, MS Klapwijk and N Davies 2018. All Rights Reserved)

afterward transferred to a nursing home because they need more care and staying at home is not safe anymore or the partner or relatives can't deliver the amount of care or guidance that is needed.

Figure 2 shows the different journeys for people with dementia; many live at home, but with the increase in care dependency, people are transferred to a hospital or a nursing home. Sometimes people are also admitted from home to a hospice or from a hospital or nursing home to a hospice. The discussions may then gradually move on to consider more specific decisions, such as treatment and scenarios of future health. These may include treatment such as artificial nutrition and hydration, the use of antibiotics for recurrent infections, and cardiopulmonary resuscitation. As with patients and families, physicians also differ in whether they feel comfortable with discussing future scenarios or rather focus on care goals and values with specific decisions postponed to when the situation occurs (van Soest-Poortvliet et al. 2015). There is a growing amount of literature surrounding planning with some placing high importance on what they regard as the necessity for people with dementia to complete advance care plans (Dixon and Knapp 2018).

3.4 Barriers

Despite many efforts internationally to encourage ACP for people with dementia, they are often not consulted about their wishes. ACP is less well developed across Europe, with much more work in Australia, Canada, and the USA. Several studies have identified a number of barriers why ACP does not occur including a lack of knowledge of ACP, difficulty of talking about such sensitive topics, fear of facing one's own mortality, organizational context, discontinuity of care, lack of a relationship with practitioners as well as within families, lack of time, as well as being made more complex in dementia by it often not being acknowledged as a terminal illness (van der Steen et al. 2014c). Many health and social care professionals are reported to lack the confidence, feel inexperienced, and need additional training and support in this area (Sampson et al. 2012). Health and social care staff in some countries believe that if they do not call emergency services in a crisis, there will be repercussions for them (Harrison Dening et al. 2012). This issue highlights the legal ambiguity that is often seen across countries of ACP (Jones et al. 2016). For example, in the UK, the legal document as part of ACP is the advance decision. The advance decision,

however, is only legally binding if it complies with the Mental Capacity Act (2005), is valid (e.g., it is signed by the individual and a witness, and it specifies clearly the treatments the individual wishes to refuse), and applies to the situation. It is important to check the legal framework of decisions at the end of life in your country or region as this does differ.

3.5 Facilitators and Benefits

ACP potentially gives patients and families an opportunity to think about what is important for them and plan to try to ensure these wishes are met. However, it may not always be possible for the individual's wishes to be met, for example, as in the case of Mrs. S's wish to go home in patient case/vignette part 2. To facilitate ACP, practitioners should be available to educate families, and in particular, there should be a dedicated key facilitator to educate both practitioner and family. ACP can lead to reduced hospital admissions, unnecessary interventions, reduced costs (Robinson et al. 2012), and even reduced stress among family caregivers as discussed in Sect. 8.2 of this chapter.

Patient Case/Vignette Part 3 Finally Mrs. S has been moved from the rehabilitation unit to a unit (wing) for people with dementia in a nursing home. At first she seems to experience problems with her new environment; later she seems to feel better in her new rhythm of the unit.

At one point she starts to frown sometimes and to behave in an agitated manner. She cannot verbally express what she is feeling at those moments. At first nothing is found which could explain this. One day a nurse hears Mrs. S moaning and sees her frowning. Physical examination and a urine test lead to a diagnosis of a urinary tract infection, which is then treated with antibiotics.

4 Symptom Management

At the beginning of the disease, people with dementia live at home and are often still capable of expressing their feelings, for instance, pain. But with the progression of the disease, people often lose this ability to communicate verbally due to neuropathological changes. This is also reflected in functional and physical impairment and behavioral and psychological symptoms, for which people often have to be admitted to a nursing home. As the dementia progresses, the need for help rises, and the last year of living with dementia is known for a high level of disability with a high need for assistance in activities for daily living. Symptoms that are often described in studies of people with dementia include pain, shortness of breath, and agitation or other neuropsychiatric symptoms.

The clinical course of dementia shows that family or medical staff working with people with dementia should pay particular attention for symptoms of pain, shortness of breath, or anxiety (Hendriks et al. 2015; Hendriks et al. 2016). Often with the progression of the disease, people get urinary incontinence and later bowel incontinence and are at high risk for swallowing problems and aspiration, weight loss, pressure ulcers, infections (pneumonia and urinary tract infections), and febrile episodes, as can be seen in the case of Mrs. S (patient case/vignette part 3) (Mitchell et al. 2009).

4.1 Pain

The gold standard for the assessment of pain is self-report. This is often not possible in a later stage of dementia when people are often not capable of verbally expressing the experience of pain or lose the capacity of pain memory. Pain can result in behavior that challenges, for example, agitation or aggression if left untreated. In the case of Mrs. S, she can be seen to frown at times, and this is often coupled with agitation; this may be an indication that she is in pain. Pain can be experienced differently in people with different kinds of dementia or at different stages, related to the different neuropathological changes. Pain is however very common, 12–76%, in people with dementia, in all stages (van der Steen 2010).

Previous studies had suggested that people with dementia in nursing homes receive less pain

medication compared to people without dementia; however, newer evidence suggests that there is no difference in people with or without dementia (Haasum et al. 2011) or it is even higher among people with dementia in some studies (Lövheim et al. 2008). Studies have also expressed concern about the overuse of opioids in people with dementia. It is therefore vital to ensure pain is a central component of continual assessment with a person with dementia, and an approach to maximizing comfort and quality of life is taken.

There are a number of instruments (pain scales) which can be used to assist staff identify pain in people with dementia if they are not able to verbally express this pain, such as the case with Mrs. S The team is alerted by the moaning and frowning suggesting she is in pain. The involvement of family and caregivers may be a very good way of assessing the patient, especially at home or just after admission in a nursing home, as they are familiar with changes in behavior or expression that may indicate distress. There are a large number of available instruments which have shown different reliability and validity, currently over 30, but for clinical practice, the Pain Assessment in Advanced Dementia (PAINAD) and Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC) are often recommended (Ellis-Smith et al. 2016). Research continues to look for an instrument that is reliable and valid and which can identify expressions specifically indicative for pain. In clinical settings it is important to evaluate the possibility of pain regularly and sometimes try the effect of analgesics, as well as assessment of current pain medication being received; is it still adequate and is it still necessary?

4.2 Shortness of Breath

Shortness of breath is often reported in studies of people with dementia with a range of 16–26% (Hendriks et al. 2015; Mitchell et al. 2009). Shortness of breath can be caused by different problems; common causes include pulmonary infection such as pneumonia or cardiac problems. Pneumonia may also be related to aspiration. Angina and pulmonary embolism are very difficult to recognize in people with dementia in cases where there are difficulties verbally expressing pain (chest) or shortness of breath.

4.3 Unmet Need/Challenging Behavior

Many feelings, for instance, pain as mentioned above, are the result of a sensation that is unpleasant, and they can lead to a change in the individual's behavior, which may be considered challenging. Many neuropsychiatric symptoms are seen in people with dementia and can have a great impact on the quality of life of that person and those surrounding them: family and caregivers.

Neuropsychiatric symptoms (NPS) (or behavioral and psychological symptoms of dementia (BPSD)) include delusions, hallucinations, depressive mood, anxiety, irritability/lability, apathy, euphoria, disinhibition, agitation/aggression, aberrant motor activity, and sleep or appetite changes (Cerejeira et al. 2012). The range of NPS prevalence in community-dwelling people with dementia is generally more than half of people (Borsje et al. 2015). These different types of behavior, often called challenging behavior, can also be frequently seen in nursing homes. Family or a regular staff member that know the person with dementia can often provide extra information on the cause of the behavior or have useful information on how to diminish this.

Infections such as a urinary tract infection are known to be a frequent cause of challenging behavior or even cause an episode of delirium; this is often the cause of admission to hospital for many people with dementia. The prevalence and incidence of delirium can be high in people with dementia, ranging from 8% in nursing homes to 89% in hospital and community populations (Boorsma et al. 2012; Fick et al. 2002). Many tools have been developed to assess delirium, including tools that are also used for people with dementia to ensure early recognition (Morandi et al. 2012), including the Richmond Agitation and Sedation Scale (RASS) and modified-RASS (m-RASS) (Morandi et al. 2016).

Agitation is often reported as one of the biggest behavioral challenges in people with dementia, and numbers ranging from 57% to 71% were found (Hendriks et al. 2015). However, for many, families are more concerned with pain, breathing problems, and memory problems than agitation (Shega et al. 2008). Pain and agitation are often reported simultaneously but a strong association was not found (van Dalen-Kok et al. 2015). Anxiety is also frequently reported in people with dementia, but this is also complex and difficult to test, due to an overlap with depression (Seignourel et al. 2008).

As can be seen in the case of Mrs. S, these symptoms and challenges often result in family caregivers acting as proxy, making decisions about the person with dementia's care when there is no advance care plan or in case of an advance care plan to check if the decision is in accordance with the ideas/wishes of the person with dementia. These are very difficult decisions for families as discussed in Sect. 6. One of the most difficult decisions is whether to move the person with dementia into a nursing home; in the case of Mrs. S, the family believe this is in the best interest of Mrs. S; however, they feel guilty about this decision as Mrs. S would like to return home (patient case/vignette part 2).

Patient Case/Vignette Part 4 After a few months in the nursing home, Mrs. S gets a fever, is short of breath, and coughs, and the amounts of fluids and food she takes are less than normal according to the nursing staff. The visiting physician diagnoses pneumonia and wants to talk to the family to discuss if Mrs. S should be sent to a hospital or not.

Mrs. S recovers from pneumonia, but she eats and drinks less every week. She can still walk but she is less stable and has a high risk of falling. She sometimes coughs during the meals. Her son asks if his mother should receive artificial hydration and feeding.

5 Treatment Options of Common Complications

In this section we refer to pharmacological and non-pharmacological treatment options for a variety of complications/symptoms which may arise before the person with dementia is in the dying phase. Later in this chapter (Sect. 9.2), we will discuss treatment in the dying phase.

5.1 Non-pharmacological Treatment Options (Including Spiritual Care)

In recent years person-centered care has been introduced in the care for people with dementia, and more evidence is showing the benefits of nondrug treatment, particularly for behavioral and psychological symptoms in relation to pain. Person-centered care is discussed in more detail later in this chapter in Sect. 7. The care for people with dementia should be multidisciplinary and include spiritual care. Studies show an effect of therapies like music therapy, massage, and aromatherapy, and these should be considered and need to be prioritized in clinical and research settings (Winblad et al. 2016). For example, music therapy has shown a reduction in the short term of depressive symptoms following at least five sessions, but there was little to no effect on agitation or aggression, and the long-term effects are yet to be studied (van der Steen et al. 2017b).

Every time when behavior changes, one has to pay attention to the possibility of medical conditions causing this change, for instance, infections, constipation, bladder retention, pressure sores, pressure sores or infections in the mouth, and side effects of medication, but also, for instance, changes in environment. Regular evaluation in a multidisciplinary team including the nursing staff, psychologist, physiotherapist, social care practitioner, occupational therapist, spiritual care counselor, dietitian, and a physician with evaluation on, among others, behavior, pain, medication, mobility, swallowing, weight change, and incontinence can help improve the quality of care for a person with dementia.

There are several environmental factors which should be considered when caring for someone with dementia. These may range from consideration about the aesthetics of the individuals' room and environment through to consistency of staff. In the home or nursing home, small alterations

may help with orientation such as using different colored doors or pictures to help identify different rooms. It is important to ensure continuity of care when delivering palliative care for someone with dementia (van der Steen et al. 2014b). Continuity encompasses, ensuring the individual is able to remain in their preferred place of care with minimal disruption and minimizing the need for transfers between settings, continuity of the provision of care even if there is a transfer, and continuity of staff caring for the individual.

5.2 Pharmacological Treatment Options

Infections in persons with dementia are usually treated following national or regional antibiotic guidelines, like Mrs. S in the patient case/vignette part 3. As the dementia progresses, there should be a process of ongoing discussions as to what to expect from treatment (this may be part of ACP), for instance, antibiotics, and the likelihood of response to treatment. In some cases, a patient may not respond to treatment when they are too sick and are not capable of drinking and eating anymore. The use of antibiotics should be discussed with the family or advocate including the person with dementia if possible; it is viewed differently in different countries. In some countries the families have more influence on treatment decisions, and the practitioner may simply provide choices, whereas in others this may be a medical decision, in discussion with the wider multidisciplinary team and family. Antibiotics can prolong life but sometimes just for several days (van der Steen et al. 2012). See Sect. 6 on controversies and decision-making in this chapter.

When people with dementia are transferred to a hospital, they often receive intravenous treatment with antibiotics or fluid or even tube feeding. This treatment increases at the end of life but practice in different countries varies (Klapwijk et al. 2014; Mitchell et al. 2009), and they also vary over time; for example, there is a decline in feeding tubes used in the USA (Mitchell et al. 2016).

As pain medication, acetaminophen (paracetamol) is often used as a first-line treatment (Hendriks et al. 2015; Sandvik et al. 2016a), followed by the use of opioids to treat more severe pain which is nonreactive to acetaminophen (commonly used, up to 24%) (Hendriks et al. 2015; Pieper et al. 2017; Sandvik et al. 2016a; Griffioen et al. 2017). Antipsychotic drugs are frequently used to treat challenging behavior in dementia, often with no positive result and many adverse effects, like extrapyramidal symptoms, stroke, or death. Research and the EAPC white paper recommend that non-pharmacological treatment (see above) should be tried first for behavior which challenges (van der Steen et al. 2014b). Several other types of medication besides (typical and atypical) antipsychotic drugs are also used to treat neuropsychiatric symptoms: anxiolytics, sedatives, antidepressants, and anti-dementia drugs. More research is needed to gain a better understanding of how and when to start and stop these pharmacological treatments to optimize prescription in people with dementia, including for cases of delirium (Agar et al. 2017). Bronchodilators are often used in the treatment of shortness of breath; studies show different prevalence, ranging from 29% to 67% (Hendriks et al. 2015).

6 Controversies and Decisions

6.1 End-of-Life Decisions

The decisions which need to be made toward the end of life are often medically focused, relating to the complex symptoms which pose a dilemma for practitioners. However, many other nonmedical factors are also important and need to be considered, for example, spiritual care. As discussed in the previous section, difficult decisions both medical and nonmedical can include spiritual care, place of care, cardiopulmonary resuscitation, treatment of infections, management of eating and drinking problems, pain, shortness of breath, behavioral problems and hospitalization, as well as any comorbid conditions. In the case of Mrs. S, as she begins to eat and drink less, the son wishes to discuss the potential use of artificial hydration and feeding (patient case/vignette part 4).

In some countries, many are raising the option of euthanasia for people with dementia. This is legal in a small number of countries including the Netherlands when strict criteria are met, but many physicians are reluctant to fulfill such a preference in the absence of clear communication with the patient.

6.2 Who Should Make the Decisions?

Ultimately, health- and care-based decisions should be made by the individual/patient themselves. However, in many cases, by the time dilemmas such as difficulty with eating and swallowing arise, it is not possible due to a diminished capacity. Hence, the individual does not have the ability to make informed decisions. Despite efforts to increase advance care planning (ACP) with people with dementia, many people reach the end of life without one (see Sect. 3 earlier in this chapter). Some are not ready to have conversations about death and face their own mortality, and decision-making is left to families (Davies et al. 2014). Practitioners rely on families to know the wishes of the individual and to relay these with confidence and accuracy when making end-of-life decisions. However, caution should be taken by practitioners as family caregivers/proxies have been shown to have a low to moderate agreement with the person with dementia about preferences for end-of-life treatments (Harrison Dening et al. 2016). Practitioners should engage closely with families to understand the individuals' previous wishes and work with the family through a shared decision-making process.

6.3 What Gets in the Way of Making Decisions?

Many barriers have been identified by family caregivers/proxies which prevent them from making decisions about end-of-life care, including a lack of information, poor communication, difficult dynamics/conflict within families, limited emotional and practical support, and dynamic care systems (Davies et al. 2014; Lamahewa et al. 2018). Practitioners should provide clear information which is communicated in a sensitive and supportive manner, helping to facilitate the decision-making process. Social care practitioners can also act as mediators in family conflict to encourage supportive family relationships and aid decision-making.

It is not just family caregivers/proxies who have difficulties in making decisions; many practitioners lack the confidence to hold such difficult conversations and shy away from these discussions (Davies et al. 2013; Lamahewa et al. 2018). These difficult conversations require a high level of skill and a vast amount of experience to be conducted sensitively; many practitioners, and even experienced practitioners, dread such conversations. This leaves family caregivers often not knowing how to approach such conversations, being left to make difficult decisions and care plans, with many feeling doubts about their status.

6.4 Approaching Challenging Decisions/Dilemmas

There are relatively few professional guidelines which address end-of-life care for people with dementia. Until recently, many palliative care guidelines have focused on cancer such as the National Institute for Health and Care Excellence (NICE) (England and Wales). Practitioners should consult their national guidelines for both dementia and palliative care (see EAPC Atlas of Palliative Care in Europe), Alzheimer Europe, and consult the EAPC white paper on optimal palliative care for people with dementia (van der Steen et al. 2014b) as discussed in the symptom management, Sect. 4.

A recent practical toolkit for making decisions specific for end-of-life care of people with dementia used in conjunction with available guidance (Davies et al. 2016) consists of a series of heuristics (schematic patterns that can be applied in complex situations and function as prompts to initiate thinking and action) which offer a

clinically familiar approach, are brief, are easy to remember, and lead to action. The toolkit covers key decisions including eating and swallowing difficulties, agitation/restlessness, reviewing treatment and interventions at the end of life (e.g., routine medication), and providing routine care at the end of life (e.g., changing dry bedsheets in the final days to hours of life). Examples of the heuristics are given in Figs. 3 and 4 and are discussed below with reference to common dilemmas and controversies.

6.5 Common Decision-Making Dilemmas and Controversies

A number of challenges and controversies around providing end-of-life care for people with dementia have been identified.

6.5.1 Hospitalization

In the process of attempting to manage symptoms and maintain quality of life, many people at the end of life often experience what are termed as avoidable hospital admissions (van der Steen 2010). This description of "avoidable" may be for a number of reasons including the nature and consequences of the condition, such as an infection (van der Steen 2010). These admissions often cause more pain and distress to both the individual and their family than remaining in their normal place of care. It is important, as in the example of Mrs. S (patient case/vignette part 4), to discuss the possibility of hospitalization with the relatives, discuss expectations, and make this decision together. Individuals can go to hospitals which have a focus on cure as opposed to care and may receive what is described as unnecessary tests or aggressive and invasive procedures. Cardiopulmonary resuscitation should be avoided in people with dementia, as it is less likely to be successful in people with dementia compared to those without. CPR can be very distressing for all those involved including both the person with dementia and the families, with those who are successfully resuscitated often being transferred to intensive care and dying a short while later.

6.5.2 Artificial Nutrition and Hydration

A common medical decision toward the end of life (like in the patient case/vignette part 4) is the introduction of artificial feeding when the individual is no longer able to swallow food, liquid, or medication. Many people, families and

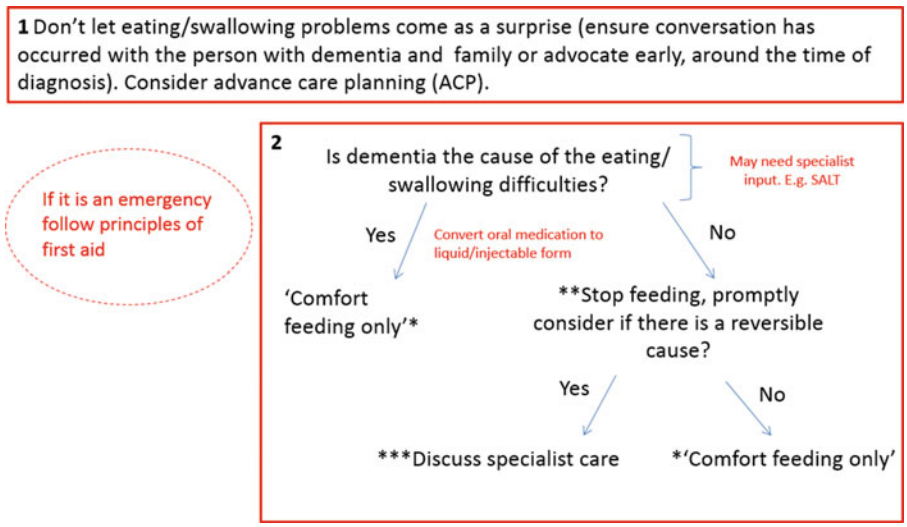

Fig. 3 Heuristic for eating/swallowing difficulties. *Comfort feeding may carry associated risks of aspiration; **Closely observe all intake particularly if changes to swallow function are suspected; ***Consider appropriateness on individual basis (Published with kind permission of © Nathan Davies and Steve Iliffe 2016. All Rights Reserved)

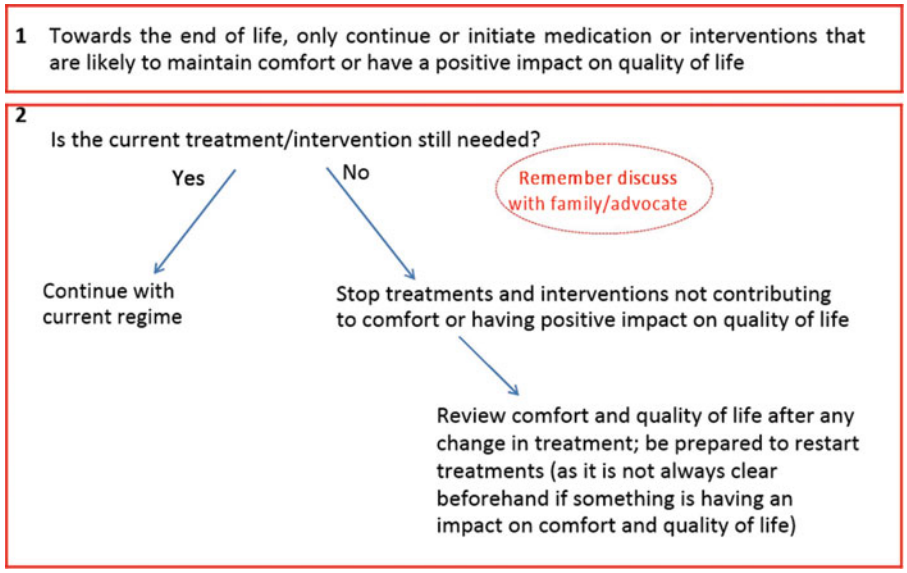

Fig. 4 Heuristic for initiating medication and interventions (Published with kind permission of © Nathan Davies and Steve Iliffe 2016. All Rights Reserved)

professional caring teams, believe that they cannot allow the individual to "starve to death," and they feel that the use of artificial feeding will extend life and prevent discomfort or further complications such as aspiration, potentially leading to an improvement in quality of life (Mitchell and Lawson 1999). In the UK, the Netherlands, and many other countries, the adoption of artificial nutrition and hydration has been a controversial topic for some time and remains so. The EAPC recommends that hydration (preferably subcutaneous) should only be provided if appropriate in the management of potentially reversible causes, such as infection, but should not be used in the dying phase when an individual loses their ability to swallow (van der Steen et al. 2014b). However, the EAPC white paper was unable to reach a consensus on this topic with the professionals they consulted, acting only to further highlight the controversy within this topic. It is unclear if rehydration therapy affects discomfort or indeed survival. A study of Italian nursing home patients with advanced dementia demonstrated that for almost all patients treated with intravenous rehydration therapy, the goal of treatment was to reduce symptoms and suffering. Despite this goal, discomfort was high overall, but symptom relief may be improved (van der Steen et al. 2018). More work to explore the effects of rehydration therapy and discomfort is needed.

The EAPC also recommends that permanent artificial feeding, using a gastrostomy or a nasogastric tube, should be avoided (van der Steen et al. 2014b). Careful and skillful hand feeding or comfort feeding should be provided. Comfort feeding refers to the process of eating for pleasure, providing small amounts of food, even though there may be associated risks such as aspiration. Practitioners together with families must balance the risks of feeding with the potential comfort and pleasure that eating may provide for the individual – Fig. 3 illustrates a heuristic which conveys a practical approach to how these decisions can be considered in the case of Mrs. S.

Currently there are no studies which show an association that artificial feeding offers benefits to the individual. On the contrary some studies have demonstrated they increase the chance of infection, aspiration, further complications (Palecek et al. 2010), and potentially mortality (Ticinesi et al. 2016). As with the limited understanding of pain in dementia, we similarly have a limited understanding around feelings of hunger and thirst in

people with dementia. Data in the USA indicates a reduction in the use of feeding tubes in people with dementia (Mitchell et al. 2016).

6.5.3 Medication: Antimicrobial Treatment

The ability of antimicrobial treatment for recurrent infections in people with dementia to extend life or improve comfort is not well understood; however, some studies have demonstrated increased survival following antimicrobial treatment compared to no treatment or a palliative approach (van der Steen et al. 2012). The use of antimicrobials including oral, intramuscular, and intravenous for pneumonia has increased survival but was also associated with more symptoms reported in retrospect in the period from before to after the pneumonia in a nursing home population with advanced dementia (Givens et al. 2010). However, this was in the USA, where people with dementia and pneumonia with fewer symptoms were more likely not to be treated with antibiotics (van der Steen 2011). Another study used discomfort observed by independent, blinded observers measured with validated tools after antibiotic treatment, and discomfort levels were lower after antibiotic treatment (van der Steen 2011). A more recent study with the same strong methods showed that, with more symptom-relieving treatment provided, antibiotics were no longer associated with discomfort (van der Maaden et al. 2016). Antimicrobial use might be more beneficial for people in the earlier stages of dementia compared to the later stages, with no difference in mortality at in more advanced dementia between those receiving antimicrobial treatment and palliation and those not (Fabiszewski et al. 1990). Some studies have shown that increased survival after antibiotic treatment, but this may only last for a few days in some cases (van der Steen et al. 2012), which may be simply prolonging the dying process (van der Steen et al. 2012). Antimicrobial treatment is associated with renal failure, diarrhea, the use of intravenous lines, and skin rashes. After nearly 25 years of research investigating the effectiveness of antimicrobial treatment for people with dementia, the effects (benefits and adverse effects) are still unclear.

It is important to identify the source of the infection which may be causing symptoms such as fever and balance the benefits of treatment with the potential side effects and consequences. The EAPC recommends that antibiotics are appropriate for treating infections which have a goal of increasing comfort, but life-prolonging effects should be considered carefully (van der Steen et al. 2014b). This can be demonstrated through the heuristic in Fig. 4.

6.5.4 Other Medications

Treatments with other medications for preventive or symptomatic use can cause dilemmas too. Acetylcholinesterase inhibitors, HMG-CoA reductase inhibitors (statins), antihypertensive drugs, antihyperglycemic drugs, and anticoagulants are prescribed often in people with advanced dementia, but many medical guidelines provide an understanding of initiating such treatments but often do not include when and how to stop them. Discontinuation should be considered, but it can be difficult to determine what the effect can be and if stopping will contribute to a better quality of life (see Fig. 4); however, it can reduce the risks of side effects and drug interaction. Multidisciplinary meetings, medication review, and educational programs can help to improve appropriate medication use for people with advanced dementia in nursing homes.

7 Person-Centered Care

For many, being viewed as a person and treated with respect and dignity is, in addition to good symptom management, fundamental to a good death. This is consistent with what experts regard as the most important domains in palliative care with dementia: optimal treatment of symptoms and providing comfort and person-centered care, communication, and shared decision-making (van der Steen et al. 2014b). It can be argued that person-centered care is always important, but it may help to emphasize its importance in patients at risk of not being seen as a person anymore, which is the case with advanced dementia or when patients are not very responsive due to

illness or at the end of life. Indeed, with admission to a nursing home, for example, as is the case with Mrs. S, family caregivers may be concerned that staff do not know the patient well enough to provide person-centered care, and as they live in a nursing home, they continue to lose their identity and may struggle to maintain this identity which is so important to person-centered care (Davies et al. 2017).

8 Family Caregivers of People with Dementia

8.1 Importance of Family Caregivers

An estimated 46.8 million people are living with dementia worldwide (Alzheimer's Disease International 2015), many of whom will be cared for by family caregivers and can be referred to as lay carers, untrained carers, informal carers, caregivers, or proxies. In the UK the Alzheimer's Society has insisted that without the help and support of family caregivers, the formal care system would collapse. Traditionally there are distinct boundaries between caregivers and the cared for. Caring in palliative care however may differ from caring for someone with a nonterminal physical or intellectual impairment. The boundary between the "caregiver" and the "cared for" is said to be somewhat blurred, because of the increasing need for support for the individual from the caregiver in palliative care. The caregiving career involves a variety of tasks in addition to meeting the physical and mental needs of the person with dementia. These include interaction with health and social care professionals, doing daily household chores, and escorting the person with dementia to various medical, dental, optical, and hairdressing appointments.

8.2 Effects of Caring for Someone with Dementia

It is well known that caring in general can be a stressful role and that the burden placed on the individual caregiver is often great, with limited opportunity to have breaks, socialize, and have whatever one may classify as a "normal" life. However, caring for an older person or a relative with dementia is thought to be one of the most stressful and difficult forms of caring. Caregivers as described in the portraits by Sanders and colleagues face the difficulty of coming to terms with the diagnosis and the loss of the person they once knew (Sanders et al. 2009). They may find difficulties with the individual's behavioral and cognitive decline, the loss of their own "normal" life, the role of caring, and finally the eventual death of the person. Uncertainty of death and the treatment options for people with dementia can lead to feelings of guilt among family caregivers; this is illustrated in patient case/vignette part 2. Caregivers of people with dementia have higher rates of various health problems, both physical and psychological, including depression and cardiovascular problems, resulting in increased doctor visits and an economical burden on health-care services, with a higher risk of mortality (Brodaty and Donkin 2009).

8.3 Supporting Caregivers

The lack of definitive split between the person with dementia and the caregiver can be conceptualized as what Twigg termed as carers as co-clients (Twigg 1989). Despite caregivers being seen as having a caring "career," the experience is not the same for all. Something which is often forgotten or not considered is that not all caregivers are loved by their relatives and conversely can be mistakenly labeled as "loved ones." The caregiver may endure a trajectory of caring from the encounter stage, where they are coming to terms with both the diagnosis of dementia and also their new role, moving onto an enduring stage at which point the caring intensity increases, through to the exit stage where they face the death of the individual and adapting to their new life (Lindgren 1993). As we discussed in Sect. 2 of this chapter, palliative care may cover all stages of this "caregiving career," and each individual caregiver may require more or less support at various stages

(Davies et al. 2014). A thorough caregiver's assessment should be completed with the family caregiver of the person with dementia, to identify their needs and levels of support required. This should be a holistic assessment considering medical as well as psychosocial aspects of care and support.

8.4 Grief, Loss, and Bereavement

Grief and loss when someone dies is to be expected with most people and is considered a normal response to death. Grief has been defined as "the reaction to the perception of loss with symptoms including yearning, sadness, anger, guilt, regret, anxiety, loneliness, fatigue, shock, numbness, positive feelings and a variety of physical symptoms unique to the individual" (Rando 2000).

Throughout the course of dementia, family caregivers may be experiencing a series of multiple losses, for example, loss of intimacy, companionship, control, personal freedom, and well-being among them (Chan et al. 2013). These losses can be described as part of anticipatory grief, that is, grief which occurs before the death of the individual (Rando 2000). Anticipatory grief occurs in 47–71% of family caregivers of people with dementia (Chan et al. 2013). The sometimes long projected course of dementia means that anticipating the death of the individual and ambiguity of what the future holds can be common among family caregivers. Anticipatory grief has been shown to have an association with depression, and depression is increased with anticipatory grief (Sanders and Adams 2005). However, some studies have suggested that what appears as clinical depression may actually be a grief reaction (Sanders and Adams 2005). Other factors which appear positively associated with increasing anticipatory grief include burden, non-English primary language in English-speaking countries, living with the person with dementia prior to being placed in a care home, and less satisfaction with care (Chan et al. 2013).

Grief appears to be more severe during the moderate to severe stages of dementia (Chan et al. 2013). However, as suggested, the needs of individual caregivers may differ, and this may also relate to their response to grief and loss. Individual caregivers may experience grief at different stages, and this should be carefully considered when supporting family caregivers. In particular, there may be a marked difference between spouses and adult children responding differently at different stages. Adult children appear to experience minimal grief in the early stages of dementia, most intense at the moderate stage, and the grief lessens toward the advanced stages with feelings of relief when the individual moves into a nursing home, for example. For spouses, grief appears to reflect a linear pattern increasing as dementia progresses; however, another work has suggested grief remains stable in advanced dementia and therefore may not continue to increase for all (Givens et al. 2011). It is important to reassure caregivers that relief after death is common and they should not feel guilty about this feeling; it can be part of the post-death grieving process (Chan et al. 2013). For some, grief may continue for some time after death, termed complicated grief if more than 6 months; this is termed as *persistent complex bereavement disorder* in the DSM-5, marked by an individual "incapacitated" by grief affecting their daily life.

Particular consideration and attention may be needed toward male caregivers who can find it difficult to openly accept their feelings of grief, strain, and distress (Sanders et al. 2003). Grief in some may be expressed in different ways or using different language, for example, portraying emotional dissociation from the person with dementia (Sanders et al. 2003). Males often have less stable social support networks and are less likely to seek assistance in dealing with their grief than females. This may be particularly pertinent in spouse male caregivers, who may be older and for whom grief may be particularly challenging, as they come to deal with the emotions associated with being alone at a time when their own social networks will be dwindling (Sanders et al. 2003).

In addition to regular caregiver assessments and reviews as mentioned, post-bereavement support should be offered to families (van der Steen et al. 2014b), including helping them adjust to a life of post-caring when much of this previous world

will have disappeared. This may include as in the case of Mrs. S patient case/vignette part 5 a meeting at the nursing home with the family after their relative has died. Practitioners should identify caregivers who are at increased risk of grief (anticipatory, normal, and complicated grief), such as those with high levels of burden and depression, offering caregiver support at an early stage.

8.5 What Do Caregivers Want from Care?

The individuality of caregivers is not only reflected in the needs of them as a caregiver but also in their views of how palliative and end-of-life care should be provided for someone with dementia. Caregivers' views regarding the appropriate treatment in particular referring to the dilemmas discussed in Sect. 6 of this chapter lie on a spectrum of beliefs from provision of care purely aimed at comfort by relieving symptoms through to active/invasive/aggressive treatment which is aimed at "cure" (Davies et al. 2014). It is important to reflect on the stage of the dementia and provide information and education to family caregivers as to the progression of dementia (see Fig. 1) and appropriate treatment options (van der Steen et al. 2014b). However, it is also important to acknowledge that there is a great deal of diversity when families want to receive the information (individual and between countries). When considering families' views, there should be a recognition that they may not have the complex medical knowledge that many practitioners have and this may be their first experience caring for someone who is dying. Caregivers may focus on the psychosocial aspects of care as their main priorities (Davies et al. 2017). This is important to emphasize as we discussed previously that not all decisions are medically focused.

Patient Case/Vignette Part 5 Mrs. S gets weaker and is not able to walk anymore. She has lost a lot of weight in the past few months. She gets another case of pneumonia, is in bed all day, and doesn't eat or drink anything anymore; the nurses think that Mrs. S is going to die this time. For the daughter of Mrs. S, this comes as a surprise. The physician and the nursing staff make all sorts of arrangements, for example, on pain relief, treatment in case of shortness of breath, and prevention of pressure ulcers and constipation. A spiritual counselor is asked by the nursing home to visit Mrs. S. Mrs. S's daughter stays with her mother all the time. She frequently asks when her mother is going to die. After 3 days and nights, Mrs. S dies in the presence of her daughter.

A few weeks after the death of Mrs. S, the family is invited to attend a meeting with the nursing staff and the physician. They talk about the stay of their mother in the nursing home and the final days to death.

9 Dying with Dementia

A prognosis is very difficult to provide to a person with dementia (Brown et al. 2013). With the disease comes a decline in cognitive functioning, but it is very difficult to predict if a person with dementia is in the last months of life, whereas with cancer patients, end of life seems more predictable. People do not always reach the last phase of dementia, and about half of people with dementia may die before the advanced stages (Hendriks et al. 2016). In people with cancer and dementia, a high number of symptoms are found while dying in various settings, such as a hospice and nursing home. In the USA hospice generally refers to hospice care as a service. In many other countries across the world, such as the UK, a hospice is a physical building which delivers palliative care (see Fig. 2); however, few people with dementia will receive care here (Reyniers et al. 2015).

The 6-month mortality rate in nursing homes is high and often higher than anticipated (van der Steen et al. 2007). The most frequent causes of death are respiratory infections or cardiovascular disorders, and in later stages, people are often more dehydrated and cachectic due to eating/swallowing difficulties like Mrs. S in the patient case/vignette part 5 (Hendriks et al. 2014). Also in the earlier stages of dementia, there is an association between eating and drinking less and mortality (Hendriks et al. 2016).

Many people with dementia die in a nursing home, but the numbers differ between countries related to the available system of care for people with dementia. In some countries a large proportion of people will still die in a hospital (Reyniers et al. 2015). The different journeys from home to sometimes hospital, nursing home or hospice to death, and the increased need for palliative specialist care are shown in Fig. 2.

Prognosis for someone with dementia is difficult; however, the prediction of short-term mortality, for example, 1 week, is much more accurate (Casarett et al. 2012; Klapwijk et al. 2014). Even when death is expected within days, it is not possible to predict when exactly someone is going to die such as in the case of Mrs. S (patient case/vignette part 5).

Many studies on the last days of life of dementia show often burdensome symptoms like pain or shortness of breath, and this is also indicated by relatives, who in many cases experience death as a struggle. Only 50% of the relatives perceive death as peaceful in a Dutch study (De Roo et al. 2014).

In the literature a minority of nursing home residents with advanced dementia enter or are transferred to a hospice (Reyniers et al. 2015), but this also depends on available care system and the care that is required; not all people with dementia will require a hospice placement (see Fig. 2). Hospice care is often more for symptomatic treatment, often scheduled treatment of pain and shortness of breath. All people with dementia should get good quality of care at the end of life, not only in a hospice.

9.1 Symptoms in the Dying Phase

Several studies on the last days of life with dementia show high percentages of pain in the days before death, ranging from 15% to 78%; however, there are differences among studies, possibly also due to different measurement scales or methods (Hendriks et al. 2014, 2015; Klapwijk et al. 2014; Sandvik et al. 2016b). There is a high prevalence of shortness of breath in people with dementia increasing in the period to death sometimes even to 80% of people (Hendriks et al. 2015; Klapwijk et al. 2014; van der Steen 2010). Different behaviors are seen in the days before death. People are often in bed and can be unconscious. Restless behavior, anxiety, and agitation are seen in several studies, and also delirium has been reported (Hendriks et al. 2014, 2015; Vandervoort et al. 2013; Mitchell et al. 2009).

9.2 Treatment Options

9.2.1 Non-pharmacological Treatment Options (Including Spiritual Care)

Many of the non-pharmacological treatment options as described in Sect. 5.2 can also be used in the last days before death. The Namaste Care program, offering meaningful activities by a trained nursing assistant in nursing homes for people with advanced dementia, specifically describes the use of the program for the dying phase (Volicer and Simard 2015).

When a person with dementia reaches the dying phase, nursing staff and medical team should pay close attention to prevent constipation, bladder retention, and pressure sores. Regular mouth care should be started. People should be offered drinks and food, but it should not be forced upon them. The medication should be evaluated, and if oral medication can't be swallowed, it should be stopped. Regular evaluation of pain, shortness of breath, or discomfort is needed; observational instruments for pain or discomfort can be used in this phase, for example, the Discomfort Scale-Dementia of Alzheimer Type (DS-DAT) (Hurley et al. 1992). The presence of a pacemaker or implantable cardioverter defibrillator (ICD) should be checked, and in case one of these is present, it should be explained what to do to nursing staff and family.

It is important to highlight the needs of people are individual and some people have personal needs and may want spiritual counseling. Spiritual counseling is often overlooked; a study from a UK hospital showed that the religious beliefs of people with dementia were documented less than those without dementia (Sampson et al. 2006). Spiritual care has been associated with an improved perception of

quality of care from families at the end of life (Daaleman et al. 2008) and families' satisfaction with physicians' communication shortly after admission to a nursing home (van der Steen et al. 2014a).

It is very important for the nursing staff and medical team to explain the course of symptoms and possible treatment options to the family (including the presence of Cheyne-Stokes respiration, rattle, and time of death) and to make a clear description of medication with explanation what to give when and also if necessary extra medication which can be given. It is vital to include families as much as possible and to ask for the wishes of the family, when the team should contact the family and who. An end-of-life care plan can help to improve communication and care in the last days of life (Detering et al. 2010).

9.2.2 Pharmacological Treatment Options

Pain and shortness of breath are often treated with opioids; a high percentage of people use opioids on the last day before death, often requiring an increase on the last day (Hendriks et al. 2014, 2015; Klapwijk et al. 2014; Sandvik et al. 2016b). Agitation is treated with anxiolytics, but also palliative sedation may be initiated, with a Dutch study demonstrating palliative sedation was started in around 21% of cases (Hendriks et al. 2014, 2015).

Response to opioids should be closely monitored when prescribed for pain or shortness of breath to ensure effective response without excessive side effects. Special caution should be taken when prescribing for patients with renal failure as there is a risk of accumulation of renally excreted opioids.

Death rattle is sometimes treated with hyoscine (also known as scopolamine) subcutaneously; however, evidence is limited with a lack of consensus on the best approach (van der Maaden et al. 2015).

10 Conclusion

As this chapter demonstrates, palliative care for people with dementia shows similarities to palliative care for people with other conditions such as cancer in particular with relation to symptoms. However, there are also differences which make palliative care for people with dementia unique, including communication difficulties with the individual, recognition of dementia as a terminal illness, and large elements of uncertainty in several areas including patient wishes and prognosis. Advance care planning is important for people with dementia. Person-centered care should be adopted throughout the care journey, but in this chapter, we have also highlighted the importance of family caregivers. Families should be involved in care decisions and processes, but also we highlight their need for care themselves, as such palliative care for people with dementia is not a dyad relationship of health and care team and the person with dementia but a triad of the person with dementia, family, and the health and care team.

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Palliative Care and Stroke

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Peter Eastman and Brian Le

Contents

Abstract

There have been significant advances in the prevention and management of stroke over the last few decades. Despite these important developments, stroke, both in the acute and chronic phases, remains a major cause of morbidity and mortality. The value of integrating palliative care principles and practices into stroke care management is being increasingly recognized across a range of domains including symptom management, assistance with complex decision-making, discharge planning, and end-of-life care. This chapter will explore the logistics, benefits, complexities, and challenges associated with the evolving relationship between stroke and palliative care services.

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_59

1 Introduction

There have been significant advances in the acute treatment and rehabilitation of stroke over the last few decades. Contributing factors include improved early detection/recognition, timely hospital presentation, the use of thrombolytic and endovascular therapies, early initiation of rehabilitation, and the introduction of organized stroke care. Ongoing improvements in stroke prevention, treatment, and rehabilitation are crucial as stroke prevalence is expected to increase with the aging population. The lifetime risk of having a stroke has been reported to be approximately one in five for females and one in six for males (Mozaffarian et al. 2015) although this figure was calculated from a predominantly Caucasian cohort within the United States and may therefore not be easily generalizable. Stroke incidence varies between countries and is influenced by a range of health, cultural, geopolitical, and socioeconomic factors. Globally the burden of stroke is increasing as measured by the absolute number of people affected, stroke survivors, and disability-adjusted life years lost (Feigin et al. 2014). Much of this burden is seen in low- to middle-income countries.

Strokes constitute a heterogeneous group of conditions which can be described by mechanism and/or location of injury. Approximately 80–85% of strokes are ischemic in nature, with the remainder being either intracerebral hemorrhage (ICH) or subarachnoid hemorrhage (SAH). ICH generally occurs following arterial wall rupture in vessels weakened by chronic hypertension while SAH typically follows aneurysmal rupture within the circle of Willis or trauma (Simmons and Parks 2008). Ischemic subtypes include thrombotic strokes due to occlusive arterial atherosclerotic disease, embolic strokes which are typically cardiac in origin, and lacunar infarcts which occur following the occlusion of the small arteries that supply deep brain structures. Broadly speaking the extent of injury or damage associated with a stroke will depend upon the blood vessels involved and the areas and extent of brain affected.

The most important factor in the initial management of acute stroke is time. The sooner a stroke is recognized and treatment commenced, the better the outcome is likely to be. Another key factor in optimizing chance of recovery is venue of care. There is clear evidence that patients who are managed in a designated stroke center or unit with a specialist multidisciplinary team do better than patients managed elsewhere. In a Cochrane review of 28 trials and 5855 participants which compared stroke care unit (SCU) care with alternative care, SCU was associated with significant reductions in the odds of death, dependency, and/or institutionalized care (Stroke Unit Trialists' Collaboration 2013). The benefits of management within a SCU have been demonstrated for all subtypes of ischemic strokes (Smith et al. 2010a) as well as for ICH (Langhorne et al. 2013).

After initial cardiorespiratory stabilization, immediate stroke management is individualized according to a range of factors including type and severity of stroke, presence of contraindications, medical comorbidities, and patient and family wishes. Following an ischemic stroke in appropriate patients who do not have contraindications, the initial goal is to provide intravenous (IV) thrombolytic therapy as quickly as possible. The provision of a single dose of IV recombinant tissue plasminogen activator (IV rt-PA) within 4.5 h of the commencement of symptoms has been associated with a substantially improved chance of independent function at 3 months post stroke (Maldonado et al. 2014). The use of endovascular therapies following ischemic stroke is an area of ongoing research and development. Therapies under this umbrella include endovascular thrombolysis, thrombectomy, and stent retriever technology. It has been suggested that these approaches may provide superior recanalization in situations such as proximal vessel occlusion when systemic thrombolysis may be less efficacious although until recently results from randomized trials were mixed. Two recently published trials however, both of which were stopped early due to efficacy, have shown significant improvements in functional outcome (Campbell et al. 2015; Goyal et al. 2015) as well as mortality (Goyal et al. 2015) for the combination of endovascular thrombectomy and IV rt-PA compared to IV rt-PA alone, in ischemic stroke with proximal cerebral arterial occlusion.

The management of ICH involves acute stabilization including management of blood glucose and temperature, careful blood pressure control, quality nursing care, prevention of complications, early rehabilitation, and prevention of recurrent hemorrhage (Hemphill et al. 2015). Time is again crucial as it is common for deterioration to occur in the period soon after an ICH. While the benefits of surgical removal of hemorrhage for most supratentorial ICH have not been proven, prompt surgical management is recommended for patients with a cerebellar ICH who are deteriorating neurologically or have brain stem compression (Simmons and Parks 2008; Hemphill et al. 2015). Emergent therapies under investigation in ICH include minimally invasive surgical techniques and the use of biological neuroprotective agents.

Despite advances in prevention, acute treatment, and rehabilitation, stroke remains a prominent cause of morbidity and mortality worldwide. It is a major cause of disability in the United States where up to a third of patients require admission to a long-term care facility following stroke (Mozaffarian et al. 2015). A range of psychological and physical sequelae have been reported by stroke survivors including anxiety and depression, pain syndromes, and communication difficulties. Not surprisingly high levels of distress and caregiver burden are also common among relatives and loved ones. The ideal model for managing the important physical and psychosocial needs of stroke survivors and their families is yet to be established, and it is not clear where palliative care services sit in this paradigm.

While mortality rates vary internationally and have decreased over the last 20 years (Feigin et al. 2014), stroke remains the second commonest cause of death worldwide (World Health Organization 2014). A range of important and diverse needs have been reported by dying patients and their families including symptom management, psychosocial support and assistance with prognostication, treatment decision-making, and future planning. The utilization of palliative care principles and practices would seem appropriate in meeting these needs, and there is increasing recognition, including from international guidelines, of the importance of integrating palliative care into stroke care (National Stroke Foundation 2010; Holloway et al. 2014; Casaubon et al. 2016; Intercollegiate Stroke Working Group 2016). However a range of challenges to effective integration have also been identified from both a stroke and palliative care perspective. The aim of this chapter is to explore the relationship between stroke services and palliative care in both the acute and longer-term setting. The current level of involvement and proposed models of integration will be discussed as well as some of the common palliative care needs and issues identified by patients, families, and health professionals. It is hoped this will provide a contemporaneous overview of the current situation and highlight some important areas for future thought, research, and investment.

2 Palliative Care and Acute Stroke

There is growing recognition that some patients and families following an acute stroke have needs that will be best met by integrating palliative care philosophies and practices into their stroke management.

2.1 Palliative Care Recognition Within International Stroke Guidelines

There is increasing recognition of the relevance of palliative care principles for some patients following a stroke within published international stroke guidelines. While the depth and breadth of information varies across guidelines, there is general agreement concerning the importance of high-quality end-of-life care within stroke services and some support for palliative care throughout the stroke care trajectory.

In a comprehensive scientific statement from the American Heart Association/American Stroke Association, Holloway and colleagues explored the dynamics, logistics, and complexities associated with palliative and end-of-life care in stroke (Holloway et al. 2014). The authors advocate for

the availability of palliative care for all patients and their families following a severe or life-threatening stroke, throughout the disease course. In their proposed model, the management of most palliative care problems would be carried out by the stroke service multidisciplinary team with specialist palliative care services available for secondary consultation in situations of heightened complexity. Importantly, the authors provide evidence-based recommendations and guidance to aid implementation, including practical education regarding communication skills, goal setting, and symptom assessment and management.

The Canadian Stroke Best Practice Recommendations emphasize the importance of fostering palliative care expertise within stroke centers (Casaubon et al. 2016). The guidelines make a distinction between palliative care and end-of-life care noting that palliative care can occur in combination with life-prolonging therapies and is not reserved only for those who are imminently dying. A palliative approach is suggested in the setting of catastrophic stroke or multiple comorbidities in order to support both patient and family. Replicating the recommendations of Holloway and colleagues (2014), the guidelines make clear that the stroke service multidisciplinary team should have the appropriate palliative care skills to support dying stroke patients but also that there be access to specialist expertise. Specific indications for specialist palliative care referral include the management of unstable symptoms and assistance with decision-making and with managing complex family and psycho-social dynamics. Recommendations are also made in relation to Advance Care Planning (ACP), specifically that stroke survivors, their families, and caregivers should be supported to participate in it.

In Australia, the 2010 Clinical Guidelines for Stroke Management recommend that all patients dying following a stroke have access to care that is aligned with palliative care principles and practices (National Stroke Foundation 2010). This includes consideration of physical, psychosocial, spiritual, and cultural needs as well as guidance with prognostication and the diagnosis of dying in deteriorating patients or those following a severe stroke. The guidelines note that in many less complex situations, this care will be provided by stroke service staff, and these staff will require ongoing education and support in relation to end-of-life care. The importance of clear and timely communication between stroke services, patients, and families is stressed, and family meetings are suggested as an appropriate forum for these discussions.

The 2016 fifth edition of the UK National Clinical Guideline for Stroke include, among their key recommendations, the proposition that multidisciplinary stroke teams should consider high-quality end-of-life care as a core component of their work (Intercollegiate Stroke Working Group 2016). The need for enhanced education and support for stroke service staff in palliative care principles is emphasized, as is access to specialist palliative care and the opportunity for timely transfer to home if this is the desirable outcome. Among changes from the previous iteration, the 2016 guidelines caution against imposing burdensome restrictions upon patients dying from stroke with particular mention made about the pragmatic management of impaired swallowing and oral intake at end of life. The guidelines acknowledge the range of physical and psychological stressors that can occur following a large stroke and propose that the appropriate management of these problems can help ameliorate distress for patients and their families at end of life.

When considered together, a number of common themes are evident across the guidelines. These include:

- General support for palliative care principles as key components of stroke care.
- Recognition of the presence of multidimensional symptom issues for many patients and their families following a large stroke.
- The importance of clear and ongoing communication between stroke services, patients, and families particularly in relation to issues such as prognostication, goals of care, and management.
- Support for a service model in which the multidisciplinary stroke team provides the majority of palliative and end-of-life care with secondary support available from specialist palliative care services.

2.2 Integration of Stroke and Palliative Care

Although integrating palliative care and acute stroke services is considered important for patients, families, and health professionals alike, how this integration might actually take place is under-researched and not without its challenges. Establishing the palliative care needs of stroke patients and their families is a crucial first step in an integrated approach; however data addressing this question are limited and little is known about how these needs might change over time (Stevens et al. 2007).

Potential methods to assess palliative care needs might include triggers built into existing stroke care pathways – simple bedside prompts or more formal targeted needs assessment tools. Creutzfeldt and colleagues (2015) showed that the use of a simple four-question "palliative care needs checklist" during neurology ward rounds was an effective prompt for recognizing and meeting patient and family needs. Questions in the checklist addressed the presence of distressing symptoms, how the patient and family were coping, and whether the goals of care or treatment approach needed to be modified. Burton and colleagues (2010) used the Sheffield Profile for Assessment and Referral for Care (SPARC) tool to identify high levels of palliative care needs in a prospective study of 191 consecutive stroke admissions to two UK hospitals. The SPARC was developed to screen patients with a range of advanced diseases for specialist palliative care (SPC) referral and incorporates five domains covering physical, psychosocial, spiritual, and functional issues. The authors concluded that the use of the SPARC tool particularly in more disabled stroke patients provided a valuable trigger for staff to consider a range of palliative care issues.

In some ways acute stroke and palliative care might not be considered particularly compatible. The acute stroke environment is one of high-intensity neuro-restorative care with an emphasis on survival, while palliative care is commonly considered more meditative in approach with less concern placed upon survival and more on quality of life. Challenges in introducing palliative care into general stroke management are highlighted by qualitative studies in which stroke unit staff have questioned the juxtaposition of a simultaneous curative focused and palliative approach (Gardiner et al. 2013) and have viewed palliative care as being predominantly about end-of-life care and representative of failure of stroke management (Burton and Payne 2012). Beyond the acute stroke phase, categorizing a patient as "palliative" has been identified as a barrier to combining rehabilitation and palliative care (Burton and Payne 2012).

Traditional palliative care models developed predominantly for patients with malignant diseases may not be easily transferrable to stroke. With its typically sudden onset and decidedly unpredictable clinical course, stroke may behave differently to many cancers or other chronic non-malignant conditions in which palliative care is commonly involved. Such differences were highlighted by a study of 544 patients admitted to a tertiary SCU that found more than 50% of the 87 patients who died had been completely independent and well immediately prior to their stroke (Eastman et al. 2013). Caregivers of stroke survivors have also been noted to have different needs when compared to those of patients with cancer. They are typically older and frailer and as a result may lack important support and social networks (Stevens et al. 2007).

Despite a current lack of clarity concerning the characteristics and function of palliative care within acute stroke services (Burton and Payne 2012), there does appear to be general acceptance of a pragmatic service model in which the multidisciplinary stroke team provides the majority of palliative and end-of-life care with secondary support available from SPC (Holloway et al. 2014; Creutzfeldt et al. 2015; Casaubon et al. 2016). SPC services are also ideally placed to provide the necessary education, training, and support to enable the provision of high-quality nonspecialist palliative care. Importantly, for any model to be applicable to patients throughout the disease course as has been suggested (Holloway et al. 2014; Creutzfeldt et al. 2015), recognition will

be required from stroke services that palliative care principles can be positive adjuncts to disease-modifying therapies rather than simply applying to end-of-life care. Additionally a model combining stroke and palliative care will need to consider important system issues such as avoiding overburdening already-stretched palliative care services and not deskilling stroke unit staff (Stevens et al. 2007).

Using qualitative data obtained from patients, families, and stroke service staff, Burton and Payne (2012) constructed a theoretical framework on how the integration of stroke services and palliative care might occur. They proposed that integration was underpinned by six key mechanisms, namely, *clinical legitimacy*, *capacity*, *family engagement*, *early integration*, *recognition of complexity*, and *recognition of dying*. These mechanisms could themselves be influenced by a range of clinical and organizational factors which vary according to the existing structures and processes within individual healthcare settings. Burton and Payne (2012) propose that analysis of the relationships and interactions influencing these six key mechanisms will facilitate service development and improve the care of patients and families following stroke.

Overall the development and optimization of integrative models will depend not only on the willingness of the stroke and palliative care sectors to embrace the process but also organizational and governmental support to ensure adequate funding and support. Underpinning the whole process is the requirement for ongoing collaborative quantitative and qualitative research focusing not just on outcomes but also factors such as needs assessment, appropriate patient stratification, timing and indication for SPC referral, cost/benefit analysis, and patient, family, and health professional experiences.

2.3 Specialist Palliative Care Utilization in Acute Stroke: A Review of the Current Literature

Data quantifying the level of SPC involvement in stroke are limited and predominantly focused on inpatient consultation services. While variability is seen between health organizations internationally, there is evidence to suggest that the overall uptake of palliative care services for patients following an acute stroke is increasing. In a large cross-sectional study investigating palliative care utilization in nontraumatic intracerebral hemorrhage (ICH), Murthy and colleagues (2016) analyzed admissions to over 1000 American hospitals using the National Inpatient Sample, the largest inpatient health database in the United States. Of the 311,217 included admissions, 32,159 (10.3%) received palliative care, with a substantial annual increase in palliative care involvement seen (4.3% in 2007 to 16.2% in 2011). In an analysis of administrative data of 4894 patients who died within 30 days of an ischemic stroke, 23% of all patients were enrolled in hospice for end-of-life care, a threefold increase from previously reported rates (duPreez et al. 2008).

A small amount of research has explored predictors for SPC involvement in patients following stroke as well as differences between referred and non-referred patients. The influence of both sociodemographic and clinical factors on referral patterns has been reported with data typically obtained from either large administrative dataset analyses or retrospective cohort studies.

In an analysis of palliative care involvement for patients following nontraumatic ICH (Murthy et al. 2016), significant predictors for palliative care involvement included ICH severity, associated comorbidities, female gender, advanced age, hospital location, and ethnicity. Several of these factors were also predictors for hospice utilization in 4894 patients who died within 30 days of an ischemic stroke (duPreez et al. 2008). Predictors which increased the likelihood of hospice utilization included older age, female gender, dementia, Caucasian descent, and hospital length of stay greater than 3 days. Mechanical ventilation, gastrostomy, and uncomplicated diabetes mellitus as a comorbidity correlated with decreased hospice enrolment.

Holloway and colleagues (2010) reviewed all patients referred to an inpatient palliative care consultation service within a large US teaching hospital over a 3-year period. Compared to

patients with cancer or common nonmalignant diagnoses including chronic obstructive pulmonary disease (COPD), stroke patients tended to be more functionally impaired, less likely to have decision-making capacity, and were more likely to die in the hospital. For the 1551 stroke patients analyzed during the study period, 6.5% received palliative care consultation. Stroke patients seen by the palliative care service were older, stayed longer in the hospital, and were more likely to be discharged to hospice. However, the majority of stroke patients who died or were discharged to hospice were not seen by SPC.

In an Australian review of 544 admissions over a single year to a metropolitan, tertiary SCU, just over 11% of patients were referred to SPC (Eastman et al. 2013). The predominant reason for referral was end-of-life care, and a number of predictors for referral were identified. These included female gender, older age, increased disability pre stroke, ICH, and living alone or in a residential aged care facility prior to stroke. Sixteen per cent of all SCU admissions died during the review period with just over half seen by the palliative care team. This is approximately double the rate reported from both Swiss and Irish stroke services where only 26% and 24%, respectively, of decreased stroke patients received palliative care consultation (Mazzocato et al. 2010; Ntlholang et al. 2016). Stroke patients referred to the Australian SPC who died during the admission were older, more disabled, and had a significantly longer length of stay than those not referred. In contrast to the total SCU population, the proportion of patients with an ICH was higher in deceased stroke patients who did not receive palliative care consultation (50% vs. 37%). This in combination with the significantly shorter median survival of non-referred patients (2.5 days vs. 6 days) supports previous observations that stroke service staff are generally comfortable managing clearly terminal patients (Rogers and Addington-Hall 2005).

In a retrospective review of 54 consecutive deaths on an Irish teaching hospital stroke service over a 2-year period, several differences were found between patients referred and not referred to SPC (Ntlholang et al. 2016). Those patients whose cause of death was judged to be unrelated to their stroke were more likely to be seen by the SPC team. These patients also had a longer median time between stroke and death, again supporting the notion that stroke unit staff are more comfortable managing the palliative care needs of patients who die soon after a severe stroke, and less so in those who survive longer.

Taken together these data suggest that referrals to SPC, particularly to inpatient consultation services, following acute stroke are increasing. This may reflect increased recognition of the benefits associated with palliative care in areas such as symptom management, complex end-of-life decision-making, and communication. Referral to SPC is influenced by a range of clinical, sociodemographic, and health service factors, but not surprisingly stroke patients referred to palliative care tended to be older, frailer, and sicker. Importantly the majority of stroke patients, including those who were severely disabled or died, were not referred to SPC. While epidemiological data regarding referral rates and predictors are useful for service provision and planning, they do not answer important questions such as whether all patients with complex needs who would benefit from SPC input are currently being referred or whether non-referred "less complex" stroke patients are receiving timely and appropriate non-specialist palliative care (Stevens et al. 2007). This represents an area for ongoing research.

2.4 Shared Stroke and Palliative Care Issues in the Acute Setting

2.4.1 Prognostication

The prediction and communication of prognosis is an important but inherently difficult part of stroke care. Given the majority of patients will survive a stroke, prognostication is relevant to all stages of stroke care from initial acute presentation to post-acute recovery and finally to rehabilitation and/or discharge. Accurate prognostication provides a road map to guide treatment decision-making and allows patients and families to plan for the future. Inaccurate prognostication runs the risk of depriving some patients of the best chance of

recovery while exposing others to burdensome treatments that may only prolong suffering. In essence prognostication attempts to provide some degree of certainty while being at the same time inherently uncertain. In a qualitative study that examined patient and family members' perspectives of acute stroke care, honest discussions around prognosis despite uncertainty were valued by relatives even when it was predicted that prognosis might be poor (Payne et al. 2010).

Studies investigating prognosis following stroke have tended to focus on mortality more than functional outcome or recovery. Numerous clinical, sociodemographic, and institutional predictors for mortality have been identified, with stroke severity and older age generally reported to have the strongest associations (Smith et al. 2010b). The National Institutes of Health Stroke Scale (NIHSS) provides a quantification of stroke severity and is a highly reliable predictor of mortality after stroke both on its own and in combination with other variables (Smith et al. 2010b; Frontera et al. 2015). It is a 15-item validated bedside assessment tool which incorporates testing of consciousness, language, sensation, and motor function.

Stroke type itself is also a strong predictor of mortality. This is illustrated by a Danish study of 39,484 hospitalized stroke patients in which intracerebral hemorrhage (ICH) was associated with a fourfold increased risk of dying compared to ischemic events in the immediate post-stroke period (Andersen et al. 2009). Interestingly the difference in mortality between the two stroke types progressively decreased over time until at 3 months, stroke type no longer correlated with mortality. Temporal differences in the factors associated with mortality have also been reported after ischemic stroke. In a Canadian study of 3631 patients following ischemic strokes, stroke severity was found to be a significant predictor of mortality at all time points, while clinician experience was only significant at seven and 30 days and age and medical comorbidities only significantly associated with 30-day and 1-year mortality (Saposnik et al. 2008).

Numerous multivariate prediction models for outcome and mortality following stroke are available although the quality and clinical utility of these models varies (Holloway et al. 2014). Examples include the Hunt-Hess scale for subarachnoid hemorrhage and the ICH score which incorporates Glasgow Coma Scale, ICH volume, intraventricular hemorrhage, age, and site of ICH origin. ICH scores of three or greater have been reported to have a sensitivity and specificity approaching 80% and 90%, respectively, for mortality following ICH (Simmons and Parks 2008).

The applicability of prognostic models to the real world is related in part to the commonality of the variables included and also by the sample from which the data are drawn. Prediction models, for example, generated using data from cohorts with high numbers of clinical trial participants or only patients managed in specialized stroke centers may not be easily applicable to a broader, community-based stroke population. Similarly models that include clinical information from imaging modalities that are not widely available may also lack generalizability.

One particular concern raised by a number of stroke researchers when considering mortality prediction models is the concept of "withdrawal bias." It is argued that because current models have incorporated patients who either never commenced or had life-sustaining therapies withdrawn, there is a potential bias toward mortality (or treatment withdrawal) as well as difficulty in establishing the true effect (positive or otherwise) of these therapies following severe stroke. This is likely to be particularly relevant for stroke types with poor prognosis such as ICH. Given this the importance for clinicians to understand the strengths and limitations of these models, when using them to establish and communicate prognosis to patients and families, has been highlighted (Holloway et al. 2014; Frontera et al. 2015). This may be particularly the case when considering instigating or transitioning to end-of-life care.

Prognostication based upon clinician experience and expertise is an alternative to a model-based approach. Unlike fixed mathematically generated models, clinicians have the advantage of being able to consider an individualized range of factors and adjust their estimations in real time. Clinician-based estimates however may vary

considerably between individuals and be influenced by both optimistic and pessimistic judgements (Holloway et al. 2014; Frontera et al. 2015). The involvement of the multidisciplinary team and utilization of a second opinion (including from SPC) have been suggested as ways to overcome some of the issues with clinician-based estimates.

Despite the inherent difficulties associated with prognostication, the importance of providing patients and their families with a sense of the future cannot be underestimated. This is likely to be best achieved using a combination of clinician acumen and evidence-based estimation models individualized to each patient and their unique characteristics.

2.4.2 Limitations of Treatment

The majority of deaths after stroke follow either the limitation, cessation, or foregoing of potentially life-prolonging therapies (Kelly et al. 2012; Holloway et al. 2014; Creutzfeldt et al. 2015; Alonso et al. 2016). In the United States, up to 60% of all stroke deaths follow the removal of mechanical ventilation (Holloway et al. 2014) although this rate is likely to be different in other countries. Decision-making regarding limitations of treatment in acute stroke is complex as it needs to incorporate a range of patient, sociocultural, and clinical factors including autonomy, patient and family wishes, and prognostication. Additionally in the acute phase when uncertainty is high, management decisions need to be made quickly so as to maximize the chances of injury reversal and potential recovery. The acute stroke setting has been described as a "fast-paced, chaotic environment wrought with hope and disappointment, relief and anxiety" (Creutzfeldt et al. 2015), and therefore it is hardly surprising that decision-making in this setting is challenging. Complicating the situation further, many patients have impaired communication as a consequence of their stroke, meaning the responsibility for these complex and often life-and-death decisions will involve family and loved ones.

Treatment limitations can take numerous forms and may alter over time. In the acute setting, they may include decisions regarding thrombolytic and/or endovascular therapy or aggressive resuscitative approaches such as cardiorespiratory resuscitation or mechanical ventilation. In some patients, particularly the more elderly, frail, or those following a severe stroke, the decision to take a palliative approach with an emphasis on comfort might be taken at the outset. This might involve, among other things, the foregoing or withdrawal of antibiotic therapy, hydration, or supplementary feeding. In the majority of circumstances, these discussions and decisions will not involve SPC but be undertaken by members of the stroke team or emergency department. Relatives of stroke patients have reported experiencing discomfort when they felt excluded from the decision-making process, overly responsible for the decisions made (Cowey et al. 2015), or when participating in discussions if they knew do-not-resuscitate (DNR) orders had already been made by the medical team (Payne et al. 2010). This highlights the importance of mutual, shared decision-making between clinicians, patients, and families. The importance of good communication skills underpinned by an awareness of palliative care practice and philosophy has been advocated as a valuable component of both neurology practice and training (Holloway et al. 2014; Creutzfeldt et al. 2015).

The impact of treatment limitations on acute stroke outcomes has been fairly extensively studied with particular interest in the effect of early DNR orders (and other limitations) on stroke mortality. A number of papers have shown an association between DNR orders and increased mortality in both ICH and ischemic stroke independent of other established mortality predictors (Zahuranec et al. 2007; Holloway et al. 2014; Parry-Jones et al. 2016). In a study of 270 non-traumatic ICH, the presence of early treatment limitations (defined as DNR orders alone or in combination with early withdrawal and/or early deferral of other life-sustaining therapies) was associated with a twofold increase in mortality independent of a range of established predictors including age, Glasgow Coma Scale score, and ICH volume (Zahuranec et al. 2007). It has been suggested that the association between DNR orders and early mortality following stroke (and

ICH in particular) represents a "self-fulfilling prophecy" whereby the prediction of poor prognosis leads to limitations of care which ultimately produce a poor prognosis. Accordingly, and in the absence of clear advance care directives, caution is advised about making early treatment limitations decisions in the immediate post-stroke period.

Following the acute stroke phase, ongoing consideration of treatment goals is influenced by the evolving clinical picture, patient and family wishes, and expectations in relation to recovery. This can be a time of significant uncertainty for patients, families, and clinicians and one in which decision-making can be become more complex with emphasis on factors such as prognosis, potential withdrawal of life-prolonging therapies, and discharge planning (Rogers et al. 2005; Eastman et al. 2013). Decisions around the withdrawal of hydration and nutrition can be particularly challenging and were recorded as a source of conflict in nearly half of all interactions between family members and staff in a study of 104 patients who died in a Canadian SCU (Blacquiere et al. 2009). Assistance with this complex decision-making and communication is a common reason for SPC involvement following stroke and is valued by other health professionals. In one study, stroke staff noted that the benefits of access to SPC in these complex scenarios included "reassurance" and "support for decision-making" (Burton and Payne 2012).

For relatives of patients who have had a severe stroke, acting as a surrogate decision-maker can be a two-edged sword. On the one hand, feeling sufficiently involved in decision-making is a predictor of high satisfaction with end-of-life care for bereaved relatives of stroke patients (Young et al. 2009). On the other, when relatives have reflected upon their experiences as surrogates for patients who had suffered severe strokes, a number of conflicts and struggles were described (de Boer et al. 2015). These include the strain of making decisions under time pressure, feeling unprepared or underqualified to speak for their relative, and dealing with uncertainty and change. Despite differences in the experiences reported between interviewees, there was an overall tendency for surrogates to follow medical advice, highlighting again the importance of patient- and family-centered communication in this setting.

Longer-term positive and negative consequences have been reported for surrogates involved in making treatment decisions for others (not specific to stroke). In a systematic review (Wendler and Rid 2011) which included 2854 surrogates across 40 quantitative and qualitative studies, nine papers found that being involved in decision-making had beneficial effects for some surrogates. Importantly however up to a third of surrogates reported negative emotional consequences associated with making decisions for their loved one including stress, guilt, and doubt about whether they had done the right thing. These negative emotions were typically sustained for months and sometimes years which has important implications for bereavement services. Feeling confident they were following a treatment plan consistent with patient preferences seemed to mitigate some of the emotional burden on surrogates, perhaps highlighting the value of Advance Care Directives as a way of planning for future health care.

2.4.3 Symptom Burden Following Acute Stroke

The recognition and appropriate management of both physical and psychological symptoms has been highlighted as an unmet need for patients and their families following acute stroke (Addington-Hall et al. 1995; Stevens et al. 2007; Burton and Payne 2012). While published literature is limited, symptom burden has been reported in between 65% and 98% of dying stroke patients. A broad range of physical symptoms have been reported with varying frequency in patients following an acute stroke including fatigue, nausea, restlessness, and issues with urination and defecation. Pain has been variably described with reported prevalence rates of between 30% and 70% (Addington-Hall et al. 1995; Mazzocato et al. 2010; Ntlholang et al. 2016; Eriksson et al. 2016).

There is evidence that psychological distress is common in patients following an acute stroke, although differences in prevalence are noted in the limited available published literature. Psychological distress, including anxiety, dysthymia, and

loneliness, was found to be present in almost half of 191 consecutive stroke admissions in one UK study (Burton et al. 2010) and in 25% of dying stroke patients referred to a Swiss palliative care consultation service (Mazzocato et al. 2010). By contrast, in a separate review of 54 consecutive deaths in an Irish specialist stroke service, psychological distress was reported in only one patient (Ntlholang et al. 2016). Investigating the palliative care needs of patients following an acute stroke, Burton and colleagues (2010) found that while spiritual or religious concerns were low, up to a 25% of patients were worried about death and dying. Additionally, many were concerned about ongoing dependence and disability and the impact this might have on their loved ones. About a quarter felt that their care needs would exceed the capabilities of their families creating the potential for additional distress and even disharmony in an already emotionally fraught time.

The importance of considering the psychological impact of stroke upon patients and families was highlighted in a study investigating bereaved family members' satisfaction with the care provided to patients palliated after ischemic stroke (Blacquiere et al. 2013). While overall satisfaction with palliative care was high, lower satisfaction rates were reported for treatment of anxiety and depression and for the level of emotional support provided to families. The impact of stroke upon loved ones and families is frequently profound, in large part due to the abrupt change in function and cognition often associated with stroke. In the longer term, a number of adverse outcomes have been identified in stroke caregivers including mental health issues, worsening physical health, and financial burden (van Heugten et al. 2006; Carod-Artal and Egido 2009). This potential for longer-term adverse sequelae adds further weight to the importance of considering the psychosocial needs of stroke patients and their families in the acute phase.

While variability in symptom burden following acute stroke has been reported, respiratory symptoms including dyspnea and secretions appear to be particularly prevalent. This is likely to be due, at least in part, to their demonstrability when compared to less visibly obvious symptoms such as pain and anxiety. In one prospective cohort study of 22 patients admitted to a SCU and felt likely to die within 3 months of admission, all of the 20 patients who subsequently died experienced respiratory symptoms during their last hours of life (Rogers and Addington-Hall 2005). Respiratory secretions or "death rattle" were recorded in just over 60% of 1626 dying stroke patients in a Swedish database review (Eriksson et al. 2016), and dyspnea was the commonest recorded symptom in 54 consecutive patients who died in an Irish hospital stroke service (Ntlholang et al. 2016) and in 81% of stroke patients referred to a Swiss palliative care consultation team (Mazzocato et al. 2010). The potential difficulty of managing dyspnea in dying patients was highlighted in this study as only 48% of patients were felt to be free from dyspnea during their last 48 h of life (compared to 81% who were assessed as being free from pain).

Using data from the Swedish Register of Palliative Care, Eriksson and colleagues (2016) compared the prevalence of six symptoms (pain, "death rattle," dyspnea, anxiety, confusion, and nausea) between 1626 patients who died following a stroke and 1626 patients dying from cancer. Interesting differences in symptom prevalence, awareness, and management were noted between the groups. While all symptoms were present in the stroke group (nausea 7.6%, confusion 7.9%, dyspnea 16.3%, anxiety 18.9%, pain 42.7%, and "death rattles" 60.7%) when compared with their matched counterparts with cancer, stroke patients were significantly more likely to experience "death rattles" but less likely to experience any of the other five symptoms. Importantly however, staff caring for stroke patients were significantly less likely to know whether a patient suffered from any of the target symptoms compared to staff caring for patients with malignant disease. It might be anticipated that this difference was related to higher rates of reduced consciousness in dying stroke patients; however this does not seem to have been the case as the ability to self-determine until the last days of life was equivalent between groups (73.3% of stroke patients, 74.3% in cancer). In keeping with the differences seen in symptom prevalence and staff awareness of

symptoms, stroke patients were significantly more likely to have as-required medications charted for "death rattle" but less likely to have them for pain, nausea, or anxiety. Overall this study highlights the potential differences in palliative care needs between dying stroke and cancer patients and lends support to individualized approaches rather than assuming that one model of care will fit all. Crucially it also reinforces the importance of stroke service staff being appropriately educated and supported in the provision of general palliative care.

The considerable variability in symptom prevalence seen in the published literature is likely due to a range of factors including communication and consciousness impairment and inconsistent symptom assessment. Additionally accurate quantification of symptom burden for patients following an acute stroke is hampered at least in part by the fact that most studies addressing the question have been retrospective reviews of precollected data. Further prospective longitudinal research is required to expand the currently limited dataset addressing this question and to guide the development of appropriate interventions and approaches to meet the important needs of patients and their families.

2.4.4 End-of-Life Care and Dying Following Acute Stroke

The recognition or diagnosis of dying is complicated and largely arbitrary. Difficulties identifying the time point at which end-of-life care (EOLC) might be initiated are commonly reported by stroke care staff (Burton and Payne 2012; Gardiner et al. 2013; Cowey et al. 2015) leading to potential under- or overtreatment and delay in providing palliative and end-of-life care. A large contributor to this difficulty is the commonality between many of the features associated with dying and those seen in patients following a severe stroke who may subsequently recover. A range of factors have been used to identify dying stroke patients including stroke characteristics (including subtype and severity), clinical course (in particular the lack of meaningful recovery or ongoing deterioration), and physiological parameters (such as altered breathing patterns) (Cowey et al. 2015). In a study of patients who died in a stroke unit, disturbed consciousness, early dysphagia, and large supratentorial strokes were indications for initiation of EOLC (Alonso et al. 2016). In a separate mixed-methods study involving 23 Scottish stroke unit health professionals, over a quarter reported using intuition (at least in part) to recognize dying (Cowey et al. 2015).

The responsibility for decision-making regarding commencement of EOLC for hospitalized stroke patients has generally rested with the SCU medical team, although the importance of input and insight from other members of the multidisciplinary team cannot be underestimated. As we have seen due to the nature of stroke presentation and management, SPC services are infrequently and reactively involved in this process typically at times of increased complexity or significant uncertainty. Involvement of family members in decision-making around end-of-life care is important but not without its problems particularly if there is discordance between relatives and healthcare professionals (Rogers and Addington-Hall 2005). Feeding patients after a severe stroke has been highlighted as an area where motivations and opinions may differ between family members and staff. Rogers and Addington-Hall (2005) noted that while relatives and stroke unit staff shared the common motivation of wanting to avoid prolongation of suffering, stroke unit staff were also concerned about the patient starving or having their chance of recovery impinged due to lack of nutrition. Despite these difficulties family involvement allows a unique perspective on the patient and their place in the world and has been shown to be a predictor of high satisfaction with EOLC. As for all other areas of stroke care, the importance of clear, unambiguous, empathic, and effective communication cannot be overstated.

Two distinct patterns of dying following an acute stroke have been described, namely, a rapid, sudden death or prolonged dying. A prolonged dying phase can be particularly difficult for family members, and this is likely to be exacerbated if there was expectation of a quick death, they had not been informed of the possibility of prolonged dying, and in the setting of severe

dysphagia (Cowey et al. 2015). Not surprisingly the transition from recovery-focused care to EOLC can be challenging for family members with feelings of isolation and abandonment reported (Payne et al. 2010). However when death is considered likely, the most important things identified by relatives and stroke unit staff alike are the avoidance of distress and the maintenance of comfort and dignity (Rogers and Addington-Hall 2005; Payne et al. 2010).

End-of-life care (EOLC) pathways have been used to guide and optimize multidisciplinary, holistic care for dying patients and their families including following stroke. In this setting EOLC pathways aim to cover not only physical symptoms but also psychological, spiritual, and cultural considerations, desired place of care, and after-death management. The Liverpool Care Pathway (LCP) is an example of an EOLC pathway which has been used worldwide in both malignant and nonmalignant conditions. Recently the LCP has attracted considerable media attention and controversy in part due to concerns about its perceived overapplication at times, the inappropriate denial of nutrition and hydration in some cases, and deficits in communication with patients and families about its use. A subsequent UK government-commissioned independent review, while acknowledging the principles underpinning the LCP, expressed among a range of concerns that it was too frequently used as a "tick-box" exercise and recommended that it be progressively phased out and replaced by individualized care plans (Neuberger et al. 2013).

There is limited evidence addressing the use of EOLC pathways following severe stroke with available data seeming to be generally supportive of their use. The Australian Clinical Guidelines for Stroke Management in a small section devoted to palliative care include a recommendation that pathways for stroke palliative care can be used to improve the care of people dying following a stroke but acknowledge that evidence to support this recommendation is weak (National Stroke Foundation 2010). Very little is known about the quantitative impact of EOLC pathways on care parameters following severe stroke although improvements in both documentation and clinical practice were observed in a small retrospective audit pre- and post the implementation of the LCP on a 12-bed stroke unit (Jack et al. 2004). Examples of the changes in clinical practice seen included increases in the discontinuation of inappropriate medications (from 40% to 100%), in the charting of subcutaneous medications (from 20% to 85%), and in the assessment of religious needs. While these results appear promising, they need to be interpreted cautiously given the retrospective study design and small sample size.

Two qualitative studies have addressed the perceptions of healthcare professionals regarding the use of the LCP in English and Scottish stroke units (Gardiner et al. 2013; Cowey et al. 2015). In general satisfaction has been reported with its use, with staff in one study suggesting that the LCP was a core element of high-quality palliative care (Gardiner et al. 2013). Surveyed family members were also generally satisfied with LCP-based care although tended to be more concerned with adequate control of problems rather than whether an EOLC pathway was used (Cowey et al. 2015). Importantly family members were able to influence EOLC including when the LCP was used. This meant that management plans, including components such as the ongoing provision of parenteral hydration, were adapted to incorporate their wishes. This negotiated mutual pragmatism is perhaps what Neuberger and colleagues (2013) were envisaging when they recommended the replacement of the LCP with individualized care plans. Interestingly while both of these studies undertook their qualitative data collection prior to the 2013 independent LCP review, the paper by Cowey and colleagues (2015) was published subsequent to it. In their conclusions, the authors acknowledged the withdrawal of the LCP in the UK but noted that it continued to be used worldwide. They reiterated that in their study, family members were more concerned with distressing stroke-related problems than the LCP. In a succinct summary encapsulating the complexity of EOLC following stroke, they concluded that "such problems are enduring in nature and remain as clinical challenges whether end-of-life care pathways are used or not."

3 Palliative Care in the Post-Stroke Phase

The last couple of decades have seen emerging recognition of the role palliative care can play beyond end of life. Earlier involvement in advanced malignant disease, for example, has been demonstrated to lead to improvements in symptom burden, quality of life, and psychological well-being. Increased awareness of the substantive symptom burden and distress associated with a range of noncancer conditions, including chronic respiratory, renal, and neurological disorders, has highlighted the benefits of multidisciplinary palliative care in symptom management, complex decision-making, and care facilitation. In stroke while there is a developing evidence base for palliative care in the acute phase, the picture is much less clear for the post-stroke period. This is worthy of further consideration because as previously discussed the majority of patients will ultimately survive an acute stroke.

For those people who survive their initial stroke, the focus of most clinical programs and the literature has understandably been on secondary prevention and stroke rehabilitation. Accordingly there is comparatively little published data evaluating the involvement or potential role of palliative care services in post-stroke care. While data examining palliative care in this setting are limited, there is evidence of a range of often under-recognized symptoms and morbidity in patients, families, and caregivers following stroke.

The symptoms and issues experienced by patients and their caregivers in the chronic post-stroke phase will be familiar to many palliative care clinicians. They can include pain, depression, functional disability, seizures, bladder and bowel dysfunction, and caregiver stress/fatigue. While these symptoms are likely to share similarities with those seen in patients with cancer, end-organ failure, and/or neurological degenerative disorders, they may also display features unique to stroke. For example, the immediate onset of profound change in physical and cognitive function that often accompanies acute stroke contrasts with the subacute development of illness and disability in other malignant and nonmalignant conditions. Additionally the management of symptom burden in an environment where patient survival might be measured in years rather than weeks or months is outside the traditional skill set of many palliative care clinicians.

In some ways the chronic post-stroke period might be considered analogous to cancer survivorship as both may share features of ongoing symptoms in the context of likely long-term survival. The role of palliative care in cancer survivorship, while variable worldwide, remains relatively undefined, debatably appropriate, and influenced by a broad range of clinical and structural factors including limitations in clinician experience, workforce issues, and funding models. It seems likely that involvement in the post-stroke phase will provide palliative care, at both a clinician and organizational level, with similar challenges regarding clinical appropriateness and service provision.

3.1 Pain Syndromes

The most common types of pain reported in stroke survivors are central post-stroke pain, hemiplegic shoulder pain, painful spasticity, musculoskeletal pain, and tension-type headache (Creutzfeldt et al. 2012). Accurate pain assessment following stroke can be challenging due to the consequent communication deficits that may include dysphasia and dysarthria and/or changes in consciousness that occur in some stroke survivors.

3.1.1 Central Post-Stroke Pain

Central post-stroke pain (CPSP) is a neuropathic pain syndrome that is both highly distressing and frequently refractory to treatment. Sometimes referred to as Dejerine-Roussy syndrome, it was first described in 1906 (Vartiainen et al. 2016). There is variability in the reported rates of CPSP development among stroke survivors as well as concerns that it may be under-recognized. In an Italian population-based study which included 1494 post-stroke patients, symptoms and sensory changes consistent with CPSP were present in 11% of stroke survivors (Raffaeli et al. 2013). Other authors have reported prevalence rates of

between 3% and 8% when all stroke survivors are considered (Vartiainen et al. 2016) and up to 35% in those with specific thalamic lesions. While the pathogenesis of CPSP is not well established, postulated mechanisms for development include hyperexcitability of injured sensory networks, changes in central inhibitory mechanisms, or central nervous system neurotransmitter imbalances. The varying incidence and prevalence of CPSP is explained by the unclear etiology of this pain syndrome as well as the lack of universally accepted diagnostic criteria. The diagnosis of CPSP requires the exclusion of pain caused by joint contracture, peripheral nerve disorders, and spasticity.

The pain of CPSP may be spontaneous or evoked. Spontaneous pain can occur either continuously or intermittently, while evoked pain is typically precipitated by stimuli such as touch, movement, stress, or temperature change (Creutzfeldt et al. 2012; Vartiainen et al. 2016). Sensory abnormalities such as allodynia, dysesthesia, paresthesia, and hyperalgesia are common features (Creutzfeldt et al. 2012; Raffaeli et al. 2013). The pain is typically experienced within the area of sensory impairment and usually at the point of maximal deficit. Spinothalamic abnormalities such as temperature-sensory abnormality are frequently described. CPSP may develop at any time from immediately to years after a stroke; however onset most commonly occurs at 3–6 months (Raffaeli et al. 2013).

Management of CPSP is challenging as there is a paucity of evidence to guide practice. Optimal management is likely to be best achieved by utilizing a combination of pharmacological and non-pharmacological treatment approaches. A range of pharmacological agents have been trialed in the management of CPSP with a particular focus on antidepressants and anticonvulsants. The efficacy and tolerability of these agents has varied across trials. Amitriptyline at a final dose of 75 mg daily was associated with significant improvements in pain when compared to placebo in a small double-blind, placebo-controlled crossover study conducted in 15 nondepressed patients (Leigon and Boivie 1989). Importantly there was little in the way of adverse effect associated with amitriptyline. No statistically significant benefit was seen for carbamazepine (at doses of up to 800 mg/day) in the same study.

In terms of other agents, there is some evidence of benefit from both case series and a controlled trial for lamotrigine; however, there is limited evidence for gabapentin and none for opioids (Frese et al. 2006). The efficacy and safety of pregabalin in the management of CPSP was assessed in a double-blind, placebo-controlled randomized trial in 219 patients. The mean dose of pregabalin received was 356.8 mg, and after 13 weeks, pain had improved in both treatment arms (pregabalin baseline pain score 6.5, end-point pain score 4.9; placebo baseline pain score 6.3, end-point pain score 5.0); however there was no significant difference between the groups. Pregabalin was associated with improvements in sleep and anxiety in the study; however, more than 50% of patients in the pregabalin group reported some adverse effects (compared to 23% in the placebo group), with dizziness and somnolence being most common (Kim et al. 2011).

Non-pharmacological therapies including cognitive behavioral therapy and stimulation therapies including transcutaneous electrical nerve stimulation and acupuncture have been described in small case series; however, controlled trial evidence is lacking. Surgical pain therapies such as rhizotomy, sympathectomy, cordotomy, and deep brain stimulation have not been formally evaluated for the treatment of CPSP and should be considered only in the context of approved clinical trials.

3.1.2 Hemiplegic Shoulder Pain

Hemiplegic shoulder pain (HSP) is the most common post-stroke pain, occurring in 11–83% of patients (Creutzfeldt et al. 2012). The prevalence of HSP increases with worsening motor impairment. HSP occurs as a consequence of joint subluxation and sensory and motor deficits. Careful attention to joint positioning in hemiplegic patients and physical therapies are the mainstay of treatment, with some emerging data for intra-articular steroid injections and intramuscular injections of botulinum toxin-A. Analgesia with anti-inflammatory medications, paracetamol, and topical heat or ice and soft-tissue massage can also assist with initial pain management.

3.1.3 Spasticity and Musculoskeletal Pain

Pain due to contractures, pressure areas, and spasticity are best prevented through the use of physical and rehabilitative therapies, body positioning, and range of motion exercises. Baclofen and dantrolene are used for post-stroke spasticity; however, their side effects including sedation, confusion, and dizziness can limit their use. Botulinum toxin can be used, particularly in upper-limb spasticity, to improve functional outcome (Creutzfeldt et al. 2012).

3.2 Post-Stroke Depression

Depression is part of a constellation of neuropsychiatric disorders that are recognized to be associated with stroke. Estimates of the frequency of post-stroke depression (PSD) vary due to the heterogeneity of assessment and reporting approaches; however, a recent meta-analysis which included 61 studies and over 25,000 people found a frequency for PSD of 31% out to 5 years post stroke (Hackett and Pickles 2014). PSD onset can occur at any time following a stroke, with a prospective, longitudinal study of over 200 patients, observing rates of PSD to be relatively stable across a range of time points from 1 month to 18 months post stroke (De Ryck et al. 2014). Stroke severity and the resultant degree of physical and functional disability are the strongest predictors of post-stroke depression, with other recognized predictors including cognitive impairment, dysphasia and aphasia, apraxia, and premorbid history of depression or anxiety (De Ryck et al. 2014; Robinson and Jorge 2016). Evidence for the impact of social support and stroke lesion location upon PSD is conflicting; however, there are reports of association between left frontal and left basal ganglia lesions and PSD (Robinson and Jorge 2016).

Post-stroke depression is associated with increased mortality, poorer engagement in rehabilitation, decreased quality of life, and social isolation (Creutzfeldt et al. 2012; De Ryck et al. 2014; Robinson and Jorge 2016). An independent and direct association exists between depression severity and functional impairment although this relationship is likely to be reciprocal in many cases. The increased mortality associated with PSD has been reported to be due to greater cardiovascular mortality, with PSD associated disruptions in autonomic nervous system function postulated as a potential explanatory mechanism (Robinson and Jorge 2016).

A number of double-blind, placebo-controlled treatment trials for PSD have been undertaken using both tricyclic antidepressants and selective-serotonin uptake inhibitors (SSRI) since 1984 (Robinson and Jorge 2016). Although sample numbers were generally small across the trials, most reported improvements in depression scores when compared to placebo. A meta-analysis that included 17 trials (13 using pharmacological agents and 4 psychotherapy) and 1655 patients (Hackett et al. 2008) found that pharmacotherapy conferred a small but significant benefit in treating depression and reducing depressive symptoms; however, this was coupled with an increase in adverse effects. No evidence of benefit was demonstrated for psychotherapy; however, other studies have reported positive outcomes for brief psychosocial interventions (including psychoeducation and family support) when combined with antidepressants (Robinson and Jorge 2016). The impacts of antidepressant medications on physical and functional outcomes are less well described (Creutzfeldt et al. 2012); however, improvements in motor, cognitive, and functional capacity have been demonstrated (Robinson and Jorge 2016). There is emerging evidence that pharmacotherapy (in particular SSRIs) may have a preventative role in PSD as well as interesting data, suggesting antidepressants might improve stroke survival independent of either successful depression treatment or the presence of depression in the first place (Robinson and Jorge 2016).

3.3 Quality of Life

Of patients who survive 30 days following acute stroke, half will die within 5 years, and of the survivors, approximately 30% will remain disabled, with 14% requiring institutional care

(Hankey et al. 2002). Quality of life (QOL) while difficult to define and inherently subjective in nature is generally considered to be a multidimensional construct incorporating multiple broad domains including physical, social, and mental. Recognition of the potential impact of stroke upon QOL has seen the development of a number of stroke-specific health-related QOL scales in recent years. These scales include specific factors relevant to stroke patients including vision and language impairments, with examples being the Stroke Impact Scale and the Burden of Stroke Scale (Carod-Artal and Egido 2009).

A wide range of factors have been shown to impair QOL following stroke including dependency in activities of daily living (ADL), motor dysfunction, aphasia, presence of depression, CPSP, sexual dysfunction, and limited social supports (Carod-Artal et al. 2000; Choi-Kwon et al. 2006; Carod-Artal and Egido 2009). Reductions in QOL have been described by stroke survivors with differing levels of functional impairment from the profoundly disabled to those who regained independence in ADL function but did not get back to premorbid functional levels and in others who were not able to return to work. A Korean study that examined influences on QOL in 151 first-time stroke patients found that ADL dependency, CPSP, depression, and lower socioeconomic status were all important explanatory factors for lower QOL 3 years post stroke (Choi-Kwon et al. 2006). Although variation exists in the literature stroke type, lesion location, age, and gender have not consistently been associated with lower QOL (Choi-Kwon et al. 2006) although there is some evidence to suggest females have lower QOL following stroke than men (Carod-Artal et al. 2000; Carod-Artal and Egido 2009).

Importantly recognition of the negative influence of a broad range of factors upon QOL highlights the need for close attention to be paid to these things in the post-stroke period. In particular, vigilance when it comes to the assessment and treatment of depression and pain and rehabilitative efforts focused on maximizing functional outcomes and independence are crucial components in the preservation of QOL for patients following a stroke.

3.4 Caregiver Issues

While patients after stroke confront a myriad of issues, caregivers are also confronted with a new and often devastatingly different world. This is often exacerbated by the sudden onset of change which necessitates the rapid acquisition of new knowledge, skills, and acceptance of changed circumstances. This contrasts other more chronic illnesses where disease progression is typically gradual and predictable, allowing caregivers greater opportunity for adjustment and adaptation. Cognitive deficits including perceptual and language change along with motor deficits and functional dependency add additional complexity to the caregiver role. Additionally many caregivers are themselves elderly with their own health problems and often contracting social and support networks.

Worsening physical health, lower QOL, high levels of stress and mood disorder, social isolation, and financial burden have all been reported by stroke caregivers (van Heugten et al. 2006; Carod-Artal and Egido 2009). Anxiety and depression are common with rates of depression estimated to be upward of 25%. Given the recognized high levels of burden among stroke caregivers and the crucial role they play in supporting patients at home, increasing attention is being paid to assessing and managing stroke caregiver needs. Importantly despite the clear challenges that the caregiver role can bring, evidence suggests that many stroke caregivers still experience increased appreciation of life and role fulfillment.

A lack of attention to caregivers in established stroke guidelines prompted the development of evidence-based clinical practice guidelines specific to stroke caregivers in the Netherlands in the mid-2000s (van Heugten et al. 2006). These guidelines cover a range of topics including risk factors for caregiver burden, approaches to assessing burden, and possible caregiver interventions. Factors identified as predictive of increased caregiver burden include both patient characteristics (particularly limited functional capacity and significant cognitive impairment) and caregiver factors including preexisting psychological ill-health.

The impact of interventions upon stroke caregivers has been evaluated across a number of

studies with varying degrees of benefit reported. Interventions identified to provide at least some improvement in caregiver wellbeing include the provision of information, social and practical supports, training in the caregiver role, attention to mental health issues, and counseling (Kalra et al. 2004; van Heugten et al. 2006). Clinicians have a key role to play in preparing caregivers for their role. In retrospective surveys of bereaved caregivers, satisfaction with care following a stroke is positively correlated with involvement of doctors and nurses who are knowledgeable about stroke, clinicians being open to discussing fears and concerns, and caregivers being involving in decision-making processes (Young et al. 2009).

While after-stroke care largely focuses on secondary prevention and rehabilitation, it is clear that symptoms and complex care needs including pain syndromes, depression, impaired quality of life, functional impairment, and caregiver issues are highly prevalent following stroke. These are all things familiar to multidisciplinary palliative care clinicians, who accordingly are conceivably well positioned to address them utilizing expertise and experience drawn from other chronic diseases, as well as collaboration with colleagues from stroke and rehabilitation teams.

4 Conclusions/Summary

Despite significant advances in prevention, recognition, and treatment, stroke remains a major cause of morbidity and mortality worldwide. The value of integrating palliative care principles and practices into stroke management is being increasingly recognized particularly in relation to issues such as symptom management, complex decision-making, and establishment of goals of care. Ongoing research is required addressing not only these important patient and family needs but also the theoretical basis, clinical requirements, and departmental structures required for successful integration. In the acute phase, the majority of palliative care is currently and likely to continue to be undertaken by members of the stroke team with secondary support available from specialist palliative care services on an as-needed basis. Additionally specialist palliative care is ideally placed to provide the necessary education and guidance to ensure the provision of high-quality care.

The role of palliative care in the more chronic post-stroke phase is less clear with little published data addressing the question. There is clear evidence of significant symptom burden, reduced quality of life, and caregiver distress for patients and their families in this period, and these are all things familiar to multidisciplinary palliative care teams. In many ways palliative care clinicians are well placed to take a lead role in the management of many of these problems although their chronicity is likely to impose clinical, organizational, and workforce challenges upon the profession.

The ongoing success of the integration of palliative care and stroke services will be contingent on a number of factors, not least of which being buy-in from both specialties. For palliative care this will perhaps require a conscious shift away from the cancer-related models and ideologies of the past and an acknowledgement that adaption, conciliation, and collaboration will be crucial in moving forward. This is relevant not just for stroke but also other nonmalignant diseases and the ever-changing cancer landscape. In essence this is the challenge for modern palliative care and the next generation of specialists.

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Palliative Care in Heart Failure

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James M. Beattie and Jillian P. Riley

Contents

Abstract

Heart failure is a life limiting cardiovascular condition, frequently encountered in the increasingly aged population. People affected endure a symptomatic burden and mortality risk at least equivalent to those associated with common cancers. However, the clinical scenario is usually more complicated in that heart

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_60

failure tends to occur in multimorbid older individuals who exhibit an unpredictable disease trajectory. In most patients, cardiac function tends to decline inexorably, with a mortality of about 50% in the 5 years following diagnosis. An ever more complex evidence-based therapy, which likely materially benefits less than half of those with this clinical diagnosis, involves polypharmacy, implanted cardiac devices, and consideration for surgical intervention including cardiac transplantation. Acknowledging its prognostic ambiguity, the capricious nature of the heart failure state, and the relatively onerous treatment protocol may undermine care coordination, patient autonomy, and ultimately conflict with patients' and families' preferences for care along a progressively declining clinical course to the end of life. This chapter describes the challenges and opportunities in providing palliative care to this burgeoning clinical population.

1 Introduction

Heart failure is a common clinical and public health problem which occurs in epidemic proportions. Currently, about 38 million people suffer with heart failure worldwide, of whom approximately 6.5 million are affected in the United States, where there is an anticipated 46% increase in prevalence by 2030 (Roger 2013; Braunwald 2015; Benjamin et al. 2017). Heart failure accounts for a significant proportion of healthcare expenditure, and for 2012, the global economic burden of heart failure was estimated at nearly US$108 billion in direct and indirect costs (Cook et al. 2014). From the age of 45 years through to 95 years, the lifetime risk of heart failure is high, ranging from 20% to 45% depending on a spectrum of demographic, lifestyle, and cardiovascular risk factors (Huffman et al. 2013). Heart failure tends to occur in older individuals, being diagnosed in 1–2% of the general population, but rising to about 8% in people aged 80 years or more (Guha and McDonagh 2013). For males, the incidence of heart failure doubles for each decade between 65 and 85 years, while for females the incidence trebles over the same periods (Benjamin et al. 2017). Given the changing demography with a trend towards an aging population, the incidence of heart failure is now similar to that of breast, bowel, prostate, and lung cancers combined (Conrad et al. 2017). Despite our best efforts to address the needs of this increasingly dependent clinical cohort, heart failure remains a generally progressive condition and affected individuals are subject to a symptom burden, a poor quality of life, and a mortality risk at least equivalent to those resulting from the above cancers. Recognition of the comparable palliative care needs and the resulting literature base accruing over the past 20 years, it is evident that heart failure has been in the vanguard of the expansion of palliative care beyond its founding association with oncologic care. A suite of consensus documents and guidelines have been produced, but delivery of palliative care to the increasingly complex population diagnosed with this unpredictable clinical condition remains problematic (Goodlin et al. 2004: Jaarsma et al. 2009; McKelvie et al. 2011; Braun et al. 2016).

2 The Nature of Heart Failure

Forty years ago, Dr. Dean Mason, then chief of cardiovascular medicine at the University of California, Davis, penned a classic description of heart failure as "*the abnormal condition in which disturbed cardiac performance is primarily responsible for the inability of the heart to pump blood at a rate commensurate with systemic metabolic requirements at rest and during normal activity*" (Mason 1976). It is important to note that heart failure is not a disease per se but rather a group of acute and chronic syndromes arising from abnormalities of cardiac structure and function, representing the outcome of a diverse range of acquired or inherited cardiovascular diseases (Ponikowski et al. 2016). Given that these various etiologies result in a spectrum of disordered left ventricular physiology and remodeling, it is unsurprising that the clinical features of heart failure occur in the setting of both systolic and diastolic dysfunction.

The American College of Cardiology Foundation (ACCF), the American Heart Association (AHA), and the European Society of Cardiology (ESC) have characterized heart failure in terms of a constellation of classic symptoms and clinical signs, combined with objective assessment of ventricular function (Yancy et al. 2013; Ponikowski et al. 2016). The recent ESC guidelines have proposed a terminology describing left ventricular dysfunction with respect to the left ventricular ejection fraction (EF), that percentage volume of the blood pool within the relaxed ventricle ejected during each cardiac contraction. This is usually assessed by echocardiography or some other form of cardiac imaging. The most recent guidelines from the American Society of Echocardiography and European Association of Cardiovascular Imaging suggest that the EF should be considered abnormal if $\leq$52% for men and $\leq$54% for women (Lang et al. 2015). By the ESC criteria, symptomatic patients are said to exhibit heart failure with a reduced EF (HFrEF) when the left ventricular EF is less than 40%, commonly reflecting a background of coronary artery disease with segmental myocardial damage and eccentric remodeling.

Heart failure with a preserved EF (HFpEF) is said to apply when the EF is at least 50%. These patients predominantly exhibit diastolic dysfunction with impaired ventricular filling. In this situation, myocardial changes arise from a pro-inflammatory state linked to the commonly occurring comorbidities in obesity, diabetes mellitus, and hypertension (Paulus and Tschöpe 2013). Even in the absence of left ventricular hypertrophy, HFpEF patients may exhibit increased left ventricular mass resulting from an excess of collagen deposition in the extracellular matrix. Intrinsic cardiomyocyte stiffness might also stem from changes in the cytoskeletal protein titin, as well as slow myocyte relaxation due to impaired cross-bridge detachment and sarcoplasmic reticular Ca^{2+} reuptake (Borlaug and Paulus 2011). An intermediate group of patients has also been defined with a mid-range EF between 40% and 49% (HFmrEF) in which the heart failure state reflects a combination of systolic and diastolic dysfunction.

Table 1 The New York Heart Association classification

NYHA Functional Class	Patient symptoms
I	Objective evidence of ventricular dysfunction but no limitation of ordinary physical activity or induction of symptoms
II	Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, dyspnea, or palpitation
III	Significant limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, dyspnea, or palpitation
IV	Unable to undertake any physical activity without discomfort. Symptoms of heart failure at rest

Table 2 The American College of Cardiology Foundation/American Heart Association stages of heart failure

ACCF/AHA Heart failure stage	Objective assessment
A	Risk factors but no objective evidence of established cardiovascular disease. No symptoms and no limitation of physical activity
B	Objective evidence of structural cardiac disease without signs or symptoms of heart failure
C	Objective evidence of structural heart disease with current or prior symptoms of heart failure
D	Refractory/advanced heart failure requiring consideration for specialized intervention

The long established New York Heart Association (NYHA) functional classification (Classes 1 to 4) and the ACCF/AHA heart failure staging system (Stages A to D) offer helpful complementary information in categorizing the impact and severity of heart failure at a given time (The Criteria Committee of the NYHA 1994; Hunt et al. 2001) (Tables 1 and 2). The former offers insight into the achievable level of exercise before symptom onset, and while this classification has been criticized as being relatively subjective and prone to inter-observer variation (Raphael et al. 2007), this metric of functional

capacity remains useful and has the benefit of familiarity for many clinicians. The latter emphasizes the progressive nature of heart failure and aids in the selection of appropriate treatment options pertinent to the individual patient's heart failure stage and their changing needs.

Over the past 25 years or so, we have gained a significant understanding of the pathophysiology of heart failure, particularly in relation to HFrEF. Following an insult to cardiac function, a variety of compensatory cardiac and neurohumoral mechanisms come into play in an effort to maintain cardiac output and critical organ perfusion. These include an increase in vascular tone secondary to augmented sympathetic adrenergic activity, as well as activation of the renin-angiotensin aldosterone system (RAAS) and the release of cytokines such as interleukins and tumor necrosis factors. Responses to alterations in ventricular loading conditions are consistent with the Frank-Starling relationship. While initially protective, these various physiological responses ultimately become maladaptive and tend to promote progressive multisystem dysfunction and a spiral of decline. Elucidation of the background to this integrated cardiovascular adaptation has generated a series of landmark studies with a resultant raft of evidence-based pharmacological therapies.

Alongside these, protocols have been developed to further optimize treatment with the use of implanted electronic devices in the form of complex pacemakers as cardiac resynchronization therapy (CRT) to improve the efficiency of ventricular contraction and implantable cardioverter-defibrillator (ICDs) to reduce the risk of sudden death from malignant arrhythmias. Surgical strategies have also evolved for those with advanced HFrEF, including the use of mechanical circulatory support (MCS) in the placement of left ventricular assist devices (LVADs) as a bridge to recovery or cardiac transplantation, or long term as so-called destination therapy. The benefits of such a multifaceted approach to this life limiting condition are well established, and this is now enshrined in HFrEF treatment guidelines (National Heart Foundation of Australia 2011; Yancy et al. 2013; Ponikowski et al. 2016). In contrast, the complex mechanisms underlying the predominant diastolic dysfunction typical of those with HFpEF are only just coming to light and effective therapies to specifically modulate these are yet to emerge (Borlaug and Paulus 2011; Ponikowski et al. 2016).

In the clinical cohort exhibiting features of heart failure, 80–90% likely have HFrEF or HFpEF which are relatively evenly represented, the residual 10–20% being made up of those with HFmrEF (Lam and Solomon 2014). HFpEF is more common in the oldest old, and secular trends in age-related heart failure variants suggest that HFpEF may become the predominant clinical phenotype. It is also uncertain if the potential benefits of evidence-based HFrEF therapy are generalizable to those affected in the growing elderly population as this group was largely excluded from the pivotal clinical trials (Rich et al. 2016).

3 Health Burden of Heart Failure

Heart failure is the most common admission diagnosis in those aged 65 years or older in high income nations (Braunwald 2015). According to the National Heart Failure Audit in England and Wales, following hospital admission with acute heart failure, the projected 1-year mortality of those below and above 75 years of age has been estimated at 26% and 56%, respectively (Cleland et al. 2011). Analysis of data from the Olmsted County Registry on 4596 patients with chronic heart failure tracked by the Mayo Clinic suggested similar 1-year and 5-year mortality rates at 32% vs. 28% and 68% vs. 65% for HFrEF and HFpEF, respectively, using an EF of 50% as the cut point (Owan et al. 2006). Comparing modes of death, for both of these clinical subtypes, a cardiovascular cause predominates, manifest as refractory congestive heart failure or sudden cardiac death, but proportionately more of the HFpEF population die of non-cardiovascular comorbidities (Chan and Lam 2013).

4 Comorbidities

Given the typically elderly population affected by heart failure, many patients exhibit several comorbidities including frailty, cognitive impairment, anemia, diabetes, chronic obstructive pulmonary disease (COPD), renal dysfunction, and depression/anxiety (van Deursen et al. 2014). Some of these are discussed in more detail below. The Charlson Comorbidity Index may have limited prognostic utility in the chronic heart failure population, and evidence on how to manage comorbidities at the end of life is limited (Testa et al. 2009; Tevendale and Baxter 2011).

4.1 Frailty

In recent years, frailty has been increasingly recognized in those with heart failure and associated with greater symptom burden and poor outcomes such as increased rates of hospitalization and mortality (Chaudhry et al. 2013; Jha et al. 2015; Denfeld et al. 2018). This complex syndrome has been variously attributed to a specific age-related biological phenotype including sarcopenia, or alternatively, to the effects of composite physiologic deficits resulting in diminished reserve and increased vulnerability to stressors (Fried et al. 2001; Jermyn and Patel 2015). Significantly affected patients often struggle with mobility and the activities of daily living which can impact on self-care behaviors affecting nutrition and hydration, sometimes manifest as falls and delirium. While no frailty assessment instrument has been validated specifically for the heart failure population (McDonagh et al. 2018), evaluation tends to be focused on the five domains of the Fried Frailty Index: self-reported exhaustion, physical activity, walking speed, hand grip strength, and unintentional weight loss; parameters initially assessed in the Cardiovascular Health Study (Fried et al. 1991). Based on this model, a recent study of patients with advanced heart failure demonstrated that 65% of them were frail and 35% were prefrail (Madan et al. 2016).

4.2 Cognitive Impairment

Cognitive impairment is relatively common in those with heart failure, the reported prevalence varying between 25% and 75% by a range of assessments across diverse studies, and estimated to be about 40% overall in a recent meta-analysis (Ampadu and Morley 2015; Cannon et al. 2017). Both HFrEF and HFpEF patients may develop this (Alagiakrishnan et al. 2016). The spectrum of cognitive dysfunction is similar to that seen in non-heart failure patients and includes agitated delirium, as well as isolated memory or non-memory deficits through to dementia. The risk factors for cognitive impairment are similar for those with or without heart failure, and while we must be aware of the potential secondary effects of heart failure therapy on cerebral perfusion, to date no causal relationship to specific treatment has been identified. However, neprilysin is involved in clearing amyloid peptides from cerebral tissue. Theoretically, following the positive results of the PARADIGM HF trial, use of the recently licensed angiotensin receptor neprilysin inhibitor sacubitril/valsartan (Entresto®) might interfere with this (Cannon et al. 2017). Two clinical trials currently in progress may clarify this potential risk [ClinicalTrials.gov identifiers: NCT01920711, NCT02884206]. The presence of atrial fibrillation, whether permanent or paroxysmal, is strongly linked to cognitive decline, even when there is no evidence of a major stroke or imaging features characteristic of cerebral microembolic disease (Ampadu and Morley 2015). The effects of cognitive impairment may impact self-care decision making and are associated with a greater use of healthcare resources, higher rates of hospital readmission, and mortality (Riley and Arslanian-Engoren 2013; Alagiakrishnan et al. 2016).

4.3 Anemia and Iron Deficiency

Anemia, conventionally characterized as a hemoglobin of less than 13 g/dL and 12 g/dL for men and women, respectively, is relatively common in heart failure. However, even in the absence of

clinically overt anemia, heart failure is associated with both absolute and functional iron deficiency (McDonagh and Macdougall 2015). Absolute iron deficiency occurs when iron stores are low, generally defined as a serum ferritin level below 100 ng/ml. This may occur as a consequence of nutritional deficiency, poor iron absorption through a congested gastrointestinal mucosa, or blood loss due to the effects of antiplatelet or anticoagulant therapy. In functional iron deficiency, typically defined as a serum ferritin greater than 200 ng/ml with a transferrin saturation (TSAT) below 20%, iron stores are replete, but iron utilization is insufficient to drive adequate erythropoiesis or normal cellular metabolism. This is often mediated by the response of hepcidin, a polypeptide and key regulator of iron metabolism. Hepcidin controls intestinal iron absorption, serum iron concentrations, and cellular iron distribution by inducing degradation of its receptor, the cellular iron exporter ferroportin (Ganz and Nemeth 2012). In the early phase of heart failure, the active inflammatory state results in high levels of hepcidin which may "trap" iron in macrophages and hepatocytes (McDonagh and Macdougall 2015). However, as heart failure progresses, hepcidin levels decline with impaired iron homeostasis and resultant anemia (Jankowska et al. 2013). Iron deficiency has been shown to occur in all heart failure variants (HFrEF, HFmrEF, and HFpEF) and is associated with poor quality of life and outcomes (Martens et al. 2017). Effective therapy is now available as intravenous ferric carboxymaltose as proposed in the ESC guidelines (Ponikowski et al. 2016). Although the mechanisms are different, iron deficiency may also arise in chronic kidney disease (CKD), a common comorbidity in those with heart failure.

4.4 Renal Dysfunction

Heart and kidney function are mutually interdependent. Cardiovascular physiology relies on the maintenance of salt and water balance by the kidney, and kidney function depends on adequate blood pressure and renal perfusion provided by the heart. Both organ systems share common risk factors and disturbances of pressure and volume homeostasis are typical of both acute and chronic heart failure (Boudoulas et al. 2017). The intimate relationship between cardiac and kidney function has seen evolution of the concept of the so-called *cardiorenal syndrome* which has been subclassified as occurring as five variants (Table 3). The pathophysiological mechanisms underlying this complex interplay remain incompletely understood but may be broadly summarized as relating to:

- Hemodynamic changes due to low cardiac output and deranged venous return
- Dysregulation of the neurohumoral axis with enhanced sympathetic drive and triggering of the RAAS system
- Other factors affecting heart and kidney function such as oxidative stress due to sepsis, inflammation, anemia, and cachexia

CKD, defined as a glomerular filtration rate (GFR) persistently less than 60 ml/min/1.73m^2, is demonstrable in 40–50% of heart failure patients (Schefold et al. 2016). This is an independent risk factor for cardiovascular disease including heart failure and for heart failure progression. For those with HFrEF, a declining GFR is a more powerful predictor of mortality than the EF. While a transient reduction in GFR is commonly observed after initiation of angiotensin converting enzyme inhibitor (ACEI) therapy or angiotensin receptor blockers (ARBs), this usually recovers. However, the presence of CKD often worries

Table 3 Variants of the cardiorenal syndrome. (Modified from Boudoulas et al. 2017)

Type	Cardiorenal syndromes
1	Acute heart failure or decompensation of chronic heart failure resulting in acute kidney injury or dysfunction
2	Chronic heart failure resulting in CKD
3	Acute decompensation of renal function inducing acute heart failure
4	CKD producing chronic heart failure
5	A variety of other conditions secondarily impacting heart and kidney function

clinicians and inhibits the optimal prescription of evidence-based heart failure therapy, including that for those on renal replacement therapy as hemodialysis. The adverse cardiovascular effects of long-term hemodialysis are well established, and while renal transplantation was previously considered contraindicated in those with significant HFrEF, this has now been shown to be beneficial. Indeed this intervention may promote recovery of ventricular function (Kute et al. 2014).

4.5 Depression and Anxiety

Depression appears to be relatively common being present in at least 1 in 5 of the clinical cohort with heart failure and may be proportionately greater in those with more advanced disease. This comorbidity is associated with increased healthcare utilization, and higher readmission rates and mortality (Moraska et al. 2013). In one study of 985 patients assessed by the Beck Depression Inventory Scale during their index heart failure admission and followed over a 12-year period, the mortality was 80% for those with depression against 73% for those without (Adams et al. 2012). Anxiety is said to be 60% more frequent in those with heart failure compared to the general population, and rates are considered at least comparable or possibly greater than those with cancer and pulmonary disease depending on the method of assessment. The effect of anxiety on outcomes is less certain than for depression (Sokoreli et al. 2016), but clearly these conditions frequently co-exist. Postulated mechanisms relevant to outcomes include both health behavioral and biological effects. Depression may result in poor adherence to heart failure medication, or anxiety-related sympathetic hyperactivity may reduce the threshold for significant arrhythmia, induce coronary vasospasm and ischemia, or promote a pro-thrombotic effect (Fan et al. 2014). Safe and effective treatments for depression in heart failure are available, either in the form of cognitive behavioral therapy or with the use of drugs such as selective serotonin reuptake inhibitors (Rustad et al. 2013).

5 The Heart Failure Disease Trajectory

Heart failure patients tend to deteriorate along a roller coaster disease trajectory of progressively declining physical capacity interspersed with distressing clinical crises (Fig. 1) (Goodlin et al. 2004). These inflection points may be markers of further cardiac events leading to incremental ventricular dysfunction, life-threatening episodes of acute decompensation, or arrhythmia. Although potentially lethal arrhythmias may occur at any stage along the course of the disease, these are more frequent in the earlier, milder phase of HfrEF, particularly when there is a background of coronary artery disease resulting in patchy scarring and electrophysiological instability. Notwithstanding the absence of an ICD, rates of sudden death have declined over the past 20 years or so consistent with a beneficial response to use of the evidence-based medication developed over that period (Fig. 2) (Udelson and Stevenson 2016; Shen et al. 2017). In advanced heart failure, the usual mode of death is through congestion and irreversible multiorgan failure, the terminal phase often preceded by a cluster of unplanned hospital admissions (Udelson and Stevenson 2016). Despite this, those close to the patient often perceive the death as unexpected. This may reflect a lack of appreciation of the nature and significance of this condition (Alonso et al. 2017), or inadequate communication between health care professionals, patients, and their families (Russ and Kaufman 2005; Allen et al. 2012). It is important to emphasize that while the schematic illness trajectory shown in Fig. 1 is a reasonable representation of clinical reality on a population basis, the pattern of decline and response to treatment is unique to each individual (Fig. 3) (Gott et al. 2007).

The fluctuating, inconsistent disease course and resultant uncertainty also constitute a barrier to discussion on end of life care as heart failure professionals find it difficult to discern specific transition points when this might be appropriate (Barclay et al. 2011). Having recovered from earlier high risk episodes, patients tend to overestimate life expectancy and assume they will

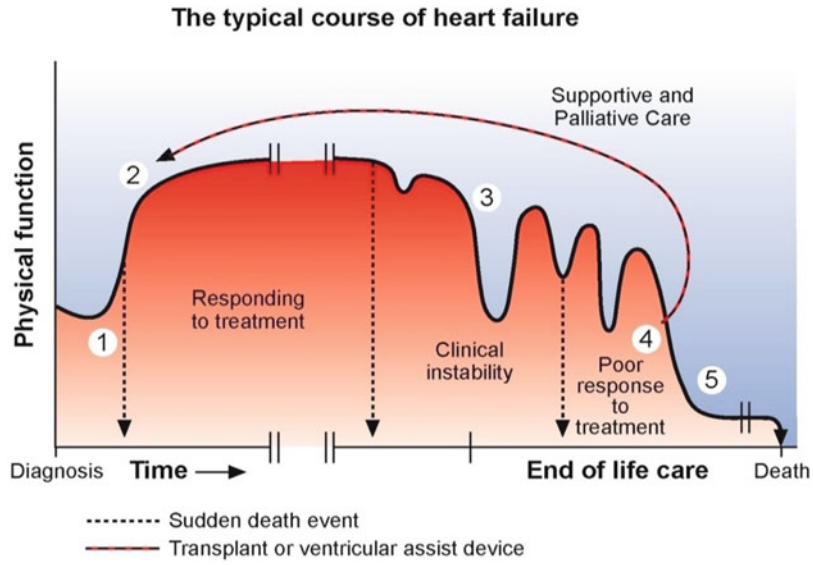

Fig. 1 A schematic of the heart failure disease trajectory (Modified from Goodlin et al. (2004) with permission)

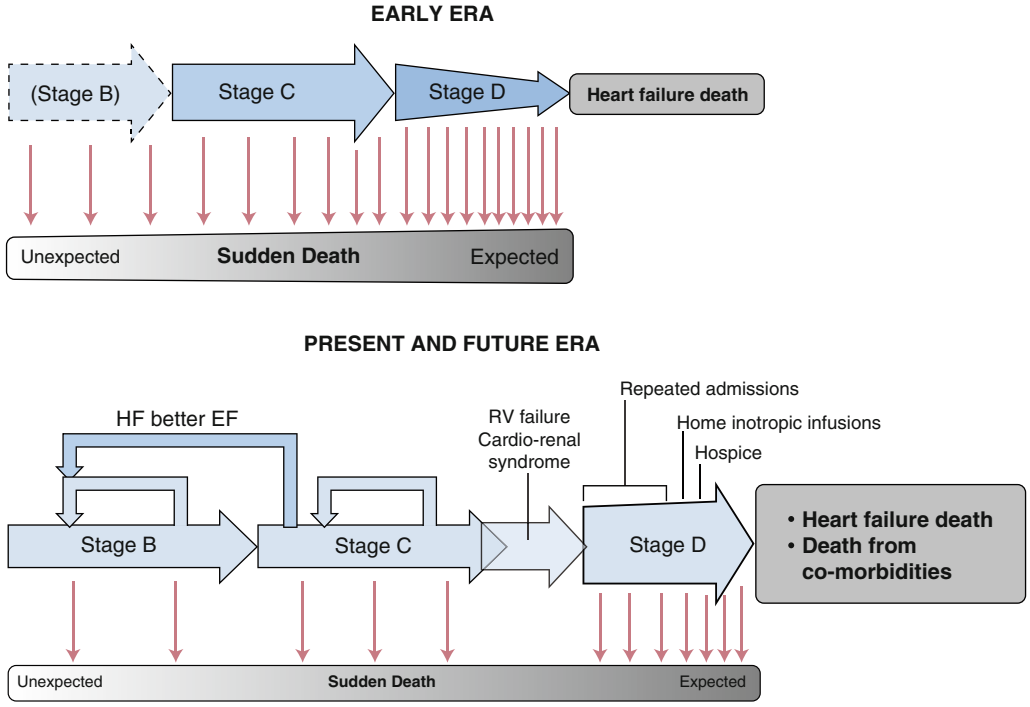

Fig. 2 The changing face of heart failure outcomes across the development of evidence-based heart failure therapy (From Udelson and Stevenson (2016) with permission)

survive against all the odds (Allen et al. 2008). While this intrinsic unpredictability needs to be acknowledged by the healthcare team, hope for the future should be maintained in fostering coping and adjustment strategies to deal with changing circumstances (Davidson et al. 2007). Themes important to those living with the uncertainty of chronic advanced illnesses, including

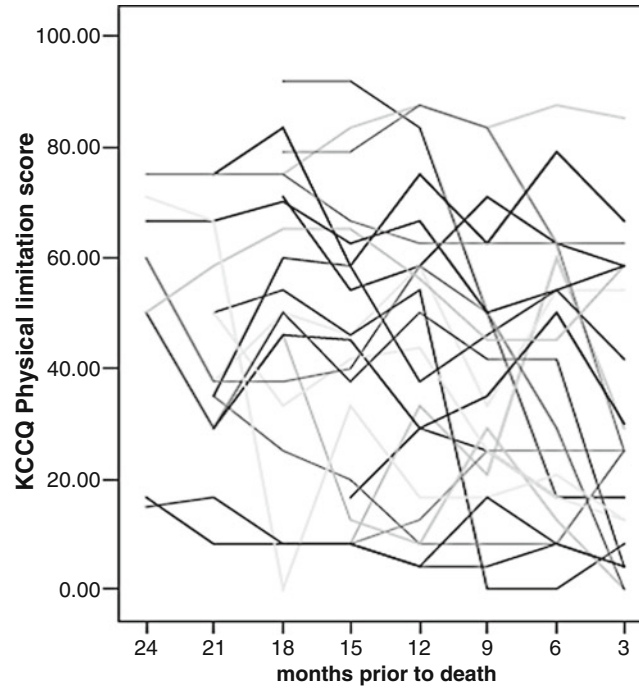

Fig. 3 The uniqueness of individual heart failure patients' disease trajectories (From Gott et al. (2007) with permission)

heart failure, have been evaluated (Etkind et al. 2017). These were shown to include their degree of engagement or control over the illness, temporal focus on the present and future, factors relating to communication, information needs and preferences, and a variety of priorities including quality of life, social factors, and concern about potential conflict between themselves and the health professionals responsible for their care.

6 Prognostication

Regardless of advances in cardiovascular therapy, heart failure in all its forms constitutes an increasingly encountered life limiting condition; about 50% of those diagnosed with heart failure die within 5 years of diagnosis (Gerber et al. 2015). Heart failure is documented on 1 in 8 death certificates in the United States (Benjamin et al. 2017). As outlined in a recent review, a variety of prognostic tools have been utilized in the assessment of survival in heart failure (Treece et al. 2017). Despite acknowledgment of subjectivity, functional assessment by the NYHA classification has been accepted as a strong prognostic indicator for both HFrEF and HFpEF (Raphael et al. 2007). In a study in England of 293 heart failure patients who self-assigned their NYHA class, subsequent mortality over 6–20 months was 19.6% for classes I/II, 34.3% for class III, and 39.2% for class IV (Holland et al. 2010).

The CardioVascular Medicine Heart Failure Index incorporates NYHA Class III/IV alongside 12 other variables related to cardiac conditions and comorbidities to stratify patients, treated across a variety of care settings, into low-, medium-, and high-risk for a 12-month mortality (Senni et al. 2006). The other variables include age, anemia, hypertension, COPD, complicated diabetes, moderate/severe CKD, metastatic cancer, absence of β-blocker, ACEI or ARB therapy, EF less $\leq$20%, and the presence of severe valvular heart disease or atrial fibrillation. A similar multivariate approach was adopted in the development of the Heart Failure Survival Score which uses 80 clinical attributes to characterize mortality risk, validated in a clinical cohort with advanced heart failure referred in consideration for heart transplantation (Aaronson et al. 1997).

The most widely used scoring system is the Seattle Heart Failure Model, developed by the

University of Washington, and validated in a cohort predominantly exhibiting HFrEF (Levy et al. 2006). This model, applicable to both ambulatory and hospitalized patients, is based on readily accessible clinical, laboratory, pharmacological, and device features and has been regularly updated to accommodate developments in heart failure therapy. More recently, a robust heart failure mortality risk assessment tool has been elaborated by the Meta-Analysis Global Group in Chronic Heart failure (MAGGIC) (Pocock et al. 2013). This is founded on 13 independent predictors derived from data collated from over 39,000 patients with HFrEF or HFpEF across 30 cohort studies comprising 6 clinical trials and 24 registries. The MAGGIC model is available via www.heartfailurerisk.org. While potentially useful on a population basis (Sartipy et al. 2014), this and the Seattle Heart Failure Model have not been specifically validated for the advanced heart failure population, and neither appear to be particularly reliable in predicting 12-month mortality for individual patients (Allen et al. 2017).

7 Palliative Care Needs Assessment

Acknowledging the underlying prognostic difficulties, and recognizing that those affected by heart failure are subject to a mortality risk and symptom burden at least equivalent to those with cancer (Xu et al. 2015), it is arguable that support should be offered at any point along the disease trajectory based on palliative care needs, rather than life-expectancy (Hogg and Jenkins 2012; Meyers and Goodlin 2016; Lewin et al. 2017). However, given the clinical complexity of the affected population and the ethos of the medical model in providing comprehensive guideline-directed heart failure therapy, of itself sometimes onerous (Jani et al. 2013), knowing when to trigger such palliative care involvement is difficult.

While potentially helpful in raising awareness, use of the "Surprise Question" – "*Would I be surprised if this patient died in the next 12 months*" – appears to offer little advantage when used alone in identifying heart failure patients who may benefit from palliative care (Small et al. 2010; White et al. 2017). Needs assessment involves comprehensive evaluation of symptom burden and functional status (Opasich et al. 2008). To some extent reflecting NYHA status, the Kansas City Cardiomyopathy Questionnaire (KCCQ) and the Minnesota Living with Heart Failure Questionnaire (MLHFQ) offer wide-ranging evaluation of heart failure-related physical and psychological symptoms, performance status, and health-related quality of life (Rector et al. 1987; Green et al. 2000). The KCCQ comprises a 21-item self-administered instrument which facilitates derivation of a summary score across domains of physical function, symptoms (frequency, severity, recent trends), social function, self-efficacy, knowledge, and quality of life. The higher summary score, the better the health status. The widely used MLHFQ is based on a psychometrically validated 21-item questionnaire covering the effects of heart failure on key elements of the physical, emotional, social, and psychological dimensions of quality of life. For each of the 21 variables, patients complete a 6-point Likert scale (0–5), indicating by how much heart failure impacts on living as they would wish. A lower score correlates with a better quality of life. The MLHFQ is available in many languages, validated against the original, and is curated by the Mapi Research Trust (www.mapi-trust.org).

A series of studies have demonstrated a moderate correlation between these heart failure instruments and palliative care assessment tools including the Karnofsky Performance Status Scale, the Palliative Performance Scale and the Edmonton Symptom Assessment Scale, but also suggest that combining these approaches might be useful in clarifying unmet palliative care needs (Opasich et al. 2008; Ezekowitz et al. 2011; Timmons et al. 2013; Johnson et al. 2014). Use of the Integrated Palliative care Outcomes Scale (IPOS) combined with specialist heart failure nurse education and training has been shown to be feasible and acceptable to patients exhibiting any of the heart failure phenotypes as HFrEF, HFmrEF, or HFpEF, as well as to their responsible health professionals (Kane et al. 2017). Similarly, an instrument specific to heart failure, the Needs

Assessment Tool: Progressive Disease – Heart Failure (NAT: PD – HF), developed in Australia, shows promise and is currently being piloted in Scotland (Waller et al. 2013; Campbell et al. 2015). In contrast, a recent review suggests that the RADboud indicators for PAlliative Care needs (RADPAC) and the NECesidades PALiativas (NECPAL), tools developed in the Netherlands and Spain, respectively, to assess the palliative care needs in those with chronic diseases, may have limited utility in those with heart failure (Thoonsen et al. 2012; Gómez-Batiste et al. 2013; Janssen et al. 2017). Palliative care needs assessment is particularly relevant to some increasingly used forms of heart failure therapy.

8 Implantable Cardioverter-Defibrillators

Since their first deployment in humans in 1980, implantable cardioverter-defibrillator (ICD) technology has been significantly refined and their use has increased exponentially in recent years (Hindricks et al. 2017; Benjamin et al. 2017). There is unequivocal evidence of their benefit in the primary or secondary prevention of sudden cardiac death in individuals deemed to be at risk from malignant ventricular arrhythmias (Russo et al. 2013; Epstein et al. 2013). These may be used as standalone ICDs or combined with cardiac resynchronization therapy (CRT-D) in appropriately selected patients with HFrEF (Yancy et al. 2013). In continuously monitoring cardiac rhythm, they offer a number of key responses:

- Automatic administration of defibrillation shocks to terminate ventricular fibrillation or fast ventricular tachycardia (VT)
- Antibradycardia pacing, often activated after a defibrillator shock as the heart transitions to normal rhythm
- Antitachycardia pacing to terminate slower VT
- Cardioversion of VT

Risks affecting quality of life sometimes accompany the benefits of these devices (Atwater and Daubert 2012). While ICD function offers no intrinsic symptomatic advantage, the discomfort associated with shock delivery, likened to being punched in the chest or kicked by a horse, or the anxiety engendered by shock anticipation, may be acceptable trade-offs in clinical scenarios when life extension is the primary goal. However, close to the end of life, when the patient is dying of progressive heart failure or an unrelated disease, futile ICD shocks constitute a painful and avoidable harm. The metabolic and biochemical derangement typical of this terminal phase may trigger arrhythmias and device activity, and such occurrences are well documented. An early study, based on experiences of bereaved families, reported that 20% of ICD patients received shocks as they were dying, and if device deactivation took place at all, this was only in a minority and very close to the point of death (Goldstein et al. 2004). In a more recent study, postmortem interrogation of explanted devices demonstrated that a third of decedents were subjected to a shock on their last day alive, often within an hour of death (Kinch Westerdahl et al. 2014). While more than half of these patients had a "Do not resuscitate" order in place, in about two-thirds of this group, the defibrillation mode of the device was still active at the time of death.

Clinical practice guidelines propose that discussion on the possibility of later device deactivation should be broached at the time of informed consent for the de novo ICD implant, and that this aspect of care should be revisited at intervals, particularly when considering device replacement due to generator battery depletion (Lewis et al. 2016). However, in real life clinical practice, these discussions are infrequent (Clark et al. 2011; Niewald et al. 2013; Hill et al. 2016). In contrast, by defaulting to a guideline-directed treatment protocol, cognitive bias has been demonstrated in that clinicians undertaking discussions before such procedures tend to over emphasize the benefits of initiating or maintaining ICD therapy (Hauptman et al. 2013; Matlock et al. 2017). A positive spin is also evident in educational materials relating to ICDs, some of which emanate from the device industry (Strachan et al. 2012). Given the framing effects evident in this information exchange, patients tend to regard the decision

on ICD therapy as binary in life or death and do not seem to recall being offered alternatives to the primary implant or the option to decline device replacement (Agård et al. 2007; Carroll et al. 2013a). Data from the United States National ICD Registry have shown that 42% of new ICDs were implanted in those aged over 70 years and 12% in those more than 80 years, yet 51% of people receiving an ICD after the age of 65 years were either dead or in hospice 5 years after implantation (Wright et al. 2013; Kramer et al. 2016). Thus, for many, particularly the relatively elderly multimorbid heart failure patients, the benefits of ICD therapy are uncertain (Kaufman et al. 2011; Barra et al. 2015; Green et al. 2016; Rich et al. 2016). As highlighted at a recently convened Hartford Change Agents Symposium (Kramer et al. 2015), a more nuanced and values-based approach is required to ensure that treatment decisions are aligned with patient preferences for care and mode of death (Joyce et al. 2013). As such preferences are prone to change (Brunner-La Rocca et al. 2012), this discourse needs to be an iterative process rather than at a single point along the individual patient's disease trajectory.

Undertaking these difficult conversations can be uncomfortable for both patients and clinicians. Perhaps linked to the anchoring heuristic set at earlier discussions in consideration of ICD therapy, patients tend to overestimate the expected benefit derived from the device, and sometimes regard the notion of deactivation as akin to an act of suicide (Goldstein et al. 2008a; Stewart et al. 2010). When proposing this intervention, ideally prior to implantation as part of the informed consent process, it would be appropriate to highlight that the perceived benefits of ICD therapy are to some extent conditional, and should be subject to review in the face of disease progression, changes in attitude to device acceptability, or other circumstances. Impartial education should be provided to ICD eligible patients and their families (Dunbar et al. 2012). While some are in development, robust decision tools to facilitate this dialogue are not yet available (Clark et al. 2012; Carroll et al. 2013b). A group at the University of Colorado, Denver, are undertaking a pilot study of ICD patient decision aids [Clinical.Trials.org identifier: NCT02026102], and through the Colorado Program for Patient Centered Decisions, have developed a web-based informational/decision support tool for patients and their families considering an ICD as primary prevention (University of Colorado 2016). It is important to include family members in this process. They often provide significant informal care to heart failure patients and may have to assume the role of surrogate decision maker if the patient loses intellectual capacity. Cognitive decline has been demonstrated in ICD recipients as early as 12 months after implantation (Kim et al. 2013). Spouses have reported feeling unprepared to take on this responsibility and have sometimes been excluded from the formal follow up process (Fluur et al. 2014). While advance care planning, including the appointment of a proxy to make decisions if capacity is lost, might obviate some of the dilemmas which may arise later, few device-specific advance directives are enacted by the heart failure population (Dunlay et al. 2012; Merchant et al. 2017).

Health professionals are sometimes uncomfortable in initiating conversations about ICD deactivation. This can stem from difficulties in prognostication, their own attitudes to dying, or a fear that such conversations might impact patients' hopes for the future and undermine the clinician-patient relationship (Goldstein et al. 2008b). Alternatively, they may falsely perceive that effective communication has been achieved. A trial has just been completed exploring means of improving clinician–patient communication in respect of ICD therapy [ClinicalTrials.gov identifier NCT01459744] but has yet to report. Some clinicians may also have unfounded ethical concerns that ICD deactivation is equivalent to euthanasia (Kramer et al. 2010, 2011), but the ethical principles supporting appropriate device withdrawal have been fully established (Wright et al. 2013; Chamsi-Pasha et al. 2014). National and international guidelines for ICD deactivation have been developed, but it is important that clinicians ensure that their handling of device issues is compatible with local legislation relevant to the state or country where their clinical practice is based (Padeletti et al. 2010; Lampert et al. 2010;

Pitcher et al. 2016). While national guidance offers a benchmark, effective device management requires the formulation of institutional, local, and regional protocols, supported by regularly updated staff education and training, and with adequate provision and unrestricted access to the required trained personnel and equipment.

Palliative care involvement may facilitate clarification of goals of care or symptom management after device withdrawal (Pasalic et al. 2016), but hospice care may present significant difficulties to heart failure patients with these devices (Lum et al. 2015). Previous surveys of hospices in the United States and the United Kingdom have shown that while most admit patients with ICDs, there was poor documentation of this on admission, a paucity of deactivation protocols, deficiencies in staff training, and poor access to equipment to facilitate urgent device deactivation (Goldstein et al. 2010; Beattie et al. 2012). Compared to those in urban centers, hospices based in rural communities report particular difficulties (Fromme et al. 2011), Planned ICD deactivation can be achieved simply by device reprogramming, and in an emergency, the shocking function can be temporarily disarmed by placing a doughnut magnet on the chest wall over the device (Pitcher et al. 2016). It is also important to remember that, if not already completed, the device should be deactivated after death to avoid a shock risk to mortuary personnel or undertakers, and that the device should be removed prior to any planned cremation to prevent an explosion hazard.

9 Mechanical Circulatory Support and Transplantation

For patients with advanced HFrEF (Stage D), aggressive surgical options include ventricular reconstructive surgery – often a form of the Dor procedure, cardiac transplantation, or the placement of a left ventricular assist device (LVAD) (Fang et al. 2015). First implanted in 1984, a LVAD is a mechanical pump inserted via open heart surgery to supplement the poor contractile function of the failing ventricle. As with implanted electronic devices in ICDs or pacemakers, refinements in technology have led to the rather bulky early devices becoming more miniaturized, with improved biocompatibility, durability, and increased functional performance. Early LVADs provided pulsatile flow based on volume displacement, but currently used axial or centrifugal continuous flow rotary pumps have fewer moving parts and are designed to provide an augmented cardiac output of up to 10 L/min. At times, when there is also right ventricular dysfunction, biventricular support in the form of a total artificial heart is implanted (Wordingham et al. 2015). The evolution and outcomes from these mechanical circulatory support (MCS) devices are collated by the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) and are described in sequential reports (Kirklin et al. 2015).

The use of MCS devices in appropriately selected advanced heart failure patients offers a significant prognostic advantage compared to optimal medical therapy, with an 80% 1-year and a 70% 2-year survival compared to about 6 months without the implant (Kirklin et al. 2015). Initially, LVAD use was intended as a bridge to recovery, sometimes effective in acute heart failure states due to conditions such as viral myocarditis or postpartum cardiomyopathy (Kirkpatrick et al. 2015). At times temporary MCS is still indicated alongside pharmacologic inotropic support for patients with critical cardiogenic shock. Such devices can be placed percutaneously or surgically and are offered as a bridge to decision in terms of potentially receiving long-term device placement depending on the outcome with respect to recovery of ventricular function, or survival (Becnel et al. 2017). More commonly, surgically placed LVADs are used as a bridge to transplant (BTT) in those with chronic heart failure. While this policy continues, given the positive outcomes in improving symptoms and prognosis, together with the scarcity of donor organs, LVAD responsive patients may be assigned a lower priority on transplant waiting lists. Alternatively, some may choose not to go on to transplantation or become transplant ineligible as they age and develop comorbidities. Consequently, many patients now receive LVADs as a long-term MCS option in destination therapy (DT).

While there are noteworthy benefits of this intervention in improved quality of life and physical capacity, living with a LVAD as BTT or DT may also be burdensome for both patients and those close to them. Implantees must adhere to relatively complex medication regimes and are physically constrained in the need to maintain device functionality through an external driveline connecting the pump to the controller and battery pack. This limits day to day activities of both patients and families, impacting their broader social but also closer interpersonal relationships. There is also existential anxiety in an heightened awareness that life itself depends on the device. Despite the hemodynamic support derived from the implant, rehospitalization may be required due to recurrent heart failure or the occurrence of device-related infections, most often linked to the driveline (Goldstein et al. 2012). Devices are being developed that can be recharged transcutaneously which might supplant the need for this external power connection. There is also a substantial risk of gastrointestinal bleeding which appears to originate in mucosal arteriovenous malformations, developing as a form of angiodysplasia in response to the moderately low pulse pressure associated with continuous flow perfusion. An acquired form of von Willebrand syndrome may also be relevant here. These clinical situations can be challenging as all continuous flow devices require anticoagulation with warfarin, usually combined with aspirin because of device-mediated changes in platelet function. Despite this, there is also a relatively high incidence of pump thrombosis, with a cumulative risk of 14%, 24%, and 25%, at 1, 3, and 5 years, respectively (Stulak et al. 2016). This almost invariably requires pump replacement. Another feared complication is that of stroke, with an incidence of 11% at 1 year and 17% at 2 years (Kirklin et al. 2015). If clinically significant, this might require consideration for withdrawal of device therapy with a consequential rapidly fatal outcome. Most patients die within an hour of LVAD deactivation. In a recent review of DT-LVAD patients from the Mayo Clinic, the most common causes of death were multiorgan failure (26%), hemorrhagic stroke (24%), and progressive heart failure (21%) (Dunlay et al. 2016). Given the complexity of this clinical cohort, the vast majority of patients die in hospital, usually in the intensive care unit.

The development and progressively mainstream use of MCS for advanced heart failure offers significant opportunities to synergize the complementary expertise of cardiologists, cardiac surgeons, and palliative care professionals (Goldstein et al. 2011). Indeed, since 2014 in the United States, the Centers for Medicare and Medicaid Services have mandated that a palliative care professional is included in all DT-LVAD program teams (Centers for Medicare and Medicaid Services 2014). Palliative care involvement may facilitate preparedness planning and goal setting against the background of clinical issues which might play out for patients and families throughout the MCS journey from just considering LVAD support, through the implant procedure and any subsequent transplant, or living with a DT-LVAD to the end of life (Swetz et al. 2011; Luo et al. 2016; Nakagawa et al. 2017; Wordingham et al. 2017). The impact of including palliative care professionals was noteworthy in aiding decision making in patients and families dealing with complications of LVADS, including consideration for LVAD deactivation. They also strengthened the expertise of the MCS team in providing enhanced symptom relief and psychosocial support and facilitated hospice referral for suitably selected patients (Sagin et al. 2016). Further, there was a perception that integrating palliative care within the MCS team improved the experience of patients and families. Care structures vary between institutions, and bereaved caregivers of LVAD patients have also reported significant confusion and care fragmentation at the end of life which underscores the need to develop effective models of collaborative care, supported by robust outcome assessment to promote and spread best practice (McIlvennan et al. 2016).

Palliative care support is also relevant to those patients who follow the clinical continuum and go on to cardiac transplantation (Banner et al. 2011). This intervention is highly effective for the privileged few graft recipients. With a 1-year and 5-year survival of 84.5% and 72.5%, respectively

(Wilhelm 2015), current data from the International Society for Heart and Lung Transplantation registry suggest a median life expectancy of 10–15 years posttransplant. However, cardiopulmonary transplantation is still associated with significant morbidity, mortality, and unmet palliative care needs (McKenna and Clark 2015).

Pretransplantation, given the significant symptomatic burden and uncertainty while waiting for a suitable donor organ, patients and families have a poor quality of life and are in need of multimodal support. Data on the effects of intervention are limited (Muhandiramge et al. 2015; Bayoumi et al. 2017), but a small pilot study of palliative care consultations jointly undertaken by a palliative care physician and cardiologist in those referred for heart transplantation demonstrated benefits for both patients and families in better continuity of care, goal setting, and reduced opioid use (Schwarz et al. 2012).

Several issues affect outcomes in the peri- and post-transplantation phases. The 30-day mortality after heart or lung transplantation lies between 10% and 30% (McKenna and Clark 2015). Despite improvements in immunosuppression, there are still significant problems with rejection. This occurs in both acute and chronic forms through cell- or antibody-mediated responses and may be manifest as accelerated allograft vasculopathy which affects about 50% of graft recipients by 10 years post-transplant (Wilhelm 2015). Infection accounts for about 30% of deaths in the first year post-intervention, the risk reducing thereafter. Pharmacologic immunosuppression is associated with a higher incidence of malignancy and more aggressive tumor biology (Collett et al. 2010). Malignancies are evident in about 15% of heart transplant patients by 5 years out and account for around 22% of the annual mortality beyond this. Skin cancer is particularly common (Wilhelm 2015).

The evidence specifically relating to palliative care provision after heart transplantation is limited. Attitudinally, some transplant teams seem to regard palliative care as a last resort and only consider this when all other forms of therapy have been exhausted, limiting involvement to end of life care (McKenna and Clark 2015). This requires education in the broader reach of palliative care and the promotion of multidisciplinary working. There are undoubtedly significant parallels in the needs and intensity of care required of the populations these disciplines serve in their different ways. The evolving collaboration between palliative care and cardiac surgical professionals related to patients requiring MCS, and indeed in those undergoing transcatheter aortic valve implantation (TAVI), might provide a useful platform to meld and expand the remit of this shared expertise (Lauck et al. 2014; Steiner et al. 2017). It is also important to emphasize that palliative care provision should be central to the continuing care of those who are assessed and deemed to be transplant ineligible. Apart from patient choice, a variety of clinical and psycho-social features may be relevant to that decision and some are outlined in Table 4. Given the irreversible nature of heart failure disease progression, in the absence of potential rescue by transplantation, addressing symptom control and planning for end of life care are likely to become the dominant goals of treatment.

Table 4 Relative contraindications for cardiac transplantation. (Adapted from Banner et al. 2011)

Active infection
Recent malignancy
Recent pulmonary embolism
Significant pulmonary pathology
Persistent severe pulmonary hypertension (>60 mmHg)
Severe obesity (>32 kg/m^2)
Diabetes with significant extra-cardiac end-organ damage
Symptomatic peripheral vascular disease
Symptomatic cerebrovascular disease
Irreversible significant renal impairment (GFR < 40 ml/min/m^2)
Cognitive impairment precluding consent
Inadequate accommodation or social support
History of non-adherence to therapy
Substance abuse (active smoking, excessive alcohol, or illicit drug use)

10 Symptom Burden

Those living with heart failure experience a symptom burden similar to that associated with cancer and other progressive long-term conditions (Solano et al. 2006; Bekelman et al. 2009; O'Leary et al.

2009). In addition to the anticipated heart failure-related symptoms of breathlessness and congestion, over the past two decades a plethora of other debilitating features has also been described including gastrointestinal, spiritual, and psycho-social dysfunction, which may be under appreciated by cardiology focused healthcare providers (Murray et al. 2007; Bekelman et al. 2009).

Pain is particularly common in heart failure patients and is frequently poorly recognized and treated (Light-McGroary and Goodlin 2013). The symptomatic spectrum in heart failure has recently been summarized and this is shown in Table 5 (Riley and Beattie 2017). The prevalence of symptoms and the extent to which they are perceived as distressing appear to vary. For example, the background to breathlessness and fatigue in heart failure is complex, but the former is both highly prevalent and highly distressing, while the latter appears to be less associated with distress (Riley and Beattie 2017). Even towards the end of life when symptoms increase in prevalence and intensity, health-related quality of life may be relatively well preserved (Levenson et al. 2000). Comparing the postulated level of symptom impact across studies is hampered by inconsistencies in methods of assessment; however, the Memorial Symptom Assessment Scale – Heart Failure (MSAS-HF), and the MD Anderson Symptom Inventory-HF, modified from instruments initially developed for those with cancer, may be particularly useful (Zambroski et al. 2005; Lee and Moser 2013). A comprehensive review suggested that heart failure patients experienced a mean of 15 $\pm$ 8 symptoms (Zambroski et al. 2005), and these may be directly linked to the heart failure syndrome or to the patients' comorbidities, perhaps particularly relevant to those with HFpEF (Blinderman et al. 2008; Eckerblad et al. 2015).

Clinicians have tended to focus on individual symptoms as distinct clinical entities, but the malaise of heart failure is multidimensional and in recent years the concept of symptom clustering has come into play. Using registry data and symptom assessment from a quality of life tool, Jurgens et al. (2009) reported three distinct symptom clusters: an acute volume overload cluster (shortness of breath, fatigue, and sleeping difficulties), a chronic volume overload cluster (ankle swelling, need to rest, and breathlessness on exertion), and an emotional cluster (depression, memory loss, and worry). They reported these symptom clusters were more common in older persons but caused less functional limitation. Another survey of more than 700 patients from the United States, Europe, and Asia described clusters of physical symptoms that included dyspnea, difficulty walking, fatigue, and increased need to rest. Worrying, feeling depressed, cognitive problems, and difficulty sleeping formed another cluster of symptoms that the researchers termed an "emotional symptom cluster" (Moser et al. 2014). A recent review from Hong Kong offers some insight into features of symptom clustering that included the physical and emotional/cognitive domains exhibited by people with advanced heart failure and describes some patterns which may presage a poor outcome (Yu et al. 2017). It is important to note that attitudes and views on the meaning of symptoms vary with cultural norms and a transcultural comparison has demonstrated dissimilar symptom clustering and resultant degrees of distressful impact in matched heart failure populations (Park and Johantgen 2017). As our understanding of symptom clustering in heart failure continues to develop, it is important that health care professionals are aware of such disparities to allow them to better target the interrelated symptom groupings and anticipated effects relevant to their local populations.

11 Symptom Relief

Symptom relief can be approached in accordance with general palliative care principles (Johnson et al. 2012a; Stewart and McPherson 2017), but the management of congestion and breathlessness are worthy of special mention. Congestion, either pulmonary or peripheral, is a cardinal sign of acute and chronic heart failure, resulting in breathlessness, discomfort, and limited physical capacity. Intuitively, salt and water restriction have been facets of both the professional and self-care of those exhibiting heart failure-related congestion.

Table 5 Symptom spectrum and associated distress in heart failure (Modified from Riley and Beattie (2017), used with permission)

	Lokker et al. (2016) n = 230		Blinderman et al. (2008) n = 103		Zambroski et al. (2005) n = 53		Wilson and McMillan (2013) n = 40	
	Frequency (%)	High distress (%)	Frequency (%)	High distress (%)	Frequency (%)	High distress (%)	Frequency (%)	High distress (%)
Physical symptoms								Unreported
Shortness of breath	95.2	89	56.3	43.1	85.2	60.5	65	
Feeling drowsy/tired	93.0	83	52.4	24.1	67.9	37.1	72.5	
Pain	91.3	76	37.9	54.1	57.4	51.7	52.5	
"I don't look like myself"	90.4	81	25.2	23.1				
Weight loss	84.8	51	19.4	25	32.1	18.8	52.5	
Lack of energy	82.2	67	66	44.8	84.9	63.6	70	
Swelling arms/legs	81.3	70	32	33.3	47.2	30.4	47.5	
Difficulty sleeping	77.0	64	44.1	44.4	64.2	60.6	52.5	
Tingling hands/feet	73.5	66	48.5	22	46.2	47.8	55	
Changes in way food tastes	73.0	61	15.5	18.5	18.9	44.4	50	
Lack of appetite	72.2	53	31.1	25.8	30.2	40	37.5	
Difficulty concentrating	67.4	30	33	29.4	50	44	40	
Problems with sexual interest/activity	52.6	8	26	46.2	46.3	50	17.5	
Cough	49.1	33	40.8	16.7	57.4	14.8	45	
Nausea	42.2	23			41.5	19	20	
Dizziness	41.3	19	27.2	32.1	51.9	38.5	45	
Feeling bloated	36.1	19	28.2	17.2	51.9	40	25	
Dry mouth	35.7	15	62.1	14.1	74.1	33.3	72.5	
Problems urinating	32.2	16	26.2	29.6	24.1	27.3	17.5	
Itching	28.3	8	34.3	22.9	43.4	47.4	40	
Constipation	26.1	15	25.2	38.5	26.4	30.8	30	
Vomiting	25.7	13			24.1	33.3	10	
Sweats	25.2	15	21.4	18.2	53.7	42.9	27.5	
Diarrhea	12.2	18			22.2	10	17.5	
Psychological problems								
Worrying	94.3	30	43.7	33.3	61.5	53.3	50	
Feeling irritable	93.5	28	33	26.5	53.7	34.6	32.5	
Feeling sad	93	18	42.7	34.1	54.7	44	37.5	
Feeling nervous	92.2	50	35.9	38.9	53.7	38.5	30	

However, recent evidence suggests that this is of little benefit and a more liberal approach should be adopted to avoid exacerbating thirst, a significant symptom in heart failure patients (Aliti et al. 2013; Allida et al. 2015). The use of loop diuretics is the cornerstone of treatment, with the intention of restoring and maintaining euvolaemia (Ponikowski et al. 2016). Furosemide is the prototype of this drug group and may be administered by a variety of routes (Carone et al. 2016). Oral diuretics may be poorly absorbed via a congested gastrointestinal tract, when intravenous therapy may be more effective. In those with decompensated chronic heart failure, a useful start point might be to prescribe the same dose intravenously that the patient was taking orally. It remains unclear whether administration by intermittent bolus dosing or continuous intravenous infusion is the better strategy. Irrespective of the mode of delivery, the duration of therapy and the dose required will be determined by individual patient responses. Prolonged use of high dose loop diuretics is associated with worsening renal function and a high mortality (Palazzuoli et al. 2017). Close monitoring, ideally with daily weighing, is required to guide dose adjustment and maintain patient safety (Felker et al. 2011). The combination of a loop diuretic with a thiazide such as metolazone may be useful in resistant congestion, but should be used with caution due to a higher likelihood of adverse events. Delivery of drugs by the subcutaneous route has been widely adopted in palliative care practice. Given the relatively light evidence base, some concern has been raised about the effectiveness of furosemide when so administered (Beattie and Johnson 2012). However, data are starting to emerge that this approach may indeed be useful (Zacharias et al. 2011; Farless et al. 2013). Subcutaneous injection of generic furosemide is sometimes associated with a tissue reaction and discomfort at the infusion site. SC Pharmaceuticals® based in Burlington, MA, in the United States have developed a buffered preparation of furosemide, together with a customized infusion pump (sc2Wear®), which appears to show potential in early clinical trials [ClinicalTrials.gov identifier NCT02329834]. Permanent catheter drainage systems are sometimes required for the palliation of diuretic resistant ascites (Bevan et al. 2016).

Multiple mechanisms contribute to the sensation of breathlessness in heart failure (Johnson and Clark 2016). Exercise training, neuroelectrical stimulation of respiratory muscles, and mindfulness approaches have been shown to be of some benefit. Opioids appear to act, at least in part, through depression of cortical centers responsible for the perception of breathlessness. Evidence suggests that low dose opioids can be helpful, particularly in stable chronic heart failure, but there may be a time lag before drug efficacy is evident (Johnson et al. 2002; Oxberry et al. 2011, 2013). Because of the possible accumulation of active drug metabolites, caution is required in those with concomitant renal dysfunction (Stewart and McPherson 2017). In the absence of demonstrable hypoxemia, long-term oxygen therapy does not appear to offer symptomatic benefit in chronic heart failure (Davidson and Johnson 2011; Clark et al. 2015), but the use of a handheld fan to blow air on the face may be effective, perhaps mediated by activation of afferent trigeminal receptors in the nasal mucosa and facial skin (Galbraith et al. 2010).

It is logical to assume that conventional evidence-based treatment for heart failure, at present predominantly relevant to HFrEF, "palliates" the effects of this syndrome to some extent in ameliorating heart failure-related symptoms, improving quality of life, and in reducing mortality. Therefore, there may be advantages in maintaining the prescription of ACEIs, ARBs, and ß-blockers where possible. Towards the end of life, when patients often develop relative hypotension or multiorgan failure including a cardiorenal syndrome, dose reduction or withdrawal of these agents may need to be considered. At that phase of the illness, when the emphasis shifts to symptom management rather than life extension, reconsideration of goals of treatment might deem acceptable the de-prescription of medication such as statins and antiplatelet therapy offered primarily for prognostic benefit. Decisions on cessation of anticoagulant therapy need to be carefully deliberated, cognizant of the specific indications for that treatment. For patients implanted with a mechanical prosthetic

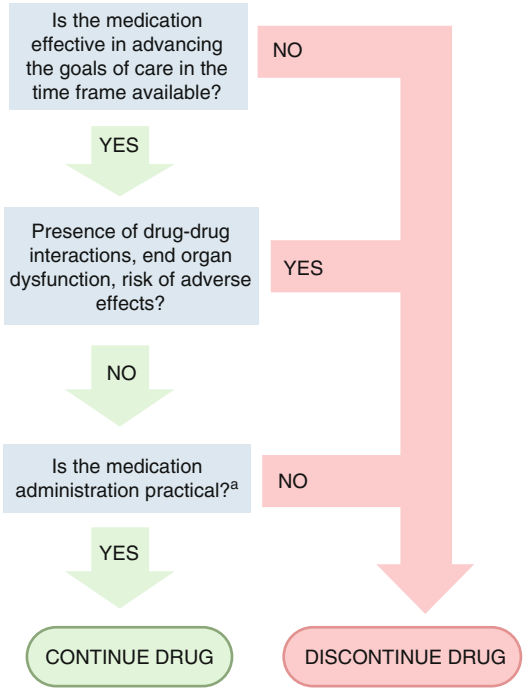

Fig. 4 An algorithm to determine appropriateness of maintaining drug therapy (From Spiess (2017) with permission)

heart valve or a LVAD, discontinuation of this therapy may be ill-advised. With such treatment dilemmas, involvement of the heart failure team may be helpful for palliative care staff. It might also be reassuring for patients to know that withdrawal of elements of their sometimes long established prescription medication was sanctioned by the team responsible for its initiation. Difficulties in routes of drug administration also arise at this terminal phase. In a recent review, Spiess (2017) has produced a useful algorithm (Fig. 4) to help guide decisions on therapy delivery through what may be the final clinical transition.

12 Palliative Care Service Provision

Providing effective heart failure palliative care relies on good communication, coordination, and timely access to specialist expertise to respond to the sometimes rapidly changing requirements of patients and families, including the opportunity for bereavement care (Low et al. 2011; Luckett et al. 2014; Siouta et al. 2016). This requires a flexible multidisciplinary approach to blend knowledgeable input from cardiology, palliative care, and other health professionals, as well as the provision of social care, to ensure optimal clinical management and support for patients and families. The composition of the multidisciplinary team and the relative contribution required of its members will be determined by the individual needs of the patient-carer dyad, but where possible, it is important that a single team member is designated as the interlocutor between the professionals and the family to ensure clear lines of communication (Ryder et al. 2011; Fendler et al. 2015). Even close to the end of life, when the emphasis of care might shift towards palliation to expertly address difficult symptoms, existential and psychosocial distress, it is important that the cardiology team remain closely involved. This will better secure the maintenance of optimal heart failure management, which might involve intermittent or chronic inotropic support (Hauptman et al. 2006). As alluded to above, this will facilitate shared decision making to determine the continuing role of established therapies, discernment of realistic ceilings of care, and definition of the preferred place of care and death. This also avoids the risk of patients and families feeling abandoned by clinicians familiar to them in this difficult final phase of the disease trajectory.

General palliative care in providing basic symptom control and supporting those with progressive disease in goal setting or advance care planning is a central tenet of general clinical care across all specialties. It has been estimated that about 5% of all heart failure patients require specialist palliative care involvement (Dunlay and Roger 2014). This would certainly be appropriate for those with refractory symptoms, complex care needs, or with features of advanced heart failure (Stage D). But it has been suggested that in other periods of the illness, generalist (primary) palliative care might be provided by those health professionals principally responsible for the patients' care. This could be their primary care physician, an internist, or a member of the heart failure team

(Gelfman et al. 2017a). This is consistent with a commentary proposing a practical model of palliative care delivery in a sometimes resource constrained specialty (Quill and Abernethy 2013), but is dependent on adequate undergraduate and postgraduate education, practical experience, and opportunities to maintain proficiency.

While palliative care teaching is increasingly featured in undergraduate medical school curricula, albeit varying widely in depth, this is yet to be offered by a third of European universities (Carrasco et al. 2015). A set of competencies for heart failure palliative care provision has been outlined for cardiology fellows in the United States, where benefits have also been demonstrated for communication skills training (Munoz-Mendoza 2015; Berlacher et al. 2017). Palliative care education is incorporated within the ESC heart failure subspecialty training program, but the reported experience of medical trainees suggests they still struggle to deliver this (McDonagh et al. 2014; Ismail et al. 2015). In contrast, sequential surveys of specialist heart failure nurses in the UK showed that after participation in palliative care training, they were better equipped to provide generalist palliative care, resulting in fewer referrals to specialist palliative care services (Johnson et al. 2012b). More research is required to define the potential role of generalist versus specialist palliative care in supporting people with heart failure.

Despite the widespread recognition of the need to include palliative care as part of a multidisciplinary approach within the clinical standards required of heart failure care, provision is inconsistent (Strachan et al. 2009; McDonagh et al. 2011; Kane et al. 2015). Service delivery is often provided on an ad hoc basis, largely supported by local champions, and subject to available resources. Unsurprisingly, care configuration is determined by the constitution of local health economies and a variety of arrangements may be applicable. This might be based on a consultancy service, in keeping with the approach in the ESC position statement (Jaarsma et al. 2009), co-management across different clinical settings including intensive care units, or in the use of dedicated palliative care units or independent hospices depending on the specific needs of patients and families. While there is increasing access to hospices by people with heart failure which may reduce acute medical service utilization and associated costs (Kheirbek et al. 2015; Taylor et al. 2017; Yim et al. 2017), numbers treated remain relatively low compared to those with cancer (Cheung et al. 2013; Cheang et al. 2015). The lack of staff experience with this condition might affect patient care. It is important to ensure that when patients are admitted to an independent palliative care unit or hospice, there is adequate transfer of clinical information, including agreed treatment policies, that any necessary heart failure therapy is readily available and that the means to deal expeditiously with any implanted cardiac devices are in place (Wingate et al. 2011; Fromme et al. 2011; Lum et al. 2016).

While some successful collaborative heart failure palliative care models have been developed (Davidson et al. 2004; Johnson et al. 2012c), there is a paucity of robust evidence from randomized clinical trials on which to base best practice (Xie et al. 2017; Gelfman et al. 2017b). However, results are accumulating confirming the benefits of a range of palliative care initiatives across inpatient, outpatient, and assisted living settings, including transitional programs between hospital and home (Pattenden et al. 2013; Evangelista et al. 2014; Brännström and Boman 2014; Sidebottom et al. 2015; Wong et al. 2016; Hopp et al. 2016; Diop et al. 2017; Gandesbery et al. 2017). While several trials are in progress and still to report, the recently published landmark PAL-HF study of 150 patients hospitalized with heart failure undertaken by Duke University and demonstrating improved quality of life by palliative care intervention provides a benchmark in taking this research forward (Rogers et al. 2017). We need to build on this growing evidence base as the foundation of quality assured comprehensive care delivered to affected patients and families.

13 Summary

Heart failure is an increasingly prevalent chronic progressive condition, occurring in epidemic proportions across the world. The widespread

implementation of the current comprehensive heart failure treatment paradigm as espoused in clinical guidelines has improved the quality of life and longevity of some of those affected. While these benefits should be celebrated, such developments may contribute to the overall burden endured by those living in fragile health and declining with this cardiovascular disease, often set against the backdrop of comorbidities typical of the changing demography. Given the prognostic uncertainty, it can be difficult to recognize when established therapies have become futile, compounded by poor care co-ordination and communication, sometimes manifest in an unconscious collusion between health professionals, patients, and their families in avoiding difficult conversations. Over the last decade or so, while the palliative care needs of those living and dying with heart failure have been increasingly recognized, care provision remains difficult. At times, the professional ethos of heart failure and palliative care specialists seem to be at odds, when in reality we need to synergize our complementary skill sets to optimize patient care from diagnosis and throughout the disease trajectory. Treatment provision will be largely determined by local healthcare structures. As agents of change, providers should endeavor to develop bespoke models of collaborative interdisciplinary working, consolidated by mutual education, to facilitate effective and coherent delivery of the dual cardiology and palliative care approaches required of this life limiting condition, and best ensure that treatment goals remain consistent with the changing needs, preferences, and values of this vulnerable population.

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Palliative Care of Respiratory Disease in Primary Care

62

Patrick White

Contents

Abstract

The palliative care of advanced progressive respiratory disease in the setting of a primary care team is concerned mainly with chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), and cystic fibrosis (CF). COPD is the commonest of these but it is perhaps the most difficult to identify in its final stages. IPF has a trajectory and prognosis more akin to malignant disease. Though relatively rare in general practice, IPF is the disease among these three that has the most easily definable terminal stage, and so primary care teams should be alert to the palliative care needs of these patients.

CF is a remarkable disease because life expectancy at birth with CF has changed from childhood or teenage years to 30 years now,

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_61

and for those aged 30 years, life expectancy is now in mid-50s. Like COPD, prognosis in CF is difficult to define. Most people with advanced disease in both groups are living with the disease. Most of these people want to continue living in the face of considerable challenges. The task in both of these diseases is to develop an approach to the amelioration of symptoms and to the support of patients and carers, that is, in keeping with the personal objectives of the patients. Information about treatment, future exacerbations, and the risk of dying is all important. Symptom control is difficult, and for intractable breathlessness, oral morphine has a role in many patients.

End-stage progressive nonmalignant respiratory disease:

the challenge/the burden from a palliative care perspective/the symptoms/issues in specific diseases/ the assessment and treatment of breathlessness in respiratory disease

1 The Challenge

The palliative care of respiratory disease presents the classic challenges of advanced progressive nonmalignant disease. The disease trajectory is often prolonged and uncertain. The transition between high dependency and dying may be imperceptible. In idiopathic pulmonary fibrosis (IPF), the end stage of the disease may resemble the terminal stage of a moderately progressive cancer. As symptoms become intractable, their management can be increasingly complex, and multidisciplinary input is likely to be needed.

In this chapter, the focus is on the advanced progressive nonmalignant diseases of the respiratory system. Lung cancer will not be treated as a separate issue here because the features of the terminal stages of lung cancer are largely indistinguishable from other malignant diseases in which metastasis to the lung is prominent.

The two most common progressive respiratory diseases that present to palliative care are chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF). They lead to contrasting experiences and different demands. COPD is likely to have progressed over 10 or 20 years. It usually does not progress to a clear terminal stage of the disease. Death may be relatively sudden from a severe acute exacerbation or pneumonia. IPF is likely to be more predictably progressive. The mean survival of IPF from diagnosis is 2.5–3.5 years. It usually has a more defined terminal stage and a more conventional opportunity for palliative care intervention than COPD.

Cystic fibrosis (CF), an inherited condition, has an altogether different onset and trajectory, from early life until premature death, which is usually in the 1950s nowadays. The need for palliative care of cystic fibrosis has only recently been addressed in the research literature. Despite its systemic effects, particularly in the gastrointestinal tract, the greatest threat in CF is progressive respiratory disease. Death may be from an acute infection. Many patients are selected for possible lung transplantation when respiratory function has been severely impaired. At that point the need for palliative and supportive care input is not likely to be in the domain of primary care.

The palliative care of advanced progressive respiratory disease shares the same basic aims of all palliative care. Timely planning and provision of clear information are the cornerstones of treatment. Neither should depend on being able to make an accurate prognosis. Symptom palliation should be determined by the severity of the symptom and the responsiveness of the underlying pathology to the treatment. Involvement of the patient, and their carers, in decisions about their care will help to ensure that care is appropriate. Providing an accurate prognosis may be challenging. That difficulty should not be used as an excuse for failing to prepare patients and their families for what lies ahead.

In advanced progressive nonmalignant respiratory disease, particularly in COPD and in CF, living with the disease is the dominant issue. The risk of death, rather than preparation for it, is the shadow that requires acknowledgment. In IPF, by contrast, the prognosis, all too clearly, is short.

The context of the stage of the disease in chronic nonmalignant respiratory disease is

important to these discussions. For some clinicians, it may be more difficult to introduce this subject because of the greater uncertainty that exists over the disease prognosis. Acknowledgment that prognosis is not the key issue here may help. Putting the issue of prognosis to one side may allow clearer thinking to be done about the risks of the disease at this stage, including the risk of dying. Will it be useful for my patient if I raise the subject of the risks associated with their illness? Is my patient someone who would like to consider the risks that they face? Have they reached the stage that life has become precarious because of the risk that the next exacerbation will be fatal?

Symptom control is the second big challenge in advanced nonmalignant respiratory disease. Patients with advanced severe disease will survive at least 2 years on average. This is not the moment to exhibit all the drugs at the clinician's disposal in the attempt to ameliorate intractable breathlessness. There is a need for a careful structured approach to symptom palliation that adopts a realistic evaluation of the patient's position. This approach will be discussed more at length in the Sect. 3. At this point the clinician should review what has been provided so far.

In this chapter the prevalence, burden, and risk of death from respiratory disease is discussed from the perspective of primary care in the UK. The population of the UK is now more than 60 million people. Where figures for prevalence are given, readers should translate those to their own country or setting. Prevalence can vary significantly. The incidence of COPD, for example, is likely to fall progressively in the UK where rates of smoking have plummeted in the last 40 years to a low of 16%. Exposure to biomass fuels in the home is virtually unheard of in the UK. This contrasts to countries in which the promotion of cigarette smoking has continued unabated and biomass fuel is commonly used for cooking. In such circumstances death from COPD is likely to be much younger because the exposure to risk factors starts earlier in life.

This chapter is written for primary care, taken from the experience of primary care in the UK. It is not directed at a particular clinical group. The issues discussed should be as relevant to general practitioners or family physicians as they are to nurse specialists, practice nurses, community nurses, healthcare assistants, and other professional clinical groups caring for patients approaching the end of their lives in the community. In other countries the organization of healthcare may differ significantly from that in the UK. Readers should translate the ideas presented here to their own setting.

2 The Burden from a Palliative Care Perspective

2.1 Chronic Obstructive Pulmonary Disease (COPD)

COPD is common. About 2% (>1,000,000) of people have diagnosed COPD in the UK (British Lung Foundation 2018). Ten percent of these have very severe disease as defined by the spirometry criterion of forced expiratory volume in the first second (FEV_1) (White et al. 2013). The prevalence of COPD in the UK is based primarily on people who have symptomatic disease. The prevalence varies quite markedly from country to country depending on the cause of the disease and whether or not screening is carried out for COPD. In many of the people diagnosed with COPD through screening, the disease causes no symptoms and has no impact on quality of life at the time of screening.

In developed countries the main cause of COPD is tobacco smoking. Occupational exposures account for a small proportion of the prevalence. In countries with high rates of poverty or large rural communities, exposure to biomass fuels is a significant cause of the disease. Exposure to biomass fuels is usually through cooking with wood or animal waste. The cooking is done in the house with poor ventilation. The whole family is exposed to smoke and volatile materials from a young age.

About 30,000 people die from COPD in the UK every year, just under 1 death from COPD for every GP each year or 3–6 deaths for a primary care team per year. This depends on the number of

patients registered with the team. This is not far below the rate of deaths from lung cancer. The mean age of death from COPD in the UK is 76 years. Comorbidities are likely to contribute to the risk of death. They may complicate the care of people with advanced COPD.

2.2 Idiopathic Pulmonary Fibrosis (IPF)

The symptoms of IPF are breathlessness, cough, and fatigue (Shaw et al. 2017). It affects more than 32,000 people in the UK or 1 in 2000 people. About 1 patient has IPF for every 30 patients with COPD. Worldwide the prevalence of IPF is 2.8–9.3 per 100,000 (Hutchinson et al. 2015). Each GP is likely to have a little less than one patient with IPF on his or her list in the UK at any one time. There are 5000 deaths from IPF in the UK each year (Navaratnam et al. 2011). On average a primary care team will have a patient who dies from IPF every 2–3 years. This is about a sixth of the deaths that might be expected from COPD.

In IPF, the diagnosis and severity are defined by the spirometric criterion of forced expiratory volume (FEV). The treatment of IPF has changed in the last 5 years with the publication of two trials of antifibrotic drugs. These two drugs, pirfenidone and nintedanib, have been shown to reduce the progression of the disease (NICE 2016; Nathan et al. 2017). It is not yet clear how well this treatment will control the impact of IPF. If successful it will significantly reduce the burden of IPF at the end of life.

2.3 Cystic Fibrosis

About 10,000 people in the UK have cystic fibrosis, the commonest inherited disease affecting Caucasians. It is a common reason for lung transplant. Dramatic changes have occurred in the life expectancy of CF (Keogh et al. 2018). At birth people with CF should now expect to live until their mid-40s. People with CF at 30 years should expect to live into their mid-50s. In 10 years life expectancy is projected to be in the mid-60s for people aged 30. Better understanding of the underlying mechanisms is likely to lead to significant improvements in the treatment of cystic fibrosis. For now, the most important intervention is early treatment of respiratory infections with the prevention of mucous plugging if possible. Respiratory failure is the commonest cause of death. It is difficult to define the burden of cystic fibrosis on palliative care services because deaths are sporadic, result from acute infections, or occur in people in lung transplant programs.

3 The Symptoms

In advanced respiratory disease, four symptoms dominate patients' experience: breathlessness, cough, weakness, and low mood.

Breathlessness is the central problem in loss of respiratory function, the chief impact of these diseases. In COPD breathlessness progresses gradually. Sometimes it deteriorates so slowly that it is the loss of functional capacity that makes the change apparent. Breathlessness is difficult to remedy. There is a variety of strategies that can ameliorate its impact in people with advanced disease, including exercise to improve muscular fitness, breath training to give greater control of the symptom, psychological strategies to reduce the anxiety that often accompanies the symptom, mechanical devices to distract from the symptom, and pharmacological interventions to reduce its perception. These are discussed in more detail later in the chapter.

Cough is usually a more prominent symptom in early disease. However, in IPF cough progresses with the disease, and 80% of patients with advanced IPF have cough (Shaw et al. 2017). In IPF the symptom is often intractable, and treatment is usually ineffective. In COPD cough is usually productive. It can become intractable in advanced disease especially when associated with difficulty in clearing secretions from the upper airway. There has been more interest in recent years in the use of mucolytics such as carbocysteine, but evidence for their effectiveness is moderate.

Weakness is the culmination of the downward spiral that results from progressive breathlessness. Breathlessness leads to reduced exercise that in turn leads to muscle deconditioning. With muscle deconditioning, there is less efficient use of oxygen so that more breathing is required to achieve the same functional result and the outcome is weakness. In advanced disease, exhaustion and demoralization can follow minor physical activity. In COPD, in IPF, or in CF, there is no evidence of inflammatory activity outside the respiratory system. The progressive weakness that occurs is not due to peripheral myopathy or neuropathy.

The most effective treatment of the progressive symptoms and disability of COPD and IPF, and possibly CF, is pulmonary rehabilitation, which converts the downward spiral of progressive weakness into a virtuous cycle (McCarthy et al. 2015). It improves breathlessness, exercise capacity, sense of mastery over the disease, and anxiety. Pulmonary rehabilitation is a treatment based on exercise, disease education, and social interaction. Participants usually attend between 8 and 12 classes spread over 6–10 weeks. The main effect of pulmonary rehabilitation is improved exercise capacity in the muscles, but there is now increased evidence, from brain scanning, that pulmonary rehabilitation is also associated with changes in the neural responses in the brain to breathlessness, which alter the perception of breathlessness (Herigstad et al. 2017). The challenge for clinicians in treating patients with advanced disease is to judge whether their patients can undertake pulmonary rehabilitation. Evidence for the effectiveness of pulmonary rehabilitation in moderate and severe disease is undisputed. There has been less study of its effect in patients with advanced disease, but such is its effectiveness in other groups; it should be considered in the most severely affected patients.

Low mood together with anxiety is a common accompaniment of chronic breathlessness and is frequently seen in COPD and IPF. The evidence for the effectiveness of the treatment of psychological symptoms in moderate or severe respiratory disease is limited. Chronic breathlessness often leads to social isolation and dependence on carers. The progressive deterioration seen in COPD, in IPF, and in cystic fibrosis is dispiriting. The chronic breathlessness also leads to insomnia and loss of established sleep patterns. In COPD, commonly caused by smoking, many patients will have suffered criticism from family, friends, and health professionals for failing to give up smoking. The implication of this criticism is that the disease has been self-inflicted, and some patients with advanced COPD feel undeserving of treatment or of the support of family and friends.

IPF by contrast with COPD is of unknown cause, has no specific treatment, and will be completely unfamiliar to most patients. IPF and CF patients may not share the sense of blame that is common in COPD. They are more likely to feel perplexed and hopeless. For all of these patients, the burden of the disease is immense, and patients' resilience is undermined further by low mood and anxiety.

4 Trajectory and Prognosis in Advanced Progressive Respiratory Disease

Prognosis is one of the more vexed areas in the management of advanced chronic respiratory disease. With IPF prognosis is worse than in many cancers. As respiratory function deteriorates, it is possible to predict roughly when a patient is likely to die (Shaw et al. 2017). The advantages that accompany this relative accuracy are the opportunities for informing patients and their families what is likely to lay ahead and for enabling patients and families to plan for the implications of the patient's death.

In cystic fibrosis prognosis is a much less precise possibility. While the disease is progressive, deterioration is determined by respiratory infection (Keogh et al. 2018). Damage is caused to the lung parenchyma by infection and mucous plugging. With each infection the process is accelerated. This is a well-documented trajectory. Death is unpredictable because it is likely to occur during an infection. The gaps between infections may be prolonged. However, the experience of people dying very prematurely from cystic fibrosis has

led to little attention to the palliative care aspects of the disorder in the research literature. Recent research on palliative care of CF has suggested that the preoccupation with preventing further progression of the disease may have drawn attention from the need to prepare those for whom death was a likely possibility. Patients and families may be unprepared for deterioration and death.

The situation with COPD is strikingly different. For many years it was the hope of most people interested in improving the management of advanced chronic respiratory disease that with more careful assessment and more careful research, it would be possible to make the prediction of the risk of death more accurate. Alas we are now more confident than ever that there is little hope of predicting the risk of death within a year in COPD.

5 Issues in Specific Diseases

5.1 COPD

The clarity with which patients with advanced COPD have indicated breathlessness as their dominant symptom, while affirming their commitment to living presents a complex dilemma (White et al. 2011; Pinnock et al. 2011). Breathlessness is a very difficult symptom for which there are limited therapeutic options. Yet patients would prefer to take their chances with the next exacerbation, with the limited treatment available, than hope for their symptoms to be relieved by death. The severity of breathlessness in COPD has been compared with that in advanced cancer (Gore et al. 2000). How is it that COPD patients with breathlessness in advanced disease manage their everyday lives? Clearly it is not easy, but a number of factors distinguish patients with COPD from those with cancer and indeed patients with IPF. The breathlessness of COPD is slow in developing, often over more than 20 years. As it progresses it is likely that patients adjust to the symptom in their perception and in their expectations. If the status quo is breathlessness on exertion, then the symptom will have no surprise element, and impaired function will the norm. As breathlessness at rest increases then, there are the accompanying problems of exhaustion, low mood, and progressive immobility. But COPD patients are often remarkably phlegmatic and accept these changes as part of the disease.

Prognosis in COPD is a thorny issue. In a landmark study in the USA in 1996, of 1016 COPD patients admitted with Type II respiratory failure (hypercapnia ± hypoxia), 50% were still alive after 2 years (Connors et al. 1996). Six years later this study was effectively repeated on a smaller scale in Spain (Almagro et al. 2002). In the later study, the survival in a similar group of patients was 65%. In such severely affected patients, the most accurate prognosis possible was a risk of dying between 35% and 50% within 2 years.

Some 15 years ago, COPD patients were reported to have expressed an interest in knowing their prognosis when asked if they wanted their physician to discuss it with them (Curtis et al. 2004). There are concerns as to whether it is ethical to ask research participants this question when an accurate prognosis was beyond the capacity of specialists or generalists. A conclusion to this question has been effectively drawn by the latest work by Almagro and colleagues (2017). They have demonstrated that a prognosis of less than 1 year is impossible to make in advanced COPD with all the disease-specific and general demographic information available.

For patients with advanced COPD or CF, and their clinicians, introducing the subject of advance care planning may seem counter to the flow of communication. One of these exacerbations may be fatal. Has important communication of this risk been considered with dependents and key intimates in their lives? Do affairs need to be put in order? Are there treatment options that should be reviewed? This opportunity must be seized because it is unlikely that a definitive prognostic moment will present itself. The opportunity is the result of increasing risk in a long trajectory of risk.

The supportive care of advanced COPD and of CF should include discussion of the stage of the disease, the likely progression of symptoms, the potential complications, and the available treatments. Progression may be accelerated by

exacerbations. The role of smoking cessation in advanced disease is uncertain. More than 40% of people with moderate, severe, or very severe disease, in whom smoking was the main cause of the disease, continue to smoke.

Since survival is important to people with advanced COPD, how can end-stage disease be identified? The terminal stage of COPD, the stage of imminent death, can be identified by a combination of conventional or generic signs of diminishing functional capacity. These include requirement of help with eating, drinking, washing, and toileting by becoming bedbound, by loss of appetite, and by severe weight loss or cachexia. In the presence of advanced COPD, with no other explanation, these signs are suggestive of imminent death. Such a case is presented in Box 1.

Box 1 A Story of Imminent Death in COPD

MD, a single man of 57 years, had COPD diagnosed at the age of 54. His COPD probably began in his mid-40s to judge from the onset of his cough and breathlessness. He was a scaffolder until 2 years ago, when his breathlessness stopped him from working. He had two hospital admissions due to his COPD in the previous 6 months. The most recent was associated with a marked deterioration. He had been ventilated during the admission and was in the hospital for nearly 3 months. No other cause was found. The doctors said there was nothing more that could be done, and he was at risk of readmission. On discharge from the hospital, he was breathless at rest and prone to confusion. He was on long-term oxygen therapy for chronic hypoxia. He was taking his inhaled drugs by nebulizer every 4 h.

He was looked after at home by his two sisters, one of whom had come to stay. Within 2 weeks of his discharge, he had deteriorated again. He was more short of breath and confused, and he was refusing food. With his sisters' help, he was using a commode. At this point his GP, who had known him for years, was shocked at his cachectic state. He wanted to readmit him to the hospital. His sisters pleaded for him not to be readmitted because he had asked them to promise not to let him be sent back. They felt that he was dying.

The GP examined him. MD was confused. His heart rate was 104/min; his respiratory rate was 36/min. He was cyanosed. There was no fever and no evidence of pneumonia. After discussion with MD's sisters, it was agreed that MD would spend the night at home and that an urgent request for assessment by the palliative care team would be made. The GP told the sisters that MD may not survive for many days in this condition. They said they knew that already.

The following day a call came from MD's sisters. He had died during the night.

The uncertain trajectory of advanced COPD, the prolonged experience of severe symptoms, and the long-term adjustments that patients make demand a palliative care approach which is about support, symptom management, and psychological adjustment. End-of-life care is not the dominant concern in COPD for the main part. Patients with advanced COPD are more likely to see themselves living with their disease than dying from it. Until they enter that final period in which cachexia and rapid loss of function are the predominant features, it is more appropriate to provide palliative care that has an outlook that matches that of the patient. Interventions should be symptom-responsive. Talk about symptom management and supportive care should be the dominant component where appropriate, not preparation for the imminent end to life.

5.2 Idiopathic Pulmonary Fibrosis

IPF presents an altogether different challenge to that of COPD. It is a disease with a limited prognosis from the outset. The annual rate of

decline of FEV_1 from diagnosis is usually between 10% and 20% of expected so that the progression of the symptoms is so rapid that there is much less time for adjustment than is seen in COPD. The loss of function is more obvious and more alarming to family and friends. The diagnosis is like that of a malignant disease, with moderate but relentless progression. As the disease progresses, so does functional impairment. The value of pulmonary rehabilitation at this stage should not be underestimated. It is common for the suggestion of the potential benefits of pulmonary rehabilitation to be lost on breathless patients. Recovering a small degree of functional improvement can make a surprising difference.

Early and effective information provision in IPF for the patient and for carers can allow for effective planning. Advance planning is needed to prepare for inevitable challenges at work, for financial commitments, for discussion with close family, and for the preparation of impending loss. Patients with IPF should be considered early for referral to multidisciplinary clinics for the management of breathlessness. The rapid deterioration in symptoms may mean that there is a greater role for psychological interventions for breathlessness and for the use of opioids.

The recent introduction of antifibrotic drugs, pirfenidone, and nintedanib, for IPF, has been shown to slow the progression of the disease in many patients (Nathan et al. 2017; NICE 2016). Should this intervention be shown to be effective in the later stages of the disease, there may be hope that its terminal stages can be postponed.

While the rate of deterioration in IPF is rapid by comparison to COPD, it is an uncommon disease, and little research has been done on the palliative care of the condition. Careful monitoring of change in FVC can be used, and from this the clinician can obtain a relatively accurate estimate of prognosis.

5.3 Cystic Fibrosis

Change in the last 50 years in the life expectancy of cystic fibrosis from birth has been remarkable. The progress of cystic fibrosis is usually intermittent, but 50 years ago the prognosis from birth was less than 15 years. Even before the disease becomes advanced, the life-threatening nature of acute infections may be unavoidable. Acute severe infections should provide a timely opportunity to consider how interventions can be optimized and the importance of early intervention with antibiotics in worsening breathlessness. They also show how such infections raise problems of antimicrobial resistance and the risk of dying. Advance care planning in CF requires good continuity of care especially as sufferers move through adolescence.

Little research has been published on the palliative care of CF. It seems likely that the patient, the carers, and the clinicians become preoccupied with early intervention and careful management of acute exacerbations of the disease. At some point there must be an opportunity to consider the increasing risk that the patient faces of an exacerbation being life-threatening. This may be addressed when patients are considered for lung transplant. There will have been appropriate and earlier occasions when the subject could have been raised. It would be remiss of services not to respond to the opportunity at the right time.

6 The Assessment and Treatment of Breathlessness

Breathlessness in advanced disease has a variable association with measures of respiratory function, particularly reductions in FEV_1 and FVC. The control of breathing and the experience of breathlessness are determined by a complex array of physiological and psychological influences and controls (Currow et al. 2016). These include the peripheral stimuli associated with movement in the muscles of respiration; the movement of air in the face, mouth, and pharynx; and drying of the mouth and pharynx with increased breathing. Internal factors include levels of oxygen, carbon dioxide and acid/base balance in the blood, and emotional factors, including expectations and learned responses. Such is the complexity of the

interactions of these different elements that it is hardly surprising that people have very different experiences of breathlessness for the same levels of disease severity. To understand the role of treatments for breathlessness in advanced disease, it is worth considering the underlying issues of low oxygen (hypoxia) and raised carbon dioxide (hypercapnia) in advanced respiratory disease.

The effect of impaired breathing due to obstruction and parenchymal damage in COPD, and due to restriction of respiratory movement in IPF, is to reduce the delivery of oxygen (O_2) into the blood and to reduce the removal of carbon dioxide (CO_2). Patients with advanced COPD usually develop tolerance in the brain to increased CO_2 (hypercapnia). The main drive to breathing in established COPD is reduced oxygen in the blood, hypoxia. In such patients complete relief of hypoxia by giving O_2 diminishes the drive to breathe. If the drive to breathe is reduced, the CO_2 level in the blood may rise to dangerous levels. This can cause the patient to become drowsy or unconscious – CO_2 narcosis – and ultimately to be in danger of dying. Patients dependent on hypoxia for the drive to breathe may be at considerable risk in receiving unlimited O_2 for symptom relief.

On the other hand, patients with persistent hypoxia may require long-term oxygen therapy to prevent pulmonary hypertension. The identification of hypoxia, O_2, below a saturation of 92% on a pulse oximeter, should lead to specialist referral for consideration of long-term oxygen therapy.

For patients that become intermittently hypoxic on exercise, intermittent oxygen may be needed. In the unusual situation that a severely ill patient becomes hypoxic at rest, then low dose (2 L/min) oxygen can be administered to relieve breathlessness until the patient is assessed by a specialist. The relief obtained is likely to be small if any.

The perception of breathlessness in the brain is complex. It varies from person to person, some people appearing to tolerate breathlessness in more severe disease than others. Breathlessness perception and the tolerance of breathlessness can be markedly affected by anxiety. Understanding the mechanisms of breathlessness is tied to the therapies that are brought to bear on the symptom in advanced disease. These are pulmonary rehabilitation, breathing training and exercises, therapy for anxiety, handheld fan, neuromuscular electrical stimulation, and the suppression of the perception of breathlessness with drugs (Higginson et al. 2014; Farquhar et al. 2016; Maddocks et al. 2017). Pulmonary rehabilitation and a handheld fan can be prescribed in primary care. If the patient needs breathing training, therapy for anxiety, neuromuscular electrical stimulation, or the use of drugs, referral should be made to a multidisciplinary center.

Breathing training and exercises work by promoting more efficient posture for breathing and by reinforcing the sense of control of breathing when the patient is more breathless through specific physical strategies to manage the breathlessness. Some people experience a cycle of worsening breathlessness in which the breathlessness causes anxiety, which in turn leads to hyperventilation and a sensation of even worse breathlessness. This combination is difficult to identify. It may be evident from an exceptional response to breathing exercise which is accompanied by a marked reduction in anxiety. The handheld fan is of variable value. It probably works by blowing air across the lips and cheeks generating a sense of greater movement of air and of more effective breathing. Neuromuscular electrical stimulation is designed to improve breathlessness by improving peripheral muscle power (Maddocks et al. 2016). It is effective in reducing the effect of exercise on breathlessness. But how long the effect is sustained has not been assessed, and it is only available in specialist centers.

The suppression of breathlessness by opioids has been used for many years in people with advanced cancer, particularly in their last days. The development of tolerance and dependence is not an issue in such circumstances. In advanced respiratory disease, the circumstances are different. Evidence is slowly coming to light about appropriate dosing and the risks of prolonged use. The case in Box 2 highlights some of the issues.

Box 2 Opioids in Chronic Respiratory Breathlessness? A Case History

SB, a widower of 74 years, had COPD for 15 years. Having been a smoker since a teenager, he was still smoking three or four cigarettes a day. He lived alone and was a volunteer driver for the local hospital, taking patients to and from their appointments. He liked his voluntary work, but his breathlessness was increasingly troublesome. He had difficulty sleeping at night and had to sit up. He was on maximal treatment for his COPD. He was not hypoxic. His GP referred him to the local chest clinic to rule out lung cancer.

The chest physician investigated SB. No new problems were identified. There was no sign of cardiac disease. He was told to continue on his medications and discharged from the clinic. He had started pulmonary rehabilitation 6 months ago, but he did not think it was helping, so he stopped after two sessions.

After another 6 months, SB's breathlessness was worse. He now spent all of his time at home, breathless at rest. He was again referred to the chest physician who discharged him saying there was no further treatment that would help his COPD.

SB's GP did not know what to do next. She referred SB to the local palliative care breathlessness clinic. SB was seen there by a palliative care physician and palliative care nurse.

SB was referred to a psychologist to treat the anxiety associated with his breathing and to a physiotherapist for breathing exercises and breathing training. He was given a handheld fan. After 4 months there was little change. SB was then started on oral morphine 2.5 mg four times daily. His breathing improved for the first time in perhaps a year. His exercise capacity was no different, but he felt better and slept better. SB was admitted to the hospital with an exacerbation of COPD 9 months after starting morphine. He was taking 5 mg in the morning and the evening and 2.5 mg twice during the day. His breathlessness was still better. Sadly he developed pneumonia and died.

It is clear that this patient has advanced COPD. The multidisciplinary team had run out of options, and so morphine was started. He was taking relatively small amounts of morphine for a prolonged period of 9 months until an exacerbation led to his death. It is unclear if the morphine retained its effectiveness or whether the increase in dosing had an impact on his death in terms of his response to the exacerbation. The morphine had been very helpful in improving the symptom for a long period of time.

The usual dosage of morphine currently recommended for advanced respiratory disease is a starting dose of 10 mg daily as a sustained release preparation (Smallwood et al. 2015). This can also be administered as 2.5 mg of immediate acting morphine up to four times daily. The maximum dose should be 30 mg. There is no evidence of difference of effectiveness between different opioids, but most of the current evidence relates to morphine. Among the issues yet to be addressed with respect to morphine use in advanced respiratory disease are the long-term effects on survival, the development of tolerance, the sustained effect on symptoms, and the need for larger amounts during exacerbations. Within the dosage guidance described here, general practitioners may wish to start opioids for COPD patients with intractable. It may be wise to do so with the support of a palliative care team for those who are inexperienced. It should only be initiated for advanced respiratory disease in specialist centers until evidence for its use becomes clearer.

7 Supporting Carers in Respiratory Disease

Carers of people with advanced IPF have needs that are similar to those of carers with advanced cancer. The needs of carers of people with COPD

and CF are different. It is only recently that the needs of this group have begun to be examined (Farquhar 2017). They relate to the slow progression of the disease, the lack of certainty about the prognosis, the frequency of exacerbations, and the isolation that comes with caring for a person with severe functional impairment who may be housebound. Spouses or partners do much of the caring. Just as many people with COPD have comorbidities, so do many of their carers.

8 Conclusion

The goal of treatment of advanced progressive respiratory disease must be in keeping with both the aspiration of patients and the practical realities of the stage of the disease. In COPD and in CF, defining prognosis is so difficult that priority should be given to informing patients and trying to meet their hopes and expectations. In IPF, prognosis may be so limited that clear information about the risk of impending death should be available to the patient and the relatives in line with their perceived need. In COPD and in CF, breathlessness may become slowly intractable over 20 or more years so that life eventually becomes barely tolerable. In IPF this is likely to be the case at a more rapid pace over 2–3 years. There are many remedies to be considered in the breathlessness of COPD and IPF. In all three diseases, morphine may have a role in reducing the perception of breathlessness. In IPF morphine may also have a role in cough which affects 80% of sufferers and is progressive. Morphine in low doses does not suppress breathing, does not appear to generate tolerance, and seems safe in the breathlessness of advanced respiratory disease.

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Palliative Care and Liver Diseases

63

Anne M. Larson

Contents

Abstract

Liver disease leads to over 4 million visits to medical practitioners and over 750,000 hospitalizations per year in the USA. Those with chronic liver disease frequently progress to cirrhosis, end-stage liver disease (ESLD), hepatocellular carcinoma, and death. Patients with ESLD experience numerous complications, including muscle cramps, confusion (hepatic encephalopathy), protein calorie malnutrition, muscle wasting, fluid overload (ascites, edema), bleeding (esophagogastric variceal hemorrhage), infection (spontaneous bacterial peritonitis), fatigue, anxiety, and depression. Despite significant improvements in palliation of these complications, patients with liver disease still suffer reduced quality of life and must confront the fact that their disease will often inexorably progress to death. Liver transplantation is a valid option in this setting, increasing the duration of survival and palliating many of the symptoms. However, many patients die waiting for an organ or are not candidates for transplantation due to comorbid illness or psychosocial issues. Others receive a transplant but succumb to complications of the transplant itself. Patients and families must struggle with simultaneously hoping for a cure while facing a life-threatening illness. Ideally, the combination of early palliative care with life-sustaining therapy can

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_62

maximize the patients' quality and quantity of life. If it becomes clear that life-sustaining therapy is no longer an option, these patients are then already in a system to help them with end-of-life care.

1 Introduction

1.1 The Scope of the Problem

Chronic liver disease affects 30–35 million persons in the USA, 29 million in the European region, and even more worldwide (Younossi et al. 2011). It leads to over 4 million US ambulatory physician visits annually, with >3.5 million visits for viral hepatitis alone. Chronic liver disease often progresses to cirrhosis and subsequent liver failure. There are 5.5 million cirrhotics in the USA, and the global prevalence of cirrhosis from autopsy series is as high as 712 million (9.5% of the population) (Scaglione et al. 2015; Lim and Kim 2008). Annually, over 750,000 US hospitalizations can be attributed to acute and chronic liver disease. US health-care costs in this population approach almost $4 billion annually, and the incidence of hospitalizations due to cirrhosis and its complications is rising significantly. Similar figures are seen worldwide. Within a month following discharge, up to 37% of cirrhotic patients are readmitted at a mean cost of nearly $30,000. The more frequent the readmission rate, the greater the risk of subsequent mortality. In 2014, 38,170 US deaths were attributed to chronic liver disease and cirrhosis – 26.4% per 2-year interval compared to 8.4% in matched controls (Scaglione et al. 2015; Kochanek et al. 2016). In 2010, over 1.0 million deaths (2% of all deaths) worldwide were attributable to hepatitis and cirrhosis (Mokdad and Lopez 2014; World Health Organization 2017). It is estimated that globally, another million deaths were due to liver cancer and acute hepatitis. This number is likely even greater, given the scarcity of mortality data in Sub-Saharan Africa and other countries (i.e., Pakistan, Bolivia, Laos, and North Korea) (Sankoh and Bypass 2012). Chronic liver disease and cirrhosis were the 12th leading cause of death in the USA, and the age-adjusted death rate has increased from 9.6/100,000 in 1999 to 10.4/100,000 in 2014 (Kochanek et al. 2016). In 2009, malignant liver neoplasms, cirrhosis, and alcoholic liver disease were the 3rd, 4th, and 5th leading causes of death due to gastrointestinal disease, respectively.

Both the incidence and the death rate of liver cancer have also gone up in the USA and worldwide (Fig. 1). From 2003 to 2012, the US incidence increased by 2.3% per year – an overall increase of 72% (Ryerson et al. 2016). Since 2003, there has been a 56% increase in deaths from liver cancer. In 2016, an estimated 39,230 persons were diagnosed with liver and bile duct cancer and 27,170 (69%) died from the disease (Howlader et al. 2016). Liver cancer was the 13th leading cause of cancer death in the USA and accounts for 750,000 to 788,000 deaths annually worldwide, the 2nd most common cause of cancer death. The relative 5-year survival rate for liver cancer is about 16–18% overall. For those whose cancer is discovered while still at a localized stage, the 5-year survival rate is still only 30.5%. The median age at death is 67 years and the rate is highest among persons aged 55–64 years (Fig. 2).

Chronic viral hepatitis is a major risk factor for hepatocellular carcinoma (HCC) and correlates with the increasing trends in HCC incidence. Approximately 50% of cases of liver cancer are related to chronic hepatitis C virus (HCV) infection and 15% to chronic hepatitis B virus (HBV) infection (Ryerson et al. 2016). There are millions of at-risk individuals with viral hepatitis. Up to 2.2 million persons in the USA and 350 million worldwide are living with chronic HBV infection, with a prevalence as high as 25% in some countries (Zampino et al. 2015). As many as 130 to 150 million worldwide are living the chronic HCV infection with 2.7–3.5 million persons in the USA. Additionally, cirrhosis and HCC secondary to nonalcoholic fatty liver disease are rapidly increasing. It is believed that at least a quarter of chronic HCV patients have yet to be diagnosed. Other important risk factors for development of hepatocellular carcinoma include chronic liver disease secondary to excessive alcohol consumption, nonalcoholic fatty liver disease (affecting

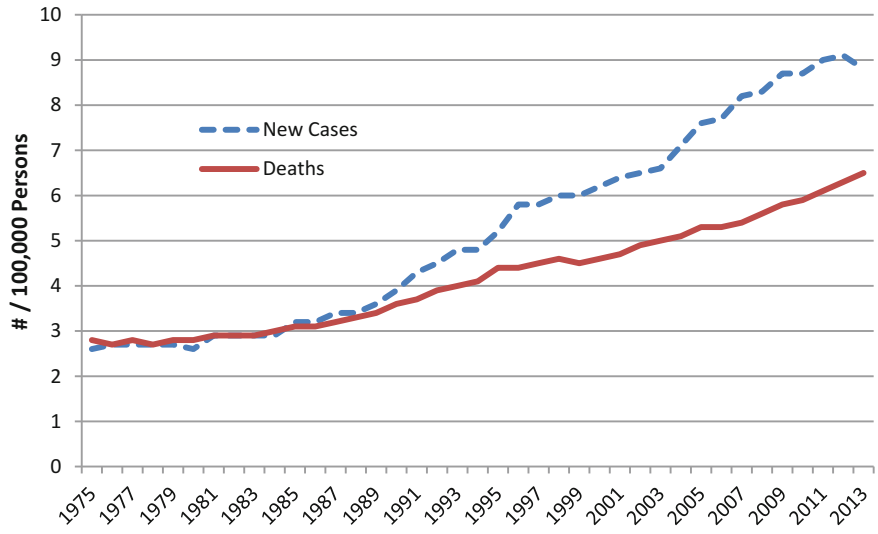

Fig. 1 New cases of hepatocellular carcinoma and age-adjusted death rate (From: SEER Cancer Statistics Factsheets: Liver and Intrahepatic Bile Duct Cancer. National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/statfacts/html/livibd.html)

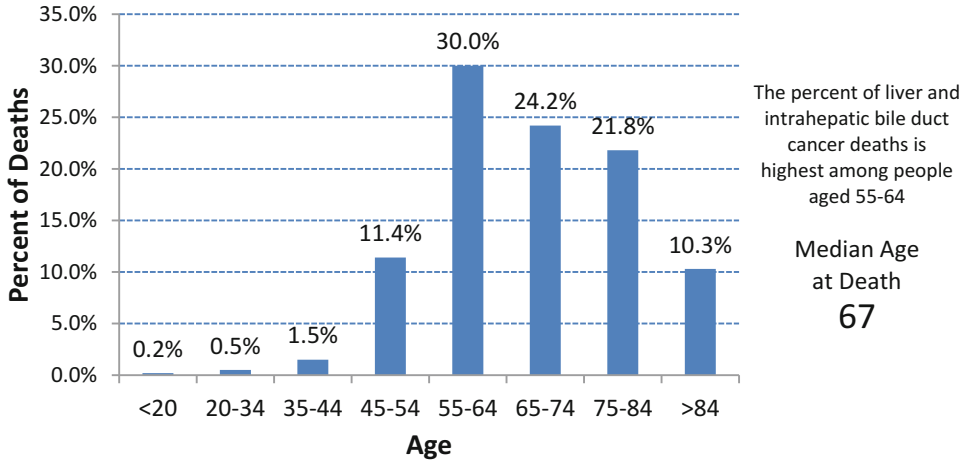

Fig. 2 Primary liver cancer death rate by age. From: SEER Cancer Statistics Factsheets: Liver and Intrahepatic Bile Duct Cancer. National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/statfacts/html/livibd.html

20% of the worldwide population), and other metabolic and genetic disorders.

2 Palliative Care and Hospice Services

Palliative care (PC) is defined as an approach that improves the quality of life (QoL) of patients and families facing the problems associated with life-threatening illness. This is accomplished through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems – physical, psychosocial, and spiritual (World Health Organization 2017). Palliative care is a board-certified specialty in the USA, and between 2000 and 2010, there was nearly a 150% increase in palliative care teams (Wordingham and Swetz 2015). Across Europe and elsewhere, specialist

palliative care (SPC) provides multidisciplinary specialist care – from a team with training and ongoing education in palliative care and working predominantly with this patient group. SPC physicians are specifically trained in the early recognition and management of both pain and non-pain symptoms, psychosocial and spiritual support, and advanced care planning. An experienced interdisciplinary PC team provides support not only to the patient and their family but to the primary team caring for the patient. Treatment is not excluded if it helps the patient and is in line with the goals of their care (Walling and Wenger 2014; Kelly and Rice 2015). Palliative care is designed to meet the preferences, goals, and values of the patient, and patient satisfaction is greater if these needs are met (Wordingham and Swetz 2015).

There is often confusion between palliative care and hospice or end-of-life care. In the USA, hospice has traditionally focused on comfort and quality of life, rather than disease-directed therapy (i.e., symptom management) (Wordingham and Swetz 2015), and hospice teams, although interdisciplinary, rely more on nursing assistants, volunteers, and bereavement specialists. Hospice is often considered a component of palliative care. In other countries, this may be seen as end-of-life care and usually is seen to be relevant in the last 6–12 months of life or more. For example, in the UK, end-of-life care is defined as "support for people who are in the last months or years of their life," and palliative care is considered a component of end-of-life care (National Health Service 2017). This confusion between palliative care and hospice/end-of-life care may lead to the avoidance of involvement of the palliative care team in patient with ESLD, particularly in the setting of potential liver transplantation. These specialists, however, can be of great assistance to patients and also help make the determination when the transition to hospice care would be beneficial for the ESLD patient (Brisebois and Tandon 2015).

Palliative care and hospice/end-of-life care are complementary entities, with palliative care supporting the quality of life and symptom burden of those with an ultimately terminal illness (Strand et al. 2014). Historically, there has been very little guidance for the use of palliative care in the setting of ESLD (Potosek et al. 2014). Palliative and hospice/end-of-life care have more traditionally been used in the setting of illnesses whose progressive disease course is clear, such as end-stage cancer. Patients with non-cancer illness such as ESLD are less likely to receive palliative care services than those with cancer (Wachterman et al. 2016; Walling et al. 2017). Palliative care is of significant value and ideally may be utilized at any stage of disease for any patient with a serious or life-threatening illness, including ESLD (Strand et al. 2014). Patients involved with palliative care experience improved quality of life, decreased depression and anxiety, and longer survival and feel that there is better alignment of their goals with their medical care (Kelly and Rice 2015; Strand et al. 2014). Early palliative care is also associated with reduced health-care costs (Harris and Murray 2013). Palliative care should therefore be considered compatible with the management of ESLD patients, including those listed for liver transplantation (Brisebois and Tandon 2015).

3 Discussing End-of-Life Issues in ESLD

Once the diagnosis of cirrhosis and end-stage liver disease is made or complications develop, patients are often frightened and wonder how they could have reached this point. They may be angry that they were unaware of the ultimate consequences of their illness. They often absorb only a small proportion of what is being told to them and have trouble piecing it all together. Patients must ultimately confront the fact that their disease will inexorably progress to death. Liver transplantation may be a valid treatment option in this setting, increasing the duration of survival and palliating many of the symptoms. These patients must be "sick enough to die" to be considered for transplant (Larson and Curtis 2006). Up to 10–15% listed for liver transplantation will die without receiving an organ, and there are many patients who are not candidates for liver transplantation.

There are medical and nonmedical contraindications to liver transplantation. The more common reasons include extrahepatic malignancy, comorbid medical disease (i.e., significant cardiopulmonary disease, active infection), multisystem organ failure, inadequate social support, inadequate finances, and ongoing alcohol or drug abuse. Furthermore, some patients will receive a liver transplant but succumb to complications of the transplant itself, including graft failure, infection, bile duct complications, or post-transplant cancers. The 1- and 3-year patient survival rates after liver transplant depend on many factors but in the USA they average about 90% and 80%, respectively.

Receiving news of a terminal or life-limiting diagnosis is stressful and evokes strong emotions such as fear, anxiety, anger, depression, despair, hopelessness, and helplessness. In addition to dealing with physical and life-threatening symptoms, patients experience psychological and emotional stress, financial concern, and worry about their family (Ryerson et al. 2016; Boyd et al. 2015). They must also deal with uncertainty regarding the development of acute, life-threatening complications (Hope and Morrison 2011; Boyd et al. 2015). Early discussion of end-of-life issues is thus essential in the management of all patients with ESLD, including those being evaluated for liver transplantation (Boyd et al. 2015). Palliative care specialists have expertise in communication, and their involvement in this setting provides benefit to both the patient and medical practitioner (Tulsky 2005; Brisebois and Tandon 2015), but all professionals seeing patients with ESLD should be able to provide honest and open communication, which improves understanding of patient's wishes and goal-oriented care (Lamba et al. 2012).

Patients and their families must fully understand the disease and its prognosis and be prepared for all potential outcomes to make realistic treatment decisions. These discussions need to occur early during the course of the disease, ideally prior to the development of significant complications such as hepatic encephalopathy, variceal hemorrhage, ascites, or hepatocellular carcinoma. Discussions become particularly challenging in the presence of hepatic encephalopathy which further impedes communication and the patient's ability to make decisions. Practitioners should anticipate this and engage the patient and their family early in advance care planning (Highet et al. 2014). Physicians face the additional challenge of supporting hope for a good outcome while providing patients with accurate prognostic information. These discussions are particularly difficult in the setting of ESLD because of its highly unpredictable trajectory. Patients often experience periods of relative health in between episodes of severe, life-threatening hepatic decompensation. Very often physicians and practitioners are overly optimistic regarding the prognosis, confusing patients further (Janssen et al. 2011; Abdul-Razzak et al. 2014; Parry et al. 2014).

There is also a substantial burden on the caregivers of patients in this setting, particularly if the patient has developed hepatic encephalopathy and can no longer adequately participate in decision-making (Bajaj et al. 2011; Rodrigue et al. 2011; Walling and Wenger 2014). Family members may be asked to be involved in helping to make decisions for the patient. Which family member is responsible for this assistance depends on country and local laws and whether there is a clear documentation as to who the patient prefers in this position. If clear documentation is not available, most governments determine who is legally responsible – i.e., in the USA it is the spouse followed by the children if no spouse is available, etc. The need for becoming the decision-maker is particularly stressful if the caregiver is unaware of the patient's wishes or family members have differing opinions on what should be done. Patients with liver disease associated with significant substance abuse may lack a strong social network. There are often inner-family disputes regarding the abuse. Family estrangement can be seen, particularly if there are feelings of abandonment, anxiety, blame, or anger toward the addicted patient. Thus, the lack of close family to provide support further complicates communication and long-term care planning (Walling and Wenger 2014).

Palliative care discussions can become particularly difficult if the ESLD patient is being considered for or has been listed for liver transplantation. Patients must face dealing with the risk of an early

death while at the same time focusing on the hope of receiving a life-saving transplant – "hope for the best and prepare for the worst." The patient must be helped to understand that they may experience a catastrophic decline in their condition before transplant can be provided or may receive a transplant only to die of post-transplant complications. These competing outcomes lead to a "roller-coaster ride" of emotions which is difficult for all involved (Larson and Curtis 2006). Throughout the transplant evaluation process, patients and their families struggle with the uncertainty of whether they will ever receive a transplant (Boyd et al. 2015). Those for whom liver transplant is not available or has failed face having their hopes dashed and confronting their terminal illness head on.

The discussion regarding the use of do-not-attempt resuscitation (DNAR) orders in the setting of ESLD is even more controversial. Decompensated cirrhotics have lower rates of DNAR orders when compared to lung cancer patients or those with other chronic illnesses (Larson and Curtis 2006; Stotts et al. 2014; Brisebois and Tandon 2015; Wachterman et al. 2016). The possibility of receiving a liver transplant adds complexity to the discussion of DNAR, and many argue that liver transplant candidates should not carry this type of directive. There is often fear that the patient may be transitioned to hospice/end-of-life care prematurely while awaiting transplantation. Resuscitation may be reasonable for patients who are still healthy enough to survive resuscitation efforts without compromising future treatment options such as transplant. As ESLD progresses, however, and patients become more critically ill, the possibility of transplant futility must be addressed (Biggins 2012; Petrowsky et al. 2014). Resuscitation is rarely successful in the critically ill ESLD patient who experiences a catastrophic event (e.g., cardiopulmonary arrest) (Roth et al. 2000; Cholongitas et al. 2006; Stotts et al. 2014). Despite successful resuscitation, the event may further compromise transplant outcome or prevent transplant altogether. In this setting, DNAR orders may be appropriate.

4 Integrating Palliative Care with ESLD Management

At the time of this writing, there are no guidelines specific to the use of palliative care in the setting of end-stage liver disease (Brisebois and Tandon 2015). Aggressive medical care is generally aimed at improving both quantity and quality of life – both of which decline as the ESLD progresses. Most patients with chronic liver disease feel well for decades, often completely unaware of the progressive nature of their illness (Scaglione et al. 2015). As the disease relentlessly progresses, however, patients may develop nonspecific symptoms such as fatigue, even in the absence of cirrhosis or liver failure. Fatigue is in fact one of the most frequently identified symptoms of chronic liver disease and cirrhosis and can lead to a substantial decrease in quality of life.

Once chronic liver disease is diagnosed or complications abruptly develop, patients often experience psychological distress which further contributes to their poor quality of life (Nardelli et al. 2013). There may be little time to adjust to the diagnosis. If disease is perceived to be "self-inflicted," there are often issues of blame and anger. Depression and anxiety frequently follow (Nardelli et al. 2013; Perng et al. 2014). Self-reported quality of life is remarkably poor in cirrhotics. The cirrhotic liver eventually decompensates, leading to end-stage liver disease (ESLD), the final phase in disease trajectory. At this point, patients experience pronounced morbidity and develop a very high symptom burden. Symptoms and complications include pain, nausea, muscle cramps, dyspnea, cognitive dysfunction (hepatic encephalopathy), anorexia, malnutrition and cachexia, fluid overload (ascites, edema), profound fatigue, and pruritus (Larson and Curtis 2006; Potosek et al. 2014; Poonja et al. 2014; Cox-North 2015). Additionally, they may experience such life-threatening complications as variceal hemorrhage, spontaneous bacterial peritonitis, or hepatocellular carcinoma. Life-saving liver transplantation is available only to a small subset of these patients.

4.1 Barriers to Palliative Care Referral

There are many barriers to the consideration of palliative care in the setting of cirrhosis and ESLD. Although the field of PC is expanding, access remains limited for a considerable portion of patients, particularly in the outpatient setting (Rakoski and Volk 2015). In US hospitals with more than 50 beds, only two-thirds reported palliative care programs in 2012 (Rakoski and Volk 2015). In London, it was reported that there were 322 hospice beds (15 providers) for a population of 9,323,570 (Cox et al. 2016). Worldwide, it is estimated that only 14% of the 40 million people in need of palliative care receive it (Palliative Care 2017). In 2013, Lynch et al. found that 42% of 234 countries surveyed had no viable palliative care services and 32% reached only a small percentage of the population (Lynch et al. 2013). Palliative care is rare or nonexistent in Mexico, South America, Africa, and Russia.

Cirrhotic patients may not appear "sick" and, therefore, may not be considered to need help with symptoms or to be at risk of dying. The marked symptom burden in these patients is frequently not identified as an important issue by physicians, caregivers, family, or friends (Poonja et al. 2014). The trajectory of liver failure is unpredictable compared with that of other terminal illnesses, such as advanced cancer (Walling and Wenger 2014). This is particularly true earlier in the disease course or if symptoms (i.e., encephalopathy or ascites) have been medically well controlled. This waxing and waning of symptoms makes care planning and projection regarding end-of-life issues more complicated. This prognostic uncertainty, however, should not be a barrier to referral to either palliative care or hospice care (Wordingham and Swetz 2015).

Discussing palliative care and advance directives may appear to be at odds with pursuit of curative or life-prolonging therapies, such as liver transplant (Potosek et al. 2014; Brisebois and Tandon 2015). Patients often have a poor understanding of their disease severity and what palliative care entails (Rakoski and Volk 2015). The discussion can be complicated further if patients refuse to accept their prognosis and focus only on life-saving interventions. The practitioner, patient, or caregivers additionally may view palliative care as synonymous with hospice/end-of-life care and appropriate only during the final days of life – seeing PC as giving up, treatment withdrawal, or imminent death (Boyd et al. 2015; Rakoski and Volk 2015; Cagle et al. 2016; Beck et al. 2016). Additionally, practitioners may be uncomfortable with end-of-life discussions – leaving both the physician and the patient with confusion and uncertainty regarding long-term care goals (Rakoski and Volk 2015; Beck et al. 2016). Patients and caregivers must be helped to prepare for future decisions regarding their care (Boyd et al. 2015). This type of discussion requires excellent communication skills on the part of the practitioner (Brisebois and Tandon 2015).

End-of-life issues in ESLD are frequently not addressed at all or addressed far too late to be of benefit to the patient and their family (Larson and Curtis 2006; Walling et al. 2013; Rakoski and Volk 2015). Poonja et al. reported that only 11% of patients who were too sick for liver transplant were referred to palliative care, despite a high symptom burden (Poonja et al. 2014). They and others have also found that goals of care and do-not-resuscitate status were rarely discussed with these dying patients. Only 28% of those in the Poonja study were designated as DNAR. Hansen et al. followed six ESLD patients who were hospitalized in the ICU and were either on the liver transplant list or being considered for liver transplant. Interviews conducted with multiple staff and family members throughout the course of the hospitalization found that what mattered most to all participants was the goal of liver transplant (Hansen et al. 2012). There was no focus on patient comfort and goals of care until all treatment options had been exhausted, and none of the patients received a palliative care consultation. Kathpalia et al. found that only 17% of patients who died or were removed from the liver transplant list had a palliative care consultation (Kathpalia et al. 2016), and half of these

consultations were within 72 h of death. A more alarming finding was that palliative care services were associated predominantly with younger or Caucasian patients. The lack of palliative and end-of-life care offered to those who are not candidates for liver transplant or have been removed from the liver transplant list often leads to feelings of abandonment by patients.

4.2 Benefit of Palliative Care Involvement in ESLD

The early integration of palliative care and medical care in the setting of ESLD provides great benefit to the patient and caregiver as well as the medical provider (Brisebois and Tandon 2015). The goals of palliative care often overlap the goals of medical care (Larson and Curtis 2006; Potosek et al. 2014; Brisebois and Tandon 2015). All practitioners involved in the patient's care can provide palliative services, including family physicians, nursing staff, transplant services staff and physicians, intensive care staff, and inpatient ward staff. Palliative care specialists provide added support for management of these complicated patients, particularly with regard to end-of-life discussions and psychologic and spiritual support (Brisebois and Tandon 2015). The palliative care specialist can also help the general clinician with the management of physical symptoms. The early integration of palliative care in the setting of chronic disease has been shown to improve QoL and results in longer patient survival. Patients have fewer emergency room visits, ICU admissions, and hospital deaths. Support for the concept of palliative care in the setting of ESLD is growing (Langberg and Taddei 2016). Palliative care services should therefore be considered in any patient who is at risk of dying within the next year from advanced liver disease.

As noted, the course of ESLD is much less predictable than many other chronic illnesses – patients experience episodic periods of exacerbation and recovery. This makes predicting the actual time course of progression to death difficult and contributes to the stress patients and caregivers feel. This also makes the timing of palliative care involvement unclear, most likely contributing to the lack of palliative care referrals in this population. However, survival significantly declines once hepatic decompensation develops (LaFond and Shah 2016). Following development of esophageal varices, the median patient survival is 7–10 years and each variceal hemorrhage carries a 10–20% risk of death (Kelly and Rice 2015). The 2-year survival following development of either hepatic encephalopathy or ascites is 50% (Potosek et al. 2014; LaFond and Shah 2016). Cirrhotics with hyponatremia (serum sodium <135 mmol/L) have a 23% 1-year survival. Patients who develop refractory ascites have a 1-year survival of 32% and those with type 2 hepatorenal syndrome have a 6-month median survival. Those with type 1 hepatorenal syndrome generally survive only a few weeks without transplantation. Thus, palliative care referral, based on needs and symptoms rather than prognosis, may be considered earlier in the disease progression when it becomes more obvious that not only are there increasing symptoms but the outlook is poor.

Early concurrent palliative care significantly benefits the patient with ESLD, and the health-care team providing this care must find ways to integrate palliative care with the possibility of life-prolonging therapy (Medici et al. 2008). It has been suggested that certain clinical findings could be used as triggers for palliative care consultation, including refractory ascites, hepatic encephalopathy, hepatorenal syndrome, bacterial peritonitis, and recurrent variceal bleeding. Additionally, symptoms such as pain, cramping, nausea, and emotional distress could also be used as a guide for referral. Patients with a high symptom burden (i.e., Edmonton Symptom Assessment Scale or SPICT™ clinical indicators) could also be referred. Prognostic scoring systems could also be utilized regarding referral timing. For patients with a model for end-stage liver disease (MELD) score > 20 as a trigger, a VA study showed an increase in PC referrals (62.5% vs 47.1%, $p = 0.38$) (Davila et al. 2012). Several have identified conditions for which a PC referral in an ESLD patient would be appropriate (Table 1) (Brisebois and Tandon 2015; Cox-North 2015; Rakoski and Volk 2015).

Table 1 Indications for palliative care in the setting of ESLD

Indication	Examples
At diagnosis	Patient and family education Planning strategies to improve functional capacity Education regarding advance care planning and goals of care Identify health-care proxies or surrogates
Physical symptoms	Uncontrolled pain Muscle cramping Hepatic encephalopathy Intractable ascites Nausea Anorexia and malnutrition Deterioration in performance status Dependence on others for care needs
Emotional or spiritual distress	Fear of dying Guilt about behaviors which may have caused the disease
Family/caregiver emotional or spiritual distress	Financial stress – time off from work to care for the patient; cost of medical care Exhaustion – continual care of a patient with hepatic encephalopathy Frustration – unpredictable hospitalizations; ups and downs of the liver disease itself
Interfamily conflict regarding goals of care	Family uncertain of patient's desires (severe encephalopathy, intubated, etc.) Family members disagree regarding patient management
Accelerating need for medical care or hospitalizations	Weekly paracenteses Modifying medications to reflect patient goals Frequent hospital readmissions
Curative care unavailable	Patient has been declined liver transplantation Patient has been removed from the liver transplant list
Patient requests palliative care	Patient does not wish to pursue life-sustaining treatment
Physician distress	Difficulty communicating a poor prognosis Lack of curative options Unable to manage symptoms appropriately

Adapted from: Highet et al. 2014, Cox-North 2015, Brisebois and Tandon 2015, Boyd et al. 2015, and Rakoski and Volk 2015

4.3 Palliative Care and Liver Transplant

Palliative care and consideration for liver transplantation are considered by many to be contradictory plans of management (Potosek et al. 2014). This often leads to PC involvement only after all medical options have been exhausted and the patient is near death. However, Baumann et al. showed that there was a clear benefit to combining palliative care with routine liver transplant care (Baumann et al. 2015). These patients had a 50% improvement in symptom scores and were more likely to have care plans in place in anticipation of further decline in health. Additionally, PC services are helpful to the patient for the management of feelings of uncertainty, fear, and the loss of control over their medical condition during the complicated liver transplant process. Goals of care and plans for future end-of-life care are more thoroughly addressed when PC services are involved. Therefore, patients should not be denied the benefit of palliative care while awaiting liver transplantation.

4.4 ESLD Symptoms Requiring Management

4.4.1 Quality of Life

Despite significant improvements in the medical management and the potential for life-saving liver

transplant, ESLD patients still suffer a profoundly reduced QoL and have an increase in health-care utilization. They often have difficulty with activities of daily living, including bathing, dressing, managing money, cooking, shopping, and ambulating safely.

This poor QoL is comparable to that reported by patients suffering from advanced chronic obstructive pulmonary disease or heart failure. Additionally, patients are frequently anxious and depressed which contributes to worse QoL, contributing to more physical symptoms – a vicious cycle. As ESLD progresses, management of the complications of cirrhosis becomes a more time-consuming endeavor and is all too often left to the busy primary care clinician. Increased disease complexity is associated with increased hospitalizations (Strand et al. 2014). Aggressive management of the symptoms of ESLD improves patient QoL. Palliative care teams can assist with this management, as well as help address the patient goals and plans for managing ever-worsening disease (Brisebois and Tandon 2015). Quality of life can be improved and health-care utilization decreased for the ESLD patient with aggressive symptom control.

4.4.2 Ascites

Ascites is the most common complication of ESLD. The development of ascites is one of the most emotionally and physically distressing symptoms for the cirrhotic patient. At least 50% of patients will develop ascites over the 10-year period following the diagnosis of cirrhosis. Ascites leads to abdominal and back pain as well as emotional distress due to an altered body habitus and decrease in mobility. It is associated with about a 50% 2-year survival after onset. Therefore, it is associated not only with an increased short-term mortality but markedly a decreased QoL.

Management of ascites is labor intensive as it progresses, but crucial for patient well-being. Early in the course, it can often be managed with sodium restriction (<2000 mg/day) and oral diuretics. This controls and appreciably reduces the discomfort caused by the ascites in about 90% of patients. Approximately 17% of patients will develop refractory ascites within 5 years of initial ascites development (LaFond and Shah 2016). Refractory ascites fails to respond to sodium restriction and diuretics and leads to an even further decline in the patient's physical and psychosocial well-being. By this point, the placement of transjugular intrahepatic portosystemic shunts (TIPS) may be limited by the presence of encephalopathy and liver failure. The use of indwelling peritoneal catheters in this setting is limited by complications, including peritonitis in 10% within 72 h of placement. Those who develop peritonitis then have a 50% 5-month mortality (Kathpalia et al. 2016; LaFond and Shah 2016). If fluid restriction is ultimately required in the setting of cirrhotic or diuretic induced hyponatremia, the patient's QoL decreases further.

4.4.3 Hepatic Encephalopathy

Hepatic encephalopathy (HE) is one of the most debilitating complications of ESLD. HE presents with a wide spectrum of neurologic or psychiatric abnormalities which range from minimal (subclinical or covert) alterations to frank coma. Minimal HE, the earliest stage, is present in up to 80% of cirrhotics. It manifests with significant impairment in attention, psychomotor speed, visuospatial perception, response inhibition, and delayed information processing (Shaw and Bajaj 2017). These patients then begin to have problems with day-to-day functioning, but this is often completely unnoticed by those around them. The presence of HE, even at the subclinical level, fundamentally complicates the patient's QoL and their medical management. Patients may make mistakes at work, sometimes leading to loss of employment and insurance coverage. Studies have shown that even minimal HE impairs the patient's fitness to drive, particularly regarding car handling, adaptation, attention deficit, and cautiousness. Therefore, independence is lost – driving is not an option once HE develops. They may not take their medications appropriately, often forgetting them, further complicating their management.

The encephalopathic patient should always be accompanied to their physician visits by a trusted family member or friend – someone to help make decisions, write out plans, learn and understand

the patient's medications, and remember details of the visit and discussions. Encephalopathy can generally be managed successfully with lactulose therapy and, if necessary, the addition of rifaximin. As the ESLD progresses, however, HE may become unmanageable and patients/caregivers may find the usual aspects of daily living very difficult. The patients may require ongoing institutional care, such as nursing homes, care homes, or skilled nursing facilities.

4.4.4 Pain Management

As many as 60–70% of patients with ESLD experience pain – at least a third of which rate this as moderately severe most of the time. In fact, patients with late ESLD report rates of moderate to severe pain like that reported by those with lung or colorectal cancer (Roth et al. 2000; Poonja et al. 2014). Pain adversely affects their QoL and often heightens other symptoms. Additionally, hospital utilization is significantly increased among ESLD patients with pain and among those who use opioids.

Pain is often undertreated in this setting for fear of complicating the liver disease. The failing liver makes pain management in the ESLD patient more complicated, and adverse events from analgesics can be seen (Soleimanpour et al. 2016). Most analgesics are metabolized through the liver, and therefore their metabolism may be altered. The alterations in hepatic blood flow, enzyme capacity, and plasma protein binding seen in cirrhosis all affect drug metabolism. As liver failure worsens, there is greater impairment in drug metabolism. The decrease in albumin synthesis by the failing liver may lead to an increased risk of adverse drug reactions by those drugs that require albumin for their metabolism (Soleimanpour et al. 2016).

Unfortunately, there are no evidence-based guidelines regarding the use of analgesics in these patients. The basic principles of pain assessment and management apply to these patients just as they do to those without ESLD; however, clinicians must often modify standard treatments (Chandok and Watt 2010). Palliative care physicians can be of assistance in this setting, having expertise in pain management as well as opioid and end-of-life medication use (Brisebois and Tandon 2015).

Acetaminophen/paracetamol is generally the preferred first-line analgesic. However, in those with cirrhosis, the half-life of the drug is double that seen in healthy controls. Its toxicity is dose dependent, and it is felt that it can be safely used in this population in daily doses of 2 g or less (Chandok and Watt 2010). However, there is no data regarding the safety of long-term use.

Selective and nonselective nonsteroidal anti-inflammatory drugs are metabolized by the hepatic cytochromes and are heavily protein bound – hepatotoxicity has been well described (Chandok and Watt 2010). These drugs should not be used in patients with cirrhosis. They inhibit platelet function and can cause gastrointestinal ulceration. The risk of gastrointestinal mucosal bleeding is even greater in patients with portal hypertension and varices, gastropathy, or gastric antral vascular ectasias. In addition, they can lead to acute renal failure, including hepatorenal syndrome, because they inhibit prostaglandin-regulated renal afferent arteriolar vasodilatation (Chandok and Watt 2010).

Opioids may be used cautiously, given that hepatic processing may be altered (Imani et al. 2014). Altered hepatic processing may result in decreased hepatic clearance (increased bioavailability) due to decreased first-pass metabolism (e.g., morphine, oxycodone, pentazocine, and tramadol). The half-life of morphine is doubled compared to healthy controls. Methadone clearance is also reduced in patients with severe liver insufficiency and drug half-life increases. Tramadol must be dose reduced in the setting of severe ESLD. Therefore, in the setting of severe ESLD, initial dosing of these drugs should be decreased by 30–50% and carefully titrated upward as needed for pain control (Soleimanpour et al. 2016). Patients should be cautioned about this and avoid taking extra pills or taking them more frequently than prescribed. As liver disease worsens, the interval between dosing may also need to be extended (Imani et al. 2014). For example, a drug normally dosed every 6 h may need to be dosed every 8 or 12 h.

Certain opioids (e.g., codeine) rely on hepatic transformation to active metabolites and therefore will be less effective. Codeine is metabolized to

morphine in the liver and should not be used in the setting of ESLD due to decreased effectiveness. Meperidine is metabolized to normeperidine, the half-life of which is prolonged. Normeperidine carries severe central nervous system toxicity, and it should be avoided in cirrhotics, particularly those with renal insufficiency. Other opioids are unaffected by the underlying liver dysfunction (e.g., fentanyl, sufentanil). All opioids can complicate or precipitate hepatic encephalopathy, as can the opioid-related constipation (Bosilkovska et al. 2012). Therefore, dosing must be carefully considered and frequent patient monitoring is essential.

Table 2 Management of muscle cramps in the cirrhotic

Medications	Dose	Comments
Baclofen	300 mg daily	Improvement in cramps compared to placebo
Branched-chain amino acids (BCAA)	4 g granules three times daily	No side effects have been reported. Improved cramps. No control groups. Expensive
Gabapentin	600–900 mg daily	No data in ESLD
L-carnitine	900–1200 mg daily	Improvement in muscle cramps. No control groups
Magnesium	400 mg 1–2 times daily	Mild diarrhea. No data in ESLD
Taurine	3 g daily	No side effects have been reported. No control groups. Cramps improved
Vitamin B complex	1 tablet daily	Most helpful in nocturnal leg cramps. No data in ESLD
Vitamin E	200 mg three times daily	No side effects have been reported. Controlled trial suggests no benefit. Use with caution in cirrhosis
Quinine sulfate	200–300 mg at bedtime	No longer available over the counter due to adverse effects. FDA recommends against prescription forms for cramps
Zinc sulfate	220 mg twice daily	Improvement in cramps. Mild diarrhea. No control groups

Adapted from: Vidot et al. 2014, Cox-North 2015 (complete citations available upon request)

4.4.5 Muscle Cramps

Painful muscle cramps are reported in 67–90% of patients with cirrhosis. These cramps are unrelated to the use of diuretics, electrolyte imbalance, or minerals (i.e., zinc) and are correlated with the severity of liver disease. They contribute to a poor quality of sleep and QoL. They are unfortunately difficult to treat, although many therapies have been tried (Table 2).

A full review of the management of all complications of cirrhosis is beyond the scope of this chapter. However, these patients suffer from a wide spectrum of symptoms which need continual management. Careful attention to this management improves their quality and quantity of life.

5 Conclusion

Chronic liver disease carries significant morbidity and mortality. These patients suffer a markedly reduced quality and quantity of life. Their management is labor intensive for all involved and is constant throughout the course of their disease. The collaboration of palliative care with primary care and specialty physician management of potential life-sustaining therapy for the ESLD patient improves not only QoL but the length of survival as well. Involvement of the palliative care team should not be interpreted as "giving up" but as integral to management of these complicated patients. When life-sustaining therapy is no longer an option, these patients are already in a system to help them with further end-of-life care.

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Palliative Care in Kidney Disease

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Fliss E. M. Murtagh

Contents

Abstract

This chapter first provides evidence about identifying which patients with kidney disease might need palliative or supportive care. Although care should be based on needs and not on prognosis, it

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_63

is nevertheless important to consider palliative needs in the context of the number of weeks, months, or years which remain. What needs to be addressed only weeks from death is often very different – and more urgent – than what needs to be addressed if there are years ahead. For this reason, there is a comprehensive overview of evidence on survival, so that the context of care can be understood.

Then a more detailed examination of how to identify and manage common symptoms is included, although details of management may vary from country to country, according to local guidelines and availability of individual medicines. Pain, constipation, breathlessness, nausea, vomiting, itch, restless legs, and fatigue are all considered. The last days of life may sometimes prove challenging in terms of symptom management, yet it is important to provide best possible care at this time, so this stage of illness is considered in further detail.

Finally, team working, communication, and planning ahead – all crucial for effective and coordinated care – are then explored, to help facilitate best palliative and supportive care for this population.

1 Introduction

As the world's population ages, the number of older adults is projected to increase dramatically; this will result in a marked increase in the incidence and prevalence of end-stage kidney failure (Stevens et al. 2010). While some reaching end-stage kidney failure will go on to have renal replacement therapy in the form of dialysis, others may choose (or be advised) not to have dialysis because it may have little to offer in terms of added survival or improved quality of life. Those receiving dialysis, often with multiple co-morbid conditions, who are doing less well and those managed without dialysis – called "comprehensive conservative care" (Davison et al. 2015) – often have complex palliative and supportive care needs (Kane et al. 2013; Wasylynuk and Davison 2015).

This chapter aims to present some of the existing and recent evidence, to inform best care and management of this population. Providing the best possible supportive and palliative care for people with advanced kidney failure and their families has the potential to markedly improve patient and family wellbeing over the last months and weeks of life, yet it has not always had sufficient attention alongside the more technological interventions available in nephrology.

2 Identifying Which Patients with Kidney Disease Need Palliative and Supportive Care

Kidney patients whose palliative and supportive care needs should be considered are those with end-stage kidney disease who:

1. Have been on dialysis but are increasingly less well (with either increasing or unstable symptoms, declining functional ability, or deteriorating overall wellbeing)
2. Are on dialysis but with a poor prognosis, often because of co-morbid conditions (especially cardiac disease, but sometimes with a new diagnosis of cancer or other life-limiting condition)
3. Are on dialysis, but finding it hard to tolerate dialysis and they and/or their kidney team are considering withdrawal from dialysis
4. Are reaching end-stage kidney disease but have declined renal replacement therapy (dialysis or transplant) through their own preference
5. Are advised against renal replacement therapy because the burden of frequent dialysis is likely to outweigh survival and quality of life benefits

These last two categories are considered to be "comprehensive conservative care" (Davison et al. 2015).

3 Survival and Prognosis

For a professional delivering palliative care to a person with end-stage kidney disease, it is important to understand, and be able to communicate, the

evidence on survival, as this provides the context for decisions about dialysis, as well as the context for preparation for ongoing care and advance care planning. It is also helpful for professionals to be familiar with the evidence about trajectory of illness and likely prognosis, and to communicate this sensitively to patients and their families, in accordance with information preferences.

One of the key questions in kidney care is whether those who are 75 years and older should have dialysis or not. While there is clear evidence that – in general – those over 75 years receiving dialysis live longer than those managed without dialysis (Foote et al. 2016), the increased survival associated with dialysis reduces substantially, or possibly disappears altogether, with increasing co-morbidity and worsening functional status. The evidence is evolving fast in this emergent field of research and is changing continually.

The recent systematic review of survival outcomes in dialysis versus conservative (non-dialytic) care for older people revealed 89 studies reporting evidence on survival, relating to 294,921 older people with end-stage kidney disease. Initial survival for older patients was similar, regardless of management type: one-year survival was 73% (95% confidence intervals 66–80%) for dialysis (type of dialysis unspecified); 78% (95% confidence intervals 75–82%) for hemo-dialysis; 78% (95% confidence intervals 74–82%) for peritoneal dialysis; and 71% (95% confidence intervals 63–78%) for those managed conservatively, without dialysis. In contrast, 2-year survival showed a marked difference; at 62% (95% confidence intervals 55–69%) for dialysis (type unspecified); 64% (95% confidence intervals 60–69%) for hemo-dialysis; 63% (95% confidence intervals 58–68%) for peritoneal dialysis; and 44% (95% confidence intervals 36–53%) for those managed without dialysis (Foote et al. 2016). However, there was very little evidence in respect of those receiving conservative care (only 724 patients or 0.2% of the total number of participants included in the review). The few studies which do include conservatively managed participants suggest that any survival advantage gained from dialysis is lost or very much reduced in those with multiple co-morbidities (especially heart disease) and/or frailty (Foote et al. 2016).

Nevertheless, it can be concluded that, regardless of whether they are receiving dialysis or not, about 1 in 4 older patients will not live more than 1 year from starting dialysis, or from an equivalent time-point if not receiving dialysis, and this falls to about 1 in 3 who will not live more than 2 years, two in three for those managed conservatively. There is a wide range however, with considerable heterogeneity among the end-stage kidney disease population, and the underlying reason for kidney failure, plus co-morbidities play a big part in understanding prognosis. It is important that more research is conducted, and better understanding of the heterogeneity of this population is gained.

4 Recognition of Palliative and Supportive Care Needs

Detailed evidence about palliative needs and interventions among people with advanced kidney disease is somewhat limited, but we do know that symptom burden in end-stage kidney failure is high (Murtagh et al. 2007a; Davison 2003a), psychological and social impacts are considerable (Murtagh et al. 2010), and there are complex transitions to be negotiated (Hutchinson 2005), especially as the illness advances towards end of life.

Communication, especially about dialysis decision-making and to support advance care planning, is very important (Davison and Torgunrud 2007) and may set the scene to facilitate or inhibit patient and family understanding of deterioration, preparation for progression of illness, and future access to palliative and supportive care services (Tonkin-Crine et al. 2015). As kidney disease advances and life expectancy reduces, the priorities and preferences of kidney patients may change, especially to take account of increasing caring burden on families. But contrary to the expectations of professionals, many patients place notably greater priority on better quality of life, improved symptom control, and accessing family support, than they do on extending life at any cost (Steinhauser et al. 2000; Morton et al. 2012). Therefore, professionals should talk early to individual patients, and families, where appropriate, about their information preferences and care priorities,

and carefully – in close communication with the patient – work to adjust the goals of care over time to match these changing preferences and priorities in the context of progressive illness.

As for any patient, palliative and supportive care assessment in kidney disease requires a holistic and patient-centered approach (Richardson 2007). This includes detailed assessment of:

- Physical symptoms
- Emotional and psychological symptoms
- Social support and networks
- Family well-being, especially in the context of informal care provision
- Preferences and priorities for communication, decision-making, and goals of care
- Planning ahead as the illness advances, in accordance with preferences

Once each of these areas has been identified and fully assessed, interventions to address the concerns and priorities raised should then be implemented.

Excellent symptom management is particularly important for those with kidney failure. These patients are among the most symptomatic of any chronic disease group (Murtagh et al. 2007a; Solano et al. 2006; Murtagh and Weisbord 2010) and are often even more symptomatic than cancer patients (Saini et al. 2006). Renal replacement therapy may improve symptoms, but it does not completely abolish them and may sometimes exacerbate overall symptom burden.

There are several factors which prevent good symptom management for those with advanced kidney disease. Symptoms may not be routinely assessed by kidney professionals and are often under-recognized (Weisbord et al. 2007; Davison 2003a). Also, patients do not always raise their symptoms for discussion spontaneously as they may be unsure whether to attribute them to kidney disease or not, and symptoms may be more often related to co-morbidities (Murtagh et al. 2016b; Davison and Jassal 2016). In addition, professionals – especially non-renal professionals – do not have the knowledge or experience in prescribing medication in end-stage kidney disease, when renal clearance is much reduced and adverse effects more likely (Douglas 2014).

5 Identifying Symptoms

Regular, proactive assessment of symptoms is therefore important. If possible, an appropriate, clinically relevant, and valid measure of symptoms and other palliative care concerns should be used for all patients at regular intervals or at least with any change in health status. There are four measures in regular use which have been adapted and validated specifically for use in those with renal disease. These are:

(i) The Palliative (or Patient) Outcome Scale symptom module (POS-S Renal), developed in the UK (see www.pos-pal.org). This assesses the full range of physical and psychological symptoms in kidney disease and has been validated in end-stage kidney disease (Murphy et al. 2009).

(ii) The renal version of the Integrated Palliative (or Patient) Outcome Scale (see www.pos-pal.org), also developed in the UK. This measure captures not only physical and psychological symptoms but also family anxiety, practical matters, information needs, and existential distress: it is a brief measure which covers the global domains most relevant in advanced disease. It has been validated in advanced disease (Schildmann et al. 2016; Murtagh et al. 2016a) and is undergoing further validation in advanced kidney disease.

(iii) The Modified Edmonton Symptom Assessment Scale (ESAS). This is a measure of physical and psychological symptoms, derived from the well-validated original ESAS measure, and which has been adapted and validated in Canada for dialysis patients (Davison et al. 2006b; Davison et al. 2006a).

(iv) The Dialysis Symptom Index (DSI), again a measure of physical and psychological symptoms, but which was developed and tested in the USA (Weisbord et al. 2004).

6 Symptom Management

Once symptoms are identified, they need to be actively managed. In this chapter, the focus is on pharmacological management, but non-pharmacological management may be equally or more important, especially for symptoms such as itch, anxiety, depression, and sleep disturbance, which have major psychological and social impact.

The aim of symptom management is to improve symptoms to a level acceptable to the patient while minimizing any adverse effects of medication. The pharmacokinetic impact of renal disease is considerable, because drug metabolism is altered, renal clearance reduced or absent, and the risk of toxicity from accumulation of renally excreted drug and/or metabolites is very high. If estimated glomerular filtration rate is $\leq$30 mL/min/1.73m^2, then prescribing needs to take into account the impact of reduced renal clearance, as well as other pharmacokinetic alterations.

In addition, for those still on dialysis, the effects of dialysis on the drug need to be factored in too. Removal of a medication from systemic circulation during dialysis depends on the molecular size of the drug, the degree of water solubility of the drug, the extent of protein binding of the drug, and a range of dialysis-related factors (such as frequency, duration, type of dialysis, type of dialyzer membrane). Handbooks such as *Dialysis of Drugs* (updated annually and now available as an app) should be used for reference.

7 Pain

Pain is common among those on dialysis (Davison 2003a), those managed without dialysis (Murtagh et al. 2007b), and those who withdraw from dialysis (Germain et al. 2007). As for any other palliative care patient, pain needs to be carefully assessed to identify the underlying cause(s), and remove or ameliorate each as much as possible in a logical and stepwise fashion. Multiple pains are common, and frequently from non-renal causes such as musculoskeletal, cardiac, or other co-morbidities (Davison 2003b).

The commonest question in managing pain among kidney patients is "which opioid to use?" It is important to fully assess the opioid-responsiveness of each pain, as general pains will be less opioid responsive than among other palliative care populations, such as those with cancer.

The World Health Organization analgesic ladder (Azevedo Sao Leao et al. 2006) suggests a step-wise use of analgesics and the Step 2 opioids, codeine, and dihydrocodeine should generally not be used if estimated glomerular filtration rate is $\leq$15 mL/min/1.73m^2 (and only with extreme caution if estimated glomerular filtration rate is between 30 mL to 15 mL/min/1.73m^2). This is because of the evidence on rapid accumulation and toxicity (Davies et al. 1996), with prolonged sedation, respiratory depression, and narcosis (Murtagh et al. 2007e).

Tramadol is a better option but is still problematic. If estimated glomerular filtration rate is $\leq$15 mL/min/1.73m^2, the dose of tramadol should be kept to a maximum of 50 mg 12 hourly (Broadbent et al. 2003). Even at this lower level, adverse effects are common, especially among older people.

All of the Step 3 opioids can cause significant toxicity, but some are less problematic. Most undergo metabolism in the liver to either active or inactive metabolites. These compounds, as well as some of the unchanged opioid, are usually excreted by the kidneys. If a significant proportion of the unchanged opioid is excreted by the kidneys and the metabolites are active, then the opioid is highly likely to cause toxicity when the estimated glomerular filtration rate is less than 30 mL/min.

Alfentanil and fentanyl are cautiously recommended and may be the preferred opioids to use towards end-of-life when an injectable strong opioid is needed, although some clinicians use low-dose oxycodone, with reduced doses and increased dose interval (King et al. 2011). Methadone has also been recommended because of its fecal route of excretion (King et al. 2011), although it should not be used unless the clinician is knowledgeable and skilled in use of methadone more generally as titration and use are complex. Several clinical and practical considerations

(other than safety) need to be taken into consideration: for instance, the short half-life of alfentanil makes it less practical for break-through pain, although it is more appropriate for continuous infusion.

Further information is available from several reviews (Murtagh et al. 2007c; Dean 2004; Broadbent et al. 2003; Mercadante and Arcuri 2004; Murtagh et al. 2007e; King et al. 2011), but all Step 3 opioids should be used cautiously, with dose reduction and increase in dosing interval, and morphine and diamorphine should be avoided in severe renal impairment because of their accumulation and adverse effects. Whichever opioid is prescribed, early review and regular monitoring is critical. Accumulation and adverse effects will occur quickly, within a matter of hours. For this reason, long-acting preparations should also be avoided.

Transdermal fentanyl patches may be useful for the ambulant patient earlier in the disease trajectory. However, professionals unfamiliar with prescribing these should recognize that even lowest strength patches represent quite a high-opioid dose and careful titration of immediate-acting oral opioids is usually needed before commencing fentanyl patches.

Transdermal buprenorphine is increasingly widely used clinically, without reports of adverse effects, although the evidence to support this remains limited. There is some evidence of biliary excretion of buprenorphine (Boger 2006) which may reduce any accumulation, but the metabolites may also be relatively inactive (Pergolizzi et al. 2008).

For oral immediate-acting preparations, oxycodone, hydromorphone, and buprenorphine all have very limited evidence to indicate whether they are safe or not, although buprenorphine is increasingly used clinically, and both hydromorphone and oxycodone are likely to be a better choice than morphine or diamorphine.

Musculoskeletal pain: Musculoskeletal pain is perhaps the most common cause of pain in patients with end-stage kidney disease (Davison 2007), and opioids are less suited to manage it, partly because of limited responsiveness and partly because of the adverse effects. Nonsteroidal anti-inflammatory drugs are likely to be beneficial for musculoskeletal or bone pain, but carry high risk of adverse effects in severe renal impairment, including risk of loss of any residual renal function. This consideration may be critical and prevent use of nonsteroidal anti-inflammatory drugs completely, but each case should be reviewed by an experienced clinician in order to make the best judgment. Sometimes, a short course of nonsteroidal anti-inflammatory drugs are prescribed as a considered risk in the absence of any residual renal function, or towards the end-of-life.

Neuropathic pain: Neuropathic (nerve) pain is unlikely to respond to opioids alone. Certain Step 3 opioids may be more useful than others in neuropathic pain. For instance, methadone may be appropriate but should only be prescribed by someone experienced in its use, usually pain or palliative care specialists. Anticonvulsants and antidepressants in low dose are commonly used as adjuvant medication to improve pain control. Antidepressants can be used in end-stage kidney disease, but it is better to avoid longer-acting preparations, reduce the dose, and/or increase the dosing interval. Anticonvulsants are more problematic, particularly gabapentin and pregabalin which accumulate markedly in renal impairment to cause adverse effects. While they can be used cautiously in those on dialysis, their use in those managed without dialysis is limited.

8 Constipation

Constipation is common among patients with end-stage kidney disease. The causes are most often from a combination of several factors, including fluid restriction to help manage kidney function; impaired mobility; a range of different medications (such as iron supplements, opioids, aluminium, or calcium phosphate binders); limited dietary intake; reduced muscle tone through edema and/or through muscle wasting; and dietary restriction of high potassium fruits and vegetables, leading to reduced fiber intake.

As for other symptoms, a detailed assessment is needed to identify causes and contributing factors, bearing in mind the likely causes listed above. Each of the reversible causes needs to be

addressed where appropriate or possible, and this will depend of the stage of illness and what causes can realistically be addressed or modified.

To address constipation, other than mild constipation, usually needs both rectal measures and oral laxatives, in combination. Moderate, severe, or established constipation is rarely addressed by oral laxatives alone, and rectal measures will not prevent recurrence without oral laxatives. Useful interventions include: improving mobility, even standing regularly for a very ill and immobile patient is helpful; increasing dietary intake with sufficient fiber and fluid, within the constraints of reduced fluid intake for kidney management – clinical judgment is needed on how important this is, according to level and rate of change of renal impairment, symptoms, co-morbidity, and prognosis; oral laxatives; and rectal measures.

Laxatives, such as softeners or osmotic laxatives, and stimulant laxatives can be used, and often a combination of softener or osmotic laxative with a stimulant is required. Laxatives which contain magnesium, citrate, or phosphate should be avoided in end-stage kidney disease. Polyethelene glycol is not ideal for renal patients because it requires high-concurrent fluid intake and also contains potassium, but it may be useful short term for constipation which does not respond to other measures.

9 Dyspnea

Dyspnea or breathlessness in the patient with end-stage kidney disease may be due to anemia, pulmonary edema (related to fluid overload or to coexisting cardiovascular disease), or co-morbidity (cardiac or respiratory disease). Identifying and treating the underlying cause is the most important, appropriate, and effective management approach. Diuretic use and fluid restriction may or may not be appropriate, depending on the clinical circumstances.

If the breathless patient is anemic, it is often hard to decide how much correction of anemia may improve the symptom, since the correlation between breathlessness and fatigue, and degree of anemia is unclear (see Sect. 13, for more on anemia management).

If all possible and appropriate treatment for underlying causes has been put in place, there may still be a degree of chronic breathlessness remaining. In this situation, an approach to symptom control of breathlessness based on the Breathing, Thinking, Functioning model of breathlessness (Spathis et al. 2017) is helpful (see Fig. 1).

All three areas in Fig. 1 are important. Physical measure to help breathing, such as sitting upright rather than lying, thus increasing vital capacity, using a fan or stream of cool air to provide effective symptom relief, and physiotherapy techniques to manage breathing are helpful. However, without also considering the anxiety, cognitive processing, and emotional experience of breathing, it is unlikely that physical measures alone will be enough. It is also critical that attention is paid to functioning and mobility and occupational therapy can help to maximize mobility and provide appropriate aids, and deconditioning may need addressing to maintain and improve mobility, and so improve breathlessness. Appropriate information, education, and support of patient and family are also a key component, including using this tripartite model to communicate and explain the important elements of management.

As end-stage kidney disease advances and breathlessness may be more severe, disease management options become limited, general and nonpharmacological measures will have less to offer, and pharmacological management of breathlessness become more appropriate. This applies only when treatment of the underlying causes of breathlessness have been exhausted. Severe breathlessness towards end of life is very distressing and should be treated actively. It is important to plan with the patient who has had one or more episode of acute breathlessness (or steadily increasing breathlessness over time) how they would like to be treated if they become more symptomatic in the future. Not all patients will, for instance, choose to be admitted for maximal treatment with intravenous diuretics in the last days or weeks of life.

Pharmacological treatments directed specifically at breathlessness include opioids. Low-dose opioids (up to the equivalent of 30 mg morphine daily) may

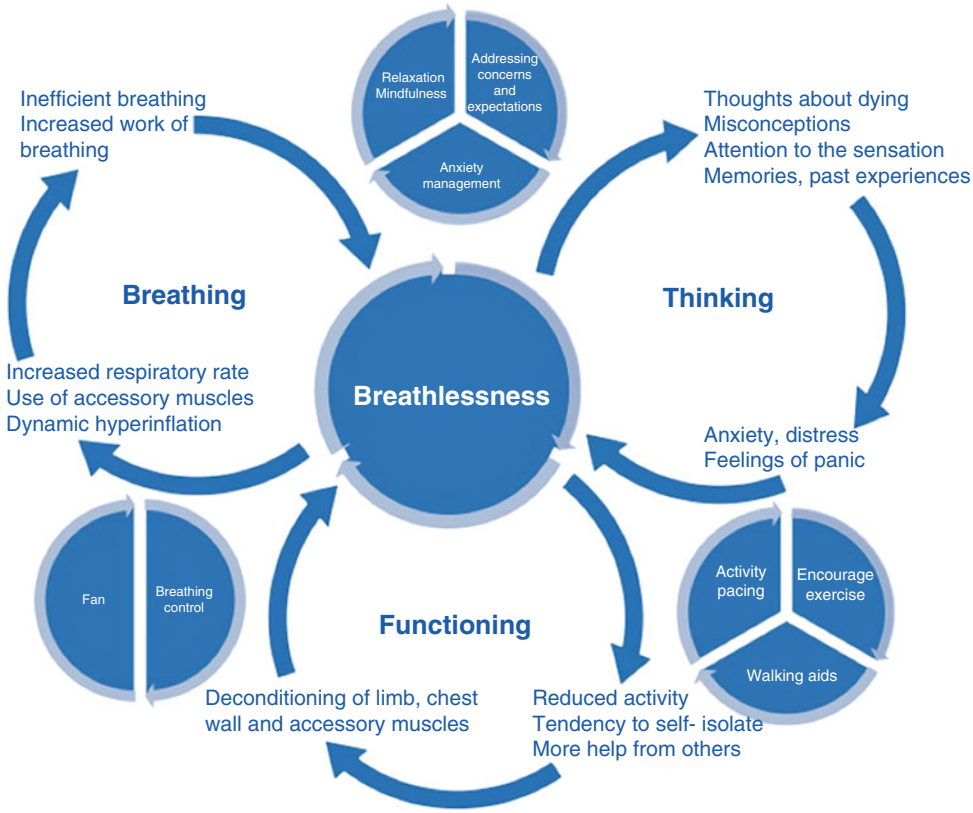

Fig. 1 The Breathing, Thinking, Functioning model to support management of breathlessness. References: see Spathis et al. (2017) and Chin and Booth (2016) for further details (Available under Creative Commons Licence at http://creativecommons.org/licenses/by/4.0/)

be helpful in relieving breathlessness near the end of life in end-stage cardiac and respiratory disease (Jennings et al. 2001) and clinical experience suggests that this also true for patients with kidney disease, although, as discussed in the Sect. 7, morphine should be avoided in end-stage kidney disease. A recent Cochrane review looking at the effectiveness of opioids to relieve breathlessness in advanced disease (Barnes et al. 2016) found evidence to suggest opioids improve the symptom of breathlessness, although the evidence was graded "low." As might be expected, the adverse effects reported included drowsiness, nausea and vomiting, and constipation. A second systematic review found no evidence of significant or clinically relevant ***respiratory*** adverse effects of opioids for chronic breathlessness (Verberkt et al. 2017), although this was not specific to end-stage renal disease.

10 Nausea and Vomiting

Nausea and vomiting are distressing symptoms. Often, the cause may be multifactorial, making these symptoms harder to manage. As with all symptoms, assessment requires a detailed history to understand the history and pattern of nausea and vomiting, considering both symptoms separately. The relationship between nausea and vomiting should also be established, as well as whether there is associated constipation, and a complete medication history. Profound nausea and/or repeated vomiting will prevent absorption of medications taken orally, and alternative routes will therefore need to be considered, at least until nausea and vomiting is controlled.

Management which is specifically directed to the underlying cause(s) is most likely to succeed. If medication or toxins are causing nausea, then nausea is usually persistent and unremitting, and sometimes without accompanying vomiting. Uremia and a variety of drugs, such as opioids, anticonvulsants, antibiotics, and antidepressants, can all cause persistent nausea. Gastroparesis or delayed gastric emptying, which may be caused by drugs such as opioids, as well as occurring secondary to uremic or diabetic autonomic neuropathy, for instance, usually presents with a history of postprandial nausea or vomiting of undigested food which relieves nausea. Bloating, epigastric fullness, flatulence, hiccough, or heartburn may also occur. Nausea related to gastritis is often associated with epigastric pain or discomfort, heartburn, or dyspepsia. Constipation exacerbates nausea and vomiting.

If gastroparesis or delayed gastric emptying is suspected, then domperidone, which increases increase gastric motility, may be preferred. If uremia is a suspected cause, then haloperidol or possibly a 5HT3 (a serotonin receptor subtype) antagonist may be the best choice. However, 5HT3 antagonists, such as ondansetron and granisetron, cause moderate or sometimes severe constipation – this must be a consideration when weighing up if they are the best choice. Drug-induced nausea can be relieved by stopping the causative drug but when this is not feasible, haloperidol is often effective. Gastritis, of which there is much higher risk in uremia, may sometimes contribute to nausea and should be actively treated with a proton pump inhibitor, to help control the related nausea. Towards the end of life, low-dose haloperidol or low-dose levomepromazine, a "broad-spectrum" antiemetic which works on several of the relevant receptors, can be effective to control nausea and vomiting. However, levomepromazine can be very sedative; it is used second or third line, and higher doses should be avoided if possible.

For all antiemetics used in end-stage kidney disease, lower than standard starting doses should be used, and then cautiously titrated to response. End-stage kidney disease patients are at greater risk than those with normal renal function of an enhanced central depressant effect, because of reduced protein binding in uremia and increased cerebral sensitivity to medication, especially where the drug crosses the blood–brain barrier (Wilcock et al. 2017). There is also higher chance of prolongation of the QT interval (risking ventricular arrhythmia) with domperidone, haloperidol, levomepromazine, and ondansetron (Wilcock et al. 2017).

11 Pruritus or Itch

Uremic itch has complex pathophysiology, and this pathophysiology is poorly understood and elucidated. Given this complexity, it is no surprise that it can occasionally be a very challenging symptom to manage. There is a very wide range of drug treatments proposed, often with limited evidence of effectiveness.

The first step is to optimize renal management. High phosphate levels may contribute to pruritus, therefore reducing phosphate levels may be important, with the consideration of dietary advice and the use of phosphate-binders. Hyperparathyroidism may also contribute and should also be considered and actively managed. Xerosis or dry skin, especially in older people, may both cause and contribute to pruritus and so should be treated actively with liberal emollients if dry skin is present. Older people living alone may find it hard to apply emollients easily and spray applications are often helpful in this instance. Preventive measures, such as nail care (keeping nails short), keeping cool (light clothing, and tepid baths or showers) are useful concurrent measures.

It is difficult to recommend specific pharmacological measures given the lack of clear evidence to support any one management over another. UVB light has good supporting evidence but may not be readily available. For those on dialysis, gabapentin may be the best choice, with some supporting evidence (Cheikh Hassan et al. 2015), including randomized controlled trial evidence (Gunal et al. 2004). However, gabapentin accumulates rapidly in those managed conservatively, without dialysis, and quickly causes adverse effects such as drowsiness or sedation; some authorities recommend avoiding gabapentin completely in the conservatively managed population, while others

propose very small doses (such as 50 mg or 100 mg alternate days), used with caution and careful monitoring. There is even more limited evidence on the clinical effectiveness of mirtazapine (Davis et al. 2003), and the dose should be reduced in renal impairment. Antihistamines are widely used, but there is little supporting evidence, and – if there is any benefit at all – it may be through the effect of a sedating antihistamine, such as chlorpheniramine, at night in helping a patient to sleep better, since itch often disturbs sleep.

12 Restless Legs

Restless legs syndrome is characterized by the urge to move the legs, uncomfortable sensations in the legs, and worsening of symptoms at rest, especially during the night. The formal International Restless Legs Syndrome Study Group (IRLSSG) criteria (Walters et al. 2003) for diagnosis are:

- Urge to move the legs, usually with unpleasant sensations in the legs
- Worse during periods of rest or inactivity like resting or sitting
- Partial or total relief by physical activity
- Worse symptoms in the evening or night rather than the day

The exact cause for restless legs is not understood as yet; it is widely accepted, however, that the dopaminergic system in the central nervous system is disrupted. There is limited evidence in uremic restless legs that iron deficiency, low parathyroid hormone, hyperphosphatemia, and psychological factors may play a role. Treatment should involve correction of these factors and reduction of potential exacerbating agents, such as caffeine, alcohol, nicotine, and medications (tricyclic antidepressants, calcium antagonists, sedative antihistamines, metoclopramide, selective serotonin uptake inhibitors, and lithium and dopamine antagonists).

There is very limited evidence about treatment of restless legs in people with end-stage kidney disease and much of the evidence is extrapolated from idiopathic restless legs. Gabapentin or pregabalin can be used with those receiving dialysis and are often effective. Dopamine agonists, pergolide or pramipexole, are also effective, although nausea is common, especially with pergolide, as are other adverse effects such as dreams or nightmares. There is also uncertainty about the use of dopamine agonists longer term, because of an association with restrictive cardiac disease and pulmonary fibrosis. Co-careldopa can be used for restless legs and is effective at low dose. However, augmentation, with the return of the symptom, often at a worse level, is very problematic, and 80% will eventually experience augmentation with co-careldopa. Augmentation does occur with dopamine agonists, although much less so than with co-careldopa. In treating restless legs, the choice of drug management should be tailored to the individual and will depend on the presence of other symptoms, age and tolerance of side effects, and whether the patient is receiving dialysis or not.

13 Fatigue

Fatigue or tiredness is highly prevalent in end-stage kidney disease (Karakan et al. 2011) – see Table 1 – and has major impact on quality of life (Bonner et al. 2010). It impairs function and mobility, and can be one of the most devastating adverse influences on quality of life (Lowney et al. 2015). Interventions to alleviate fatigue center around management of anemia and

Table 1 Mean prevalence of symptoms in end-stage kidney disease - weighted by size of study (%) (Murtagh et al. 2007d)

	Percentage
Fatigue	71%
Pruritus	55%
Constipation	53%
Anorexia	49%
Pain	47%
Poor sleep	44%
Anxiety	38%
Dyspnea	37%
Nausea	33%
Restless legs	30%
Depression	27%

supportive interventions such as rehabilitation and practical aids. However, much of the evidence on these interventions is extrapolated from other populations. Rehabilitation-based interventions currently have the best supporting evidence.

Anaemia is a common complication in end-stage kidney disease and is associated with fatigue. It is not clear whether or how much erythropoiesis-stimulating agents – acting to replace endogenous erythropoietin – may or may not be helpful in alleviating fatigue in the palliative end-stage kidney population or not. A small retrospective study in renal palliative care patients suggests fatigue and hospitalizations are reduced (Cheng et al. 2017), but more substantive and robust evidence is needed.

14 Symptom Management at the End of Life

It was believed that a uremic death was relatively symptom-free, but the evidence does not support this. Where studies have specifically reported symptoms in the last day of life, a significant minority experience severe or distressing symptoms (Cohen and Germain 2004; Cohen et al. 1995). Pain, breathlessness, nausea, retained respiratory tract secretions, and terminal agitation are all reported.

These symptoms can be relatively well controlled in the majority of patients. Agitation usually responds to low dose of anxiolytics, such as midazolam. Retained respiratory tract secretions can be improved, although not always resolved, by glycopyrronium or hyoscine butylbromide, and treatment is optimal if commenced early. Pain or breathlessness can be effectively managed with opioid medications, and often only low doses are required, although morphine and diamorphine should be avoided in severe renal impairment because of the accumulation of metabolites and subsequent adverse effects (see Sect. 7, in this chapter). If the patient has been on regular strong opioids orally and can no longer take oral medication, then convert the total daily dose of strong opioid to the equivalent for subcutaneous fentanyl or alfentanil over 24 h and start a subcutaneous infusion.

15 Team Working

Multi-disciplinary team working is inherent to the palliative care approach. For patients with end-stage kidney disease, it is important to ensure excellent liaison, not only within the palliative care team but between the nephrology team, the specialist palliative care team, care of the elderly teams, other disease-based teams, and the primary care or community-based teams. Coordination of care across providers is always important, but it becomes critically so when caring for these, usually, older people with multiple conditions.

Primary care or community-based teams may see patients with end-stage kidney disease rarely; in the UK, deaths with end-stage kidney disease represent only 1–2% of all deaths (Murtagh and Higginson 2007). Each general practitioner will care for a patient with end-stage kidney disease only once every few years; and until recently, the care and deaths of these patients has largely been in acute hospitals (Lovell et al. 2017). This may be changing however, as conservative management programs expand (Lovell et al. 2017) and home deaths increase (Okamoto et al. 2015); nevertheless, primary care teams may need specialist supportive to deliver excellent end of life care.

There are a variety of models of care of those with end-stage kidney disease, as evidenced in a recent UK-wide study (Roderick et al. 2015). However, there is little evidence to suggest which model is most effective or cost-effective. Shared care models, with collaborations between primary, palliative, and nephrology providers to optimize recognition, assessment, and management of supportive and palliative care needs, would, at present, seem to be the most highly rated by patients, families, and professionals (Murtagh et al. 2016c).

16 Advance Care Planning

Planning ahead in end-stage kidney disease is important, especially given the high levels of cognitive impairment as the disease progresses. There is good evidence of benefit from advance care planning in a range of advanced illnesses

(Weathers et al. 2016; Houben et al. 2014) but wide variation in patients' perspectives on advance care planning (Ke et al. 2017). Most are keen to discuss and plan ahead, but small proportions prefer not to discuss.

This indicates that advance care planning needs to be done in such a way as to be highly individualized. Open questions, such as "What do you understand about your illness (or health) at present?"; "Do you have any concerns about how it might change in the future?"; or "Do you have any worries about the next weeks [or months or years, as appropriate]?," are invaluable ways to open up discussions at a pace or in a way which can be led by the patient. It is always hard to make opportunities for these discussions, but the conversation can readily be dropped if it is too soon or not currently desired, whereas considerable harm can be caused by not addressing important issues in time.

The overall evidence for advance care planning in hamodialysis patients remains inconclusive (Lim et al. 2016), but this is because the research has not yet been done. Several studies are currently underway, so the evidence may emerge soon which clarifies the effectiveness (or not). The economic benefits are particularly unclear (Dixon et al. 2015), but despite this uncertainly, if advance care planning is done well, with sensitivity to individual preferences and priorities.

17 Conclusion and Summary

Although those with end-stage kidney disease represent only about 2% of all deaths, there are major challenges to delivering effective palliative care to this population. This is accompanied by an increasing awareness among clinicians and health services of the complexity of their supportive and palliative care needs. This chapter outlines the current evidence on identification, assessment, and management of these supportive and palliative care needs, as well as the gaps in that evidence, in order to inform the best ways to overcome the challenges and deliver high-quality palliative care for those with end-stage kidney disease.

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Palliative Care and Endocrine Diseases 65

Pallavi D. Rao and K. M. Prasanna Kumar

Contents

Abstract

Palliative care in endocrine diseases is similar to palliative care in any other disease. The aim will be to reduce the symptoms, avoid short-term complications and improve or maintain the quality of life by minimal interference and with least inconvenience to the patient. Palliative care in diabetes mellitus aims at avoiding hypoglycemia and symptomatic hyperglycemia, and not necessarily achieving euglycemia or postponing/preventing chronic complications of diabetes. Palliative care in thyroid disorders aims to help the patient remain asymptomatic in both hypothyroidism and hyperthyroidism and not normalizing the TSH. Palliative care in all other endocrine diseases like Cushing's disease, pheochromocytoma, pituitary tumor, insulinoma, and hyperparathyroidism is also mostly minimal medical intervention to alleviate symptoms and improve quality of life. Replacing endocrine deficiency as in Addisons disease, hypothyroidism, hypocalcemia due to hypoparathyroidism is important and similarly managed to any other endocrine deficiency.

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_112

1 Introduction

Palliative care aims to provide comfort care, supportive care, and symptoms management, and its goal is not to cure the disease but to prevent or treat, as early as possible, and to alleviate the symptoms of the disease and side effects of its treatment.

In this chapter, we aim to discuss treatment of diabetes and other endocrine disorders in life limiting disorders and towards the end-of-life.

2 Diabetes Mellitus

Diabetes mellitus is a chronic relentless disorder, needing major lifestyle changes and maintaining them as the years go by. Patients are encouraged to manage their disease, with close monitoring of the blood glucose, with the aim of reducing morbidity, further complications, and mortality.

However, the most important goal of management of diabetes in palliative care is to avoid hypoglycemia and symptomatic hyperglycemia. Tight control of diabetes is not necessary in palliative care as the life span is limited in these patients. When it comes to managing diabetes in life limiting illnesses, the targets obviously need to change, as with the medications. The majority of patients in palliative care do not need to achieve a target Hb A1C below 7%.

Strict avoidance of added sugars is often impractical, when food choices are already limited. Patients may request "sugary" nutrients, which should be provided. Calorie-dense foods (including chocolate) are encouraged despite their adverse impact on glucose concentration. Adjusting medication is preferable to limiting the diet but therapy will have to match small frequent meals (End of life diabetes care 2013).

A set of key principles underlie high quality diabetes care at the end-of-life and these have been summarized as:

- Provision of a painless and symptom-free death
- Tailored glucose-lowering therapy and minimize diabetes-related adverse treatment effects
- Avoid metabolic de-compensation and diabetes-related emergencies: frequent and unnecessary hypoglycemia, diabetic ketoacidosis, hyperosmolar hyperglycemic state, persistent symptomatic hyperglycemia
- Avoidance of foot complications in frail, bed-bound patients with diabetes
- Avoidance of symptomatic clinical dehydration
- Provision of an appropriate level of intervention according to stage of illness, symptom profile, and respect for dignity
- Supporting and maintaining the empowerment of the individual patient (in their diabetes self-management) and carers to the last possible stage. (End of life diabetes care 2013)

The goal of diabetes management in palliative care is not achieving euglycemia. Blood glucose above 5.6 mmole/l (100 mg/dl) is acceptable to prevent hypoglycemia. Blood glucose below 14 mmole/l (250 mgm/dl) is acceptable to prevent symptoms of hyperglycemia in palliative care of diabetes. In many ways, it is important to keep the blood glucose level at a level of 10–15 mmole/l so that if there are problems such as vomiting or reduced oral intake, hypoglycemia is less likely.

The palliative care of diabetes should be a team work involving care providers, endocrinologist or diabetologist, diabetes nurse educator, dietitian, primary care team, palliative care specialist, and the family of the patient.

2.1 Patients on Oral Antidiabetic Treatment

Patients who are on oral antidiabetic agents can continue medication, provided there is no hypoglycemia. However, if appetite is poor or the patients unable to eat adequately long-acting sulfonylureas need to be avoided (End of life diabetes care 2013). Repaglinide or Nataglinide can be useful for patients managing small regular meals with the dose carefully adjusted according to intake (End of life diabetes care 2013).

With liver impairment and cirrhosis, compensatory mechanisms are altered due to reduced or lack of neo-glucogenesis and glycogenolysis, and

hence sugar targets will need to be relaxed to reduce the risk of severe hypoglycemia.

Similarly, with renal impairment, many of the oral hypoglycemics cannot be continued and insulin doses may need to be reduced or a change in insulin regime may be warranted.

Low-dose insulin may be the only option for patients whose glucose levels are high despite a significantly reduced oral intake.

2.2 Patients on Insulin Regimes

In persons with Type 1 diabetes (T1DM), however, insulin will definitely need to be continued to avoid ketoacidosis, as a basal insulin.

Persons with T2 DM on insulin may not need basal bolus regimens or even pre-mixed insulin, as these are likely to cause hypoglycemia. Symptom control may be achieved with once-a-day basal insulin.

2.3 End-of-Life Care

Towards the last few weeks and days of life, the focus in diabetes mellitus treatment should shift from tight control to symptom control only. Hyperglycemic symptoms that need to be addressed and treated are excessive thirst and excessive urination.

Many factors associated with end-of-life care may precipitate hyperglycemia (steroids, concurrent infection, tumor-specific effects, and the stress response) and/or hypoglycemia (loss of appetite, weight loss, and renal or hepatic failure).

Dexamethasone or prednisolone is often used for symptom control in palliative care. Regardless of the indication, the impact of steroids on glucose control can contribute to hyperglycemic symptoms. Regular monitoring of blood sugars may be helpful, particularly if there are symptoms of hyperglycemia. Once daily steroid therapy taken in the morning tends to cause a late afternoon or early evening rise in glucose levels which can be managed by a morning sulfonylurea (such as gliclazide) or morning isophane insulin (including NPH, Detemir, Glargine, Degludac); If steroids are to be given twice daily, twice daily gliclazide or isophane insulin can be effective but early morning hypoglycemia may occur and the dose must be adjusted with this risk in mind (End of life diabetes care 2013).

3 Other Endocrine Disorders

There are no guidelines available for the management of endocrine disorders towards the end-of-life. As with diabetes mellitus, management should aim to ensure that side-effects are kept to the minimum and management is to maintain comfort and quality of life.

3.1 Thyroid Disorders

3.1.1 Hypothyroidism

The etiology of hypothyroidism in oncology patients may be pre-existing auto-immune hypothyroidism, as a result of chemotherapy agents or radiation to thyroid. In these cases, replacement thyroxine will be necessary.

In pre-existing hypothyroidism, Levothyroxine should be continued with an aim to maintain the TSH within normal ranges as before or below10 mIU/L is good enough. Changes in Levothyroxine doses, dosing schedules (weekly or bi-weekly rather than daily) and route of administration (oral/nasogastric tube) may need to be considered. Changes in the route depend on the ability of the patient to swallow tablets, absorption of levothyroxine in conditions affecting the gastrointestinal tract, and possible interaction with the chemotherapy agents (Jonklaas et al. 2014).

Management of hypothyroidism secondary to chemotherapy agents or radiation therapy is similar to that of autoimmune hypothyroidism.

Towards the end-of-life however, like in many other disorders, symptom control should take priority. There is no evidence to suggest increase in mortality or death being caused as a result of stopping thyroxine towards end-of-life.

3.1.2 Hyperthyroidism

Long-term anti-thyroid drugs (ATD), like carbimazole ormethimazol 10–15 mgm once a

day-treatment of toxic multinodular goitre (TMNG) or toxic adenoma (TA), may be indicated in some elderly or otherwise ill patients with limited life expectancy, in patients who are not good candidates for surgery or ablative therapy, and in patients who prefer this option (Jonklaas et al. 2014; Ross et al. 2016).

The required dose of ATD to restore the euthyroid state in TMNG or TA patients is usually low (5–15 mg/d). Because long-term, low-dose ATD treatment in nodular hyperthyroidism can be difficult to regulate, frequent (every 3 months) monitoring is recommended initially, especially in the elderly until stability has been documented, after which testing frequency can be decreased (Takats et al. 1999).

3.2 Parathyroid Disorders

3.2.1 Hyperparathyroidism

Hyperparathyroidism could be primary, where it is due to a parathyroid adenoma, or secondary, where it develops secondary to vitamin D deficiency or chronic kidney disease. Treating vitamin D deficiency and chronic kidney disease is the treatment of choice for secondary hyperparathyroidism. Surgery is the treatment of choice in primary hyperparathyroidism. In patients who are not fit for surgery or those who choose medical management over surgery, cinacalcet, a calcimimetic, may be used.

Cinacalcet, a calcimimetic, reduces both serum calcium and parathyroid hormone (PTH) levels and raises serum phosphorus. Cinacalcet inhibits parathyroid cell function and reduces PTH secretion by altering the function of parathyroid calcium-sensing receptors, normalizes serum calcium in PHPT, both mild and more severe, for sustained periods (Griebeler et al. 2016).

Cinacalcet can be considered for patients with hypercalcemia secondary to parathyroid carcinoma, secondary hyperparathyroidism, and primary hyperparathyroidism.

3.2.2 Hypoparathyroidism

Hypoparathyroidism is a condition of parathyroid hormone (PTH) deficiency. Primary hypoparathyroidism is a state of inadequate PTH activity. In the absence of adequate PTH activity, the ionized calcium concentration in the extracellular fluid falls below the reference range. Primary hypoparathyroidism results from iatrogenic causes or from a few rare disorders.

Secondary hypoparathyroidism is a physiological state in which PTH levels are low in response to a primary process that causes hypercalcemia.

Treatment of patients with hypoparathyroidism involves correcting the hypocalcemia by administering calcium and vitamin D. Recombinant human PTH is indicated as an adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism.

Vitamin D supplementations needs to be in a daily dose of 400–800IU to patients treated with activated vitamin D analogues. In a patient with hypercalciuria, it is important to consider a reduction in calcium intake, a sodium-restricted diet, and/or treatment with a thiazide diuretic (Bollerslev et al. 2015). Calcium excretion is increased by loop diuretics and diminished by thiazide-type diuretics and amiloride (Rose 1991).

3.3 Adrenal Disorders

3.3.1 Hypoadrenalism

Hypoadrenalism will need to be treated even towards the end-of-life to avoid adrenal crisis, as the patient does not produce corticosteroids and is dependent on the administered replacement therapy. Depending on the severity of the terminal illness, the dose will need to be adjusted to accommodate for the stress response as a result of the illness per se. Parenteral administration of hydrocortisone may be necessary if the patient is unable to take oral medication. 200 mgm i.v. bolus followed by 100 mgm i.v. 6–8th hourly.

3.3.2 Cushing's Syndrome (Steroid Excess)

Cushing's syndrome occurs when there is an excess of steroids. This may be due to administration of corticosteroids. If the etiology is unclear, the investigation and the cause may be against the principles of palliative care, and the aim is to ensure symptom control. Controlling hyperglycemia,

hypertension, and hyperlipidemia with medications as needed should be the goal.

Ketoconazole, an imidazole derivative, inhibits steroid synthesis through inhibition of cytochrome P450 enzymes 17,20-lyase, 11-B hydroxylase, 17-hydroxylase, and side chain cleavage. These effects are dose dependent and completely and rapidly reversible upon drug discontinuation (Liu et al. 2007; Sonino et al. 1991).

Metyrapone blocks the production of cortisol through the inhibition of 11B-hydroxylase, resulting in a dramatic rise in 11-deoxycortisol, a precursor steroid with mineralocorticoid activity formed immediately proximal to cortisol in the steroid biosynthesis pathway (Rizk et al. 2012; Jeffcoate et al. 1977).

Dopamine agonists are widely available and used clinically for the treatment of prolactinomas and occasionally for acromegaly. However, use in Cushing's syndrome has shown variable results possibly with better short-term than long-term results (Sonino and Boscaro 1999; Boscaro et al. 1983).

Etomidate inhibits cholesterol side chain cleavage and 11-B hydroxylase. It has been successfully used as a short-term treatment in critically ill patients with Cushing's syndrome unable to take oral medications (Krakoff et al. 2001).

Mitotane reduces cortisol synthesis through the inhibition of 11B-hydroxylase, 18-hydroxylase, 3-α hydroxylase, hydroxysteroid dehydrogenase, and several cholesterol side chain cleavage enzymes. It is also an adrenolytic agent at doses greater than 4 g per day and is used most often for the treatment of adrenocortical carcinoma (Crane and Harris 1970).

Mineralo-corticoid excess in patients where there is no indication for surgery or who, choose not to undergo surgery, can be treated with eplerenone or spironolactone (Lim et al. 2001). When blood pressure is not controlled with spironolactone or eplerenone, or side-effects limit tolerability, the addition of other antihypertensive therapies may be required.

Mineralocorticoid deficiency in life-limiting illness is best managed again with replacement with fludrocortisone to control symptoms of postural hypotension. Mineralocorticoid excess in the same way could be to control with ACE-inhibitors and aldactone.

3.4 Pituitary Disorders

3.4.1 Hypopituitarism

Treatment of hypopituitarism is by the replacement of the hormones that are not being produced. Patients with pan hypopituitarism will need to be treated with hydrocortisone until the very end, similar to the treatment with insulin in patients with insulin-dependent diabetes mellitus, and steroids for hypoadrenalism and Addisons disease.

Thyroid hormone replacement though is not as crucial as cortisone, but thyroxine should be given in adequate doses to keep serum T4 levels in the normal range.

Hypogonadism need not be treated in life-limiting disorders. Testosterone and estrogen therapy need not be started or may be stopped.

3.5 Pituitary Tumors

3.5.1 Prolactinoma

A prolactinoma leads to excess prolactin secretion with symptoms of galactorrhea/amenorrhea in women and erectile dysfunction in men. Macroadenomas can also present with visual field defects if large enough to compress the optic chiasm.

Treatment with dopamine agonists needs to be continued in macroadenomas, especially sight threatening macroadenomas. Cabergoline or bromocryptine could be stopped in postmenopausal women. In patients who do not respond to either and who are in-operable, temozolomide, a chemotherapeutic alkylating agent, could be tried.

Hormonal deficiencies as a result of compression on the normal pituitary will need to be dealt with individually as explained above.

3.5.2 Acromegaly

In acromegaly, there is excessive growth hormone (GH) secretion, leading to growth of bone soft tissue. This results in enlarged hands and feet; protruding lower jaw and brow; an enlarged nose; thickened lips and wider spacing between your teeth; coarsened, enlarged facial features; coarse, oily, thickened skin; small outgrowths of skin tissue (skin tags); fatigue and muscle

weakness; deepened, husky voice due to enlarged vocal cords and sinuses; severe snoring due to obstruction of the upper airway from soft tissue growth; impaired vision; headaches; enlarged tongue; pain and limited joint mobility; menstrual cycle irregularities in women; erectile dysfunction in men; enlarged liver, heart, kidneys, spleen, and other organs; increased chest size (barrel chest).

This condition is often diagnosed late and morbidity and mortality rates are high, particularly as a result of the associated cardiovascular, cerebrovascular, respiratory complications, metabolic, bone, and endocrine complications and malignancies. Hypopituitarism may also develop as a result of the tumor mass.

Medical management would be the treatment of choice in a subgroup of patients. These are patients who are not willing for surgery, are not fit enough for surgery, patients in whom the tumor is deemed in-operable, patients with post-operative relapse.

Medical management is with somatostatin analogues (Octreotide, Lanreotide, Pasireotide) and dopamine analogues (Bromocryptine, Cabergoline) and GH receptor antagonist (Pegvisomant).

4 Summary

In summary, palliative care of endocrine disorders and diabetes focuses on symptom control, as is more appropriate in life-limiting conditions and towards the end-of-life. The monitoring of diabetes and the endocrine condition per se should be kept to the minimum and aims to guide treatment towards symptom control only, reducing adverse effects and maintaining quality of life.

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Palliative Care in Chronic Illness and Multimorbidity

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_64

Abstract

Extended chronic phases of life-limiting illness and increasing multimorbidity present growing challenges that require a new approach to healthcare. A population-based approach is needed to harmonize policies, systems and services relating to chronic and palliative care. Partnerships are needed between different healthcare disciplines and specialties, and between health services and communities. Technology is likely to play an increasingly important role in transfer of information (including advance care plans) and enabling coordination of care. During periods of stability, patients and families should be actively involved in keeping well and helped to "hope for the best while preparing for the worst" to support sustained coping. A rapid response is needed to clinical events that helps people return to stability and takes preventive action against future events wherever possible. Transitions between chronic and terminal phases of illness and different settings (community, residential and hospital) need focal support to prevent people "falling through the gaps." The optimal timing of referral to specialist palliative care services is the subject of ongoing debate and research. Consumer advocacy may play an important role in raising awareness and advocating for appropriate resourcing and changes to policy and legislation.

1 Introduction

Aging of the population and medical advances are leading to ongoing changes to the community who have palliative care needs. Illnesses that once were a major cause of sudden death have become progressive and chronic in nature, resulting in many people living with extended and unpredictable cycles of wellness and disability. With increased longevity, people are also accumulating more than one chronic illness, together with associated symptoms and treatment side effects and progressive disability. This changing epidemiology demands innovative models of care. This chapter will use the World Health Organization (WHO) Framework for Innovative Care for Chronic Conditions to consider the implications of these changes for a needs-based approach to care from the perspectives of the patient/family, health organization, wider community, and policy.

2 World Health Organization (WHO) Framework for Innovative Care for Chronic Conditions

The WHO Framework for Innovative Care for Chronic Conditions (ICCC) is the most widely accepted framework for chronic care (World Health Organization (WHO) 2002). This framework identifies that people with chronic illness and their families require support not only from formal healthcare services but also their communities and the wider policy environment (see Fig. 1). Healthcare enablers are focused on promoting continuity and coordination, organizing and equipping healthcare teams and communities, using information systems to support coordination and communication, and supporting patients and families to self-manage health within the context of everyday life. This framework provides a useful lens for considering the supports required

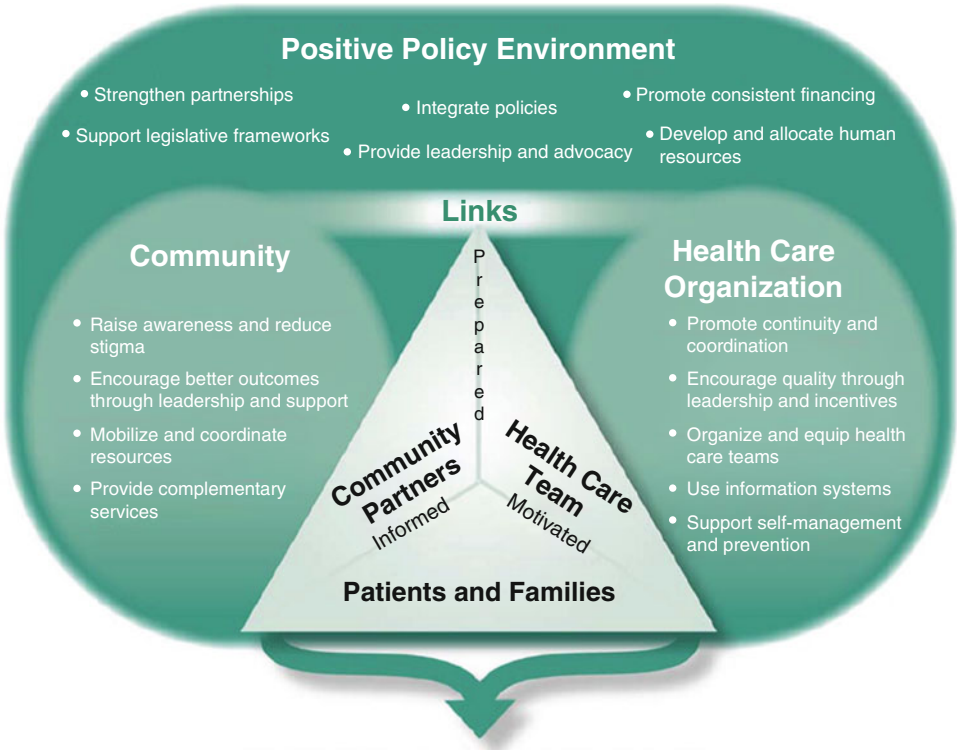

Fig. 1 World Health Organization's Framework for Innovative Care for Chronic Conditions (World Health Organization (WHO) 2002)

by patients and families during the chronic phase of a life-limiting illness.

3 Defining Chronic Illness and Multimorbidity

3.1 Chronic Life-Limiting Illness

Treatment advances are enabling people with life-limiting illness to live for many years longer than previous generations (Canadian Hospice Palliative Care Association 2013). Life-limiting illnesses that are now frequently described as chronic include respiratory, heart, cerebrovascular, and kidney disease, HIV/AIDS, dementia and other neurodegenerative disorders (e.g., Parkinson's disease), and many types of cancer. Worldwide, the most common chronic life-limiting illness is chronic obstructive pulmonary disease (COPD), affecting 26.6 million people in 2004 (World Health Organization 2004). An analysis from the UK found cancer to be the most costly for healthcare services but dementia to have the greatest social care costs (Luengo-Fernandez et al. 2012).

For some of these diseases, such as dementia, medical advances have led to incremental rather than exponential benefits. But for cancer in particular, developments over the past decade in targeted therapies have been profound. This has led to more recent and explicit consideration of what is meant by "chronic" for cancer than for other life-limiting illnesses. While references to cancer as a chronic illness go back more than half a century, definitions have changed over time to reflect developments both in treatment and healthcare (Harley et al. 2015; McCorkle et al. 2011; Phillips and Currow 2010). The most recent definition by Harley et al. (2015) refers to a "chronic phase" that is finite, unpredictable, and associated with a burden of symptoms, treatment side effects, and medical appointments (see Box 1).

Box 1 Working definition of the chronic phase of cancer provided by Harley et al. (2015), p. 344)

- A diagnosis of active, advanced, or metastatic cancer that cannot be cured.
- Active anticancer treatments are available that can lead to symptom control, slow disease progression, or prolong life.
- The patient is not considered to be at the end stage of cancer.
- The chronic cancer phase ends when the cancer no longer responds to treatment and there are no treatment options available that are expected to slow disease progression or prolong life. Patients will leave the chronic phase when they are expected to have only months to live.

The expansion of genomics, proteomics and metabolomics will continue to impact on improved cancer diagnosis, prognostication and treatment decisions (Roychowdhury and Chinnaiyan 2016). In the future, advances are likely to result in better matching between therapeutic agents and the molecular characteristics of the individual patient. Currently, however, the new generation of advanced cancer treatments are available for only some tumor types and have variable efficacy between individuals. For many, treatment response leads to recovery commensurate with prior functional status. However, for others, adverse effects such as febrile neutropenia can sometimes confer a similar trajectory to that traditionally associated with heart and lung failure (see Fig. 2).

Advances in treatments for heart and lung failure have also extended life and increased the variability in trajectories, decreasing the likelihood of acute events but often at the expense of significant disability. The field of mechanical circulatory support for heart disease has seen particular growth, with important developments in pacemakers, implantable cardioverter defibrillators (ICDs), and ventricular assist devices (VADs). Most recently, VADs have transitioned from being "bridge to transplantation" devices to destination therapy for critically ill patients with heart failure, allowing individuals to live at home (Abraham and Smith 2013). While organ transplant success rates have improved and eligibility criteria have expanded, those with multimorbidity are less likely to benefit, and an inadequate supply of organs means that many people die on the waiting list. Emergent developments in dialysis include wearable artificial kidneys that may lead to much less interruption of everyday functioning during dialysis.

The healthcare needs conferred by benefits and burdens associated with expanding chronic phases of life-limiting illnesses will be discussed in the next section, which is concerned with the "healthcare organization" component of the WHO's ICCC Framework.

3.2 Multimorbidity

In the absence of a clear definition, the term "multimorbidity" is typically operationalized as the coexistence of two or more long-term health conditions (National Institute for Health and Care Excellence 2016). The related term "comorbidity" assumes that a particular condition is the main focus and refers to each "additional co-existing ailment" (Feinstein 1970, p. 455). Distinctions between constructs such as "health condition" or "ailment" and developmental disorders (e.g., learning disability), symptoms (e.g., chronic pain), functional status (e.g., cognitive impairment), geriatric syndromes (e.g., frailty, falls), sensory impairment, and alcohol/substance misuse vary between conceptualizations; sometimes, it may also be difficult to distinguish these based on aetiology. Multimorbidity in the context of chronic life-limiting illness may either refer to more than one life-limiting disease (e.g., lung cancer and COPD) or else to diseases that have potential to become life-limiting (e.g., chronic renal disease) or non-life-limiting diseases (e.g., skin conditions) presenting comorbidly with a life-limiting illness. Chronic illnesses that are not normally life-limiting but may increase symptom burden and the complexity of care needs include diabetes, musculoskeletal disease, and mental health disorders.

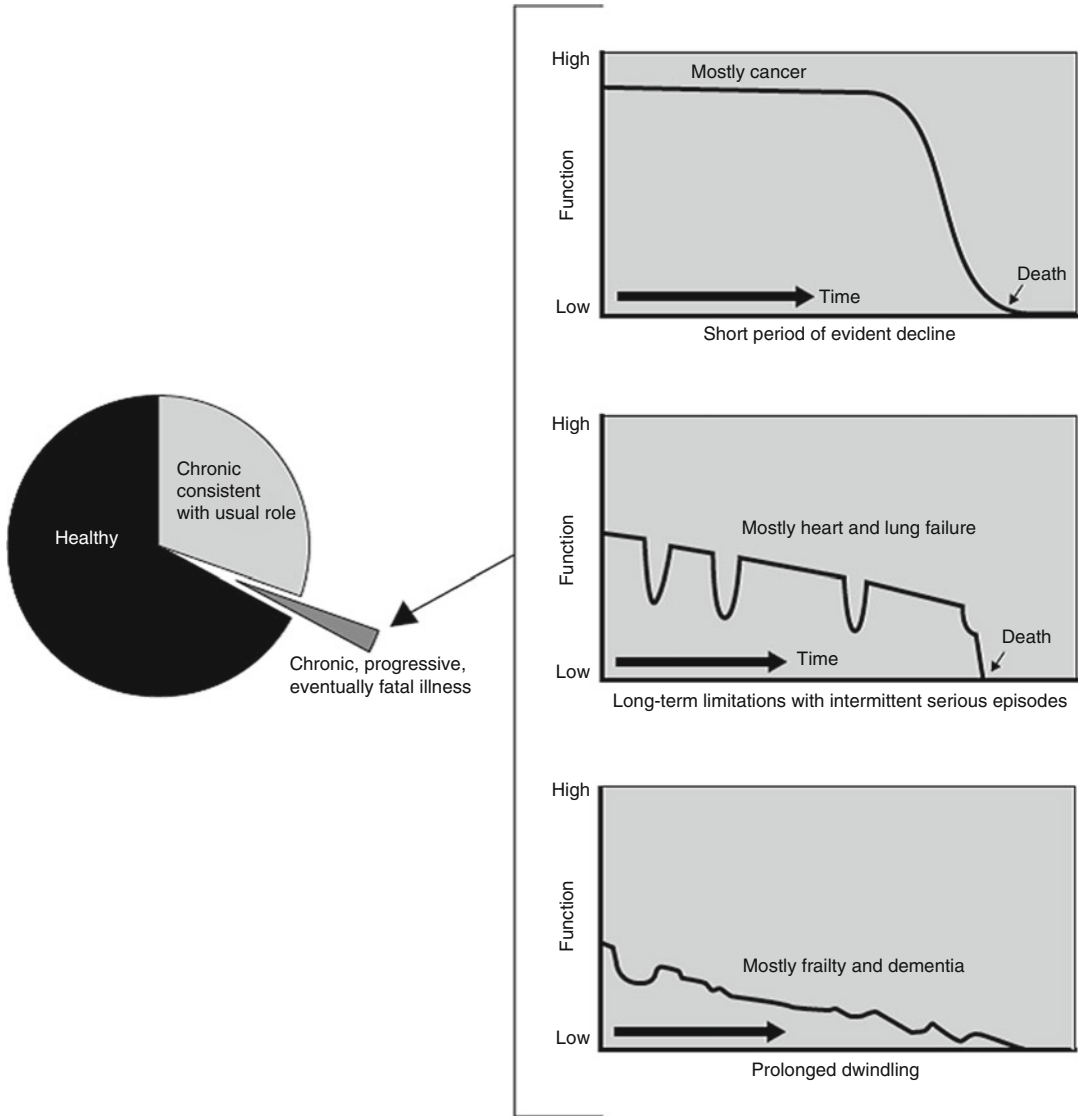

Fig. 2 Chronic illness in the elderly typically follows three trajectories (Lynn and Adamson 2003). Note that adverse effects associated with new treatments for some advanced cancer types mean the trajectory can sometimes resemble "long-term limitations with intermittent serious episodes"

Estimates of the prevalence of multimorbidity in clinical populations have varied from 20% to 98% depending on the population and definition of morbidity, but are generally more than 50% – higher than the prevalence of any single chronic disease (Marengoni et al. 2011). Multimorbidity has consistently been associated with higher age, female sex, and lower socioeconomic status. Multimorbidity is also increasing in prevalence, with the US National Health Interview Survey data collected over two time periods demonstrating a 37% increase in multimorbidity in adults aged 65 years of age and older between 1999–2000 and 2009–2010 based on self-reports of two or more of nine listed conditions (hypertension, heart disease, diabetes, cancer, stroke, chronic bronchitis, emphysema, current asthma, and kidney disease) (Freid et al. 2012). Increases over time were especially notable in hypertension, diabetes, and cancer. Multimorbidities involving

life-limiting illness identified as common in either this study or others have included hypertension combined with heart disease or cancer, and angina with asthma and COPD.

Measurement of multi- or comorbidity has tended to focus on relative burden (de Groot et al. 2003). Many such measures weight comorbidities according to their association with mortality. However, the burden for any given condition is highly variable, especially where the additional impact of each new morbidity is synergistic with others, resulting in greater overall burden than expected based on simple accumulation (Verbrugge et al. 1989). Understanding the mechanisms by which these synergies occur is a priority for future research because of its potential for informing which interventions may offer the most cost-effective opportunities for improvement in outcomes.

4 Elements of the WHO's Framework for Innovative Care for Chronic Conditions as Applied to Chronic Life-Limiting Illness and Multimorbidity

4.1 Healthcare Organization

4.1.1 Self-Management

The problems experienced by patients and families in each of the domains of palliative care – physical, psychological, social, and spiritual (World Health Organization 2002) – will vary according to a large range of factors, including the life-limiting illness in question, comorbidities, living situation, occupational roles, financial status and social support (Murray et al. 2005). However, for most people most of the time, support will be delivered within a self-management paradigm. Self-management is best promoted within a partnership or collaborative model, in which patients are considered experts on the experience of illness and its relationship to their daily life, while health professionals assume a coaching role aimed at building confidence in one's ability to manage ("self-efficacy") as well as necessary skills themselves (McCorkle et al. 2011). As well as practical aptitude in disease and symptom management, self-management skills include more generic abilities in: problem-solving; decision-making; finding and using information, services, and other resources; and building further partnerships with health professionals as needed (Lorig and Holman 2003). In addition to benefits to quality of life from improved symptom and disease management, development of self-efficacy has itself been associated with a range of positive psychosocial outcomes, perhaps because of an increased sense of control (Marks et al. 2005).

Self-Management in the Context of Multiple Comorbidities

Limited evidence is available for self-management interventions designed specifically for people with multiple comorbidities. However, a layered approach may be required where a foundation of generic skills is developed alongside skills in managing each disease and its interactions with others (see Fig. 3). An initial focus on each separate disease should be aimed at helping patients better understand the processes and consequences of each before considering the reasons and ways that management needs to be modified to accommodate interactions between symptoms and side effects from other illnesses. Developing an understanding of this kind is needed to identify safety considerations and clarify which aspects of the self-management plan are most important. Rather than expecting patients to "comply with doctor's orders," the partnership model of care supports patients in developing their own management goals and making informed choices among management options according to their priorities and preferences. Regardless of whether doctors are collaborative or paternalistic, patients will often seek participation and control by modulating the medication dose to find an appropriate balance between symptoms and side effects (Luckett et al. 2013) or by using complementary and alternative medicines in addition to, or in place of, those prescribed (Bishop et al. 2007). Encouraging open, honest communication about these decisions will not only improve management safety and quality but also foster patients'

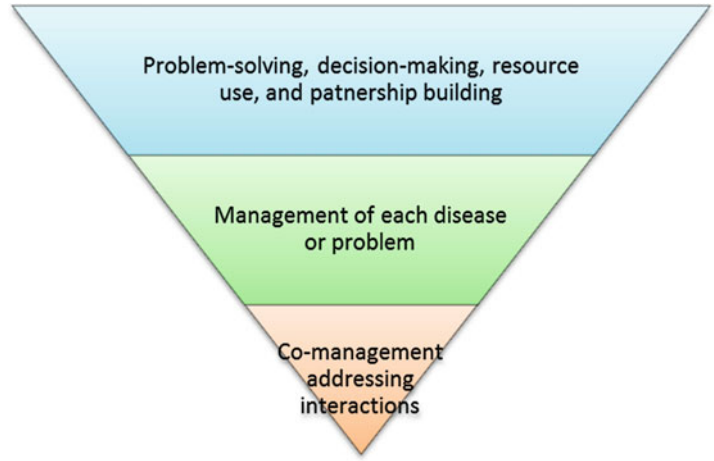

Fig. 3 Suggested foci for self-management support in people with multimorbidity, starting with generic skills identified by Lorig and Holman (2003)

feelings of participation, control, and shared responsibility in "co-producing" their own healthcare and health (Batalden et al. 2016). A partnership approach is especially essential in the context of multimorbidity because the feasibility of treatment for any given condition often becomes questionable due to competing priorities and burden from managing others (Petrillo and Ritchie 2016). Guideline recommendations also note that treatments approved for individual health conditions should be used with caution because the evidence on which approval is based has often been collected in samples specifically excluding those with multimorbidities (National Institute for Health and Care Excellence 2016).

Self-Management in the Context of Palliative Care

Self-management pertains not only to the medical aspects of illness and symptoms but also to managing changes in everyday functioning and the psychosocial consequences of chronic illness (Corbin and Strauss 1988). Unpredictability of prognosis and daily fluctuations in symptoms have led people living with chronic life-limiting illness to liken the experience to being on a "roller coaster" (Brannstrom et al. 2006). Even in the terminal phase, patients and families may continue to hope for a cure (Clayton et al. 2008); in the chronic phase, there are likely to be several transitions in hope as new treatments succeed or fail and symptoms worsen or abate. The "long-haul" nature of the chronic phase also means that maintaining a degree of normalcy is likely to be a priority for many people (Ohman et al. 2003). Where there are periods of stability, daily concerns may shift away from health altogether either because life events take precedence or people actively seek respite from the "medicalization" of their lives (Mendes 2015). However, even during periods where people are well enough to carry on everyday roles such as working and parenting, there may be insidious impacts from illness. For example, healthcare costs can sometimes mean that patients have to extend their working hours at a time when they might otherwise be reducing them to enjoy other aspects of life while they remain well (Zafar et al. 2013). This challenge is likely to become increasingly common even in countries with universal healthcare because of the delay in approval for new treatments and their high associated costs. The psychological impact on dependent children may also be especially complex during the chronic phase because of periodic reversals in the role of parents as the giver versus recipient of care and associated expectations placed on children (Kennedy and Lloyd-Williams 2009). While evidence is lacking, it may also be that "false hope" during periods of wellness and consequent disruption of anticipatory grief can have

a negative impact on bereavement outcomes after a parent dies.

4.1.2 Advance Care Planning

Psychosocial impacts of the above kinds require a balanced approach to support that empowers patients and families to self-manage their response to the challenges of chronic illness by helping them "hope for the best while preparing for the worst" (Feuz 2012). Evidence suggests that patients and families tend to welcome honest and accurate information communicated with empathy and understanding. Formally structuring this through a process of advance care planning (ACP) will enable information to be contextualized within an individualized discussion regarding patient and family values and preferences for the future. Clinicians are often reluctant to discuss ACP with people before the terminal phase for fear of undermining hope and demotivating self-management (Luckett et al. 2014b). However, when appropriately facilitated, ACP is viewed by patients as empowering rather than damaging to hope (Davison and Simpson 2006). Delaying ACP may also mean that patients lack time to thoroughly consider and discuss their wishes and risk a loss of decision-making capacity, especially for people with organ failure or respiratory disease who may face a sudden clinical crisis or increasing cognitive impairment (Shen et al. 2016).

Key considerations for ACP during the chronic phase concern the unpredictability of the disease course and likelihood that preferences for life-sustaining treatment may change dramatically in response to clinical events. These considerations warrant a "slow start" and iterative approach to ACP that:

- Helps patients consider the relative possibilities of a range of future scenarios that may each become more or less likely over time
- Enables "death awareness" to develop gradually, allowing time for adjustment (Sanders et al. 2008)
- Ensures that ensuing directives are both well considered and current

Approaches should be aimed at anticipating, identifying, and providing focal support during transitions from the chronic to terminal phases of life-limiting illness, which may otherwise lack the same attention as diagnosis. A good example of this kind of transition concerns the decision to withdraw medicines aimed at treating underlying disease. Advance discussion regarding the net benefits of continuing or discontinuing such medications as goals of care change may help frame this decision as a positive choice rather than "giving up" and decrease the likelihood that patients continue medications inappropriately (Reeve et al. 2017).

Patients with organ failure commencing life-sustaining treatment require special consideration for ACP. The dynamic ratio of benefit to adverse effects for treatments like dialysis needs careful discussion, especially in the context of increasing age and multimorbidity (Dasgupta and Rayner 2009). Patients awaiting transplant and their families will also require specific information and support to deal with uncertainties regarding organ availability and transplant outcomes (Larson and Curtis 2006). Finally, ACP for people with heart failure may need to include consideration of resuscitation status and device therapy at the end of life. Recent studies found that the majority (85%) of ICD recipients believed that "switching off" the device equated to immediate death (Stromberg et al. 2014), and few realized that almost a third (31%) of dying patients with ICDs receive shock therapy in the last 24 hours of life (Kinch Westerdahl et al. 2014). Shock therapy at the end of life is likely to cause discomfort to patients and distress to family, highlighting the importance of developing a deactivation plan.

While self-management and patient empowerment through choice are key principles in the care of people with chronic life-limiting illness, it is important to recognize that:

- Some patients will want more of an active role than others
- There is a risk of overburdening patients and families
- Caution is needed to avoid any sense of blame being attached to perceived failures in self-management or "bad" choices (Thorne et al. 2016)

4.1.3 Services and Coordination

Care Coordination

Care coordination is the most significant challenge in delivering healthcare to people with chronic life-limiting illness and multimorbidity. Unlike people at the end of life, those in the chronic phase are likely to require treatment from one or more specialties focused on their underlying condition – for example, oncology, cardiology, or respiratory medicine. At the same time, care for people with multimorbidity requires a shift from single disease practices to a patient-centered framework that recognizes the broad range of services that are likely to be needed, the burden faced by the patient and family both from the illness itself and its management, and the duration of time people will be living with the illness (National Institute for Health and Care Excellence 2016; Petrillo and Ritchie 2016). The complexity of care needs and difficulty in successfully integrating care associated with multimorbidity is evidenced by the higher rates of unplanned and emergency care seen in this population (Lehnert et al. 2011; Marengoni et al. 2011).

Case management is the service element with perhaps the most evidence for coordinating care and improving outcomes: in chronic illness (Ouwens et al. 2005); during the chronic phase of life-limiting illness (Aiken et al. 2006); for people with multimorbidity (Smith et al. 2012); and at the end of life (Luckett et al. 2014a). Case management has been found cost-effective for older people living in the community over 1 year due to avoided hospitalizations and GP visits (Black 2007). However, cost-effectiveness for people with chronic life-limiting illness has yet to be evaluated and is likely to be a "moving target" as the chronic phase becomes further extended through medical advancements in the future. Given the likelihood of exacerbations and decline in people with life-limiting illness, case management needs to pay special attention to timely prevention, response to acute events, and support for transitions to and from hospital as needed, in addition to helping patients maintain health and functioning during periods of stability.

A special challenge is faced by healthcare services trying to provide integrated care to people with chronic life-limiting illness and multimorbidity living in nursing homes. Models tested by research have typically involved in-reach from a specialized healthcare team either to deliver direct care or to train and support clinical champions within the nursing home (Goodman et al. 2016). To effect more sustainable change, models of care are needed that value and motivate nursing home personnel, support joint priority setting, and foster ongoing relational working. Successful models will likely need to make use of systems and processes for encouraging regular communication and shared decision-making, such as case conferencing (Phillips et al. 2013). Systems also need to be in place for formally monitoring changes in residents' needs and communicating information between nursing homes and acute care during transitions.

Managing the Transition from Chronic to Palliative Care

Changes in the trajectories of life-limiting illnesses mean that the optimal timing of transition from a chronic to palliative approach to care may be becoming increasingly difficult to identify and will vary between individuals (Burge et al. 2012). For many people, the optimal transition may be gradual and draw on elements of both approaches concurrently for much of the trajectory (see Fig. 4).

Involvement of Specialist Palliative Care Services

While palliative care has traditionally focused on the last 6 to 12 months of life, its ethos has much to offer those with complex care needs at any stage of the disease trajectory (Agar et al. 2015). Palliative care has an established philosophy that aims to help people focus on "living with" rather than "dying from" advanced illness. It focuses on the whole person rather than disease and is needs-based rather than discipline-based in its approach to delivering care. Indeed, if we assume that palliative care should be assigned according to needs rather than prognosis, it may be that a palliative approach is relevant from diagnosis onward for patients with life-limiting illness of any kind (Beernaert et al. 2016).

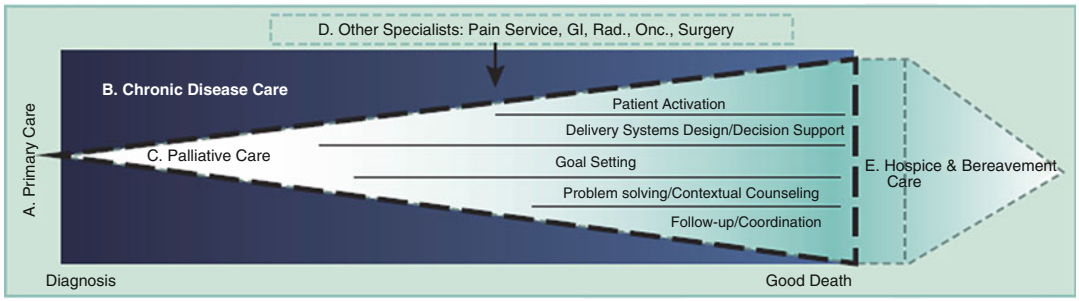

Fig. 4 Model of concurrent chronic disease palliative care for people with cancer (Canadian Hospice Palliative Care Association 2013, p. 5)

At the same time, it is important to distinguish between palliative care as an approach to care versus specialist palliative care services (SPC). Worldwide, resourcing of SPC is insufficient to enable its provision to everyone with life-limiting illness from the time of diagnosis; nor is this necessarily desirable (Glare and Virik 2001). In Australia, the New South Wales Department of Health (2007) has identified three populations of people with life-limiting illness with differing levels of need regarding input from SPC, namely, (A) those whose needs can be met almost entirely within primary care, (B) those who are predominantly managed within primary care but who experience exacerbations that require support or intervention from SPC, and (C) those with complex needs who require direct and intensive intervention from SPC. It seems likely that people in the chronic phase of life-limiting illness will generally be included in the first or second of these categories and will also be spending most of their time in the community rather than in the hospital. For these people, the responsibility for care coordination will likely sit with primary care. Indeed, it could be said that primary care health professionals are themselves the "specialists" in managing chronic illness.

The question of appropriate timing for SPC referral is the subject of much ongoing debate. Interest in "early" referral was sparked by the 2010 publication of a landmark trial which found this contributed not only to quality of life but also survival for people with advanced lung cancer (Temel et al. 2010). However, the mechanism by which early referral might have contributed to this outcome remains unclear (Irwin et al. 2013), and little research is available on referral even earlier in the disease trajectory or for other disease groups. Published guidance has tended to make use of the question "would you be surprised if this patient died in the next 6 or 12 months?" taking into account disease progression and general indicators such as functional decline, weight loss, and unplanned admissions (Boyd and Murray 2010). However, the UK Gold Standards Framework has acknowledged increasing difficulties with predicting prognosis and now advocates "instinctive, anticipatory and insurance-type thinking" which lowers the threshold at which end-of-life care planning and referral to SPC should be undertaken (National Gold Standards framework 2011). Based on this reasoning, there may be many patients with chronic illness and multimorbidity not traditionally considered life-limiting who might meet criteria for – and benefit from – referral to SPC, including people with diabetes and nonhealing foot disease (Calam et al. 2012).

A special role for SPC in the care of people with multimorbidity is supported by research suggesting that cost savings may increase with the number of comorbidities (May et al. 2016). However, further discussion is needed both within SPC and across specialties to better define the parameters of optimal SPC service provision and, if necessary, inform advocacy for funding to increase capacity. Promotion of earlier referral to SPC would also need to change perceptions among people with chronic illness and health professionals that palliative care is reserved for

people who are imminently dying (Mason et al. 2016). US research suggests that both patients and health professionals may favor the term supportive rather than palliative care even during the terminal phase (Maciasz et al. 2013). While a change in terminology of this kind is controversial in the context of end-of-life care, the fact that supportive care is currently used in oncology to refer to management of problems associated with active treatment suggests it may be a good fit for the chronic phase of life-limiting illness.

4.1.4 Information Systems

The WHO's ICCC Framework identifies information systems as being critical in organizing care for people with chronic illness. In the context of life-limiting illness, these need to include systems for sharing up-to-date information about ACP at the point of care. Transitions between care settings (e.g., aged care and hospital) are especially notorious for hampering communication about ACP as well as current care plans, test results, and medication management (Coleman 2003). Little evidence is available to support particular information system approaches, although several countries have implemented national patient healthcare information systems that enable patients to upload and share ACP information along with other medical records if they so wish. Uptake of these systems to date has been limited, and little research has been conducted on the impact on processes and outcomes of care. A recent systematic review of personal health records found evidence of benefit for chronic conditions such as HIV, asthma, and diabetes but none for cancer or multiple sclerosis (Price et al. 2015). Benefit seemed to be related to personal health records' potential for monitoring and informing self-management.

4.2 Community Perspective

The WHO ICCC Framework recognizes the need to build community capacity to support people with chronic illness in addition to formal health services. Recently, a global movement called Compassionate Communities has emerged with the aim of developing community "death literacy" and capacity to support people who are dying and their families. The movement is based on a premise that, compared with previous generations, modern communities tend to have less awareness about death and dying and weaker local networks to provide support in times of need. Research has consistently found the public to have a limited understanding of advanced illness and palliative care (Cox et al. 2013).

Initiatives aimed at improving death literacy include those promoted by the Compassionate Cities program which include "death cafe" and "death over dinner" events where people talk about their experiences of bereavement or caring for someone who is dying or death and dying more generally, visual and performing art projects, initiatives within workplaces and schools to raise awareness, and memorial events. Initiatives of this kind may be run by local government, healthcare organizations, or citizen groups. One of the largest and longest running public health and advocacy campaigns of this kind has been the Project on Death in America (PDIA) run by the nonprofit foundation, the Open Society Institute (Aulino and Foley 2001), which from 1994 to 2001 funded 94 projects to a sum of US$34 million.

Initiatives developing community capacity to support people who are dying and their families have been primarily aimed at enabling people to die at home through establishment and support of social networks that meet practical needs (e.g., preparing food, shopping), sharing knowledge about services, and, in some areas, healthcare professionals to provide training to help carers deliver care (Sallnow et al. 2016).The optimal interface between formal healthcare and community initiatives of this kind is the subject of ongoing debate. A central tenet of the Compassionate Communities movement is that care for people with life-limiting illness is "everybody's business." For some, a goal of demedicalizing death and dying is a natural corollary. Healthcare services may be viewed as "essential but not central" to care for people who are dying, with some arguing that their role is primarily to equip communities with the skills to care for themselves, providing as little

direct intervention as possible (Abel 2017). This view differs from the partnership model to self-management introduced above in that service provision is seen as community-centered rather than patient- or even family-centered.

It is unclear whether public awareness has kept pace with changes in disease trajectories, but it seems likely that this will be similar to death literacy in needing focal education and support to increase community capacity. Nongovernment organizations (NGOs) (e.g., Macmillan Cancer Support [UK], Lung Foundation Australia) may play an important role in raising awareness and advocating for resources to meet the needs of this population. Many NGOs already provide support well-suited to the needs of people during the chronic phase of life-limiting illness, including telephone helplines, wellness programs, and peer support networks. These interventions have potential to respond more quickly than healthcare systems to changing illness trajectories. They also present immediate opportunities for community engagement and leadership.

4.3 Policy Perspective

Community initiatives form just one part of a public health approach long since advocated for both palliative and chronic care (Institute of Medicine 2012; Sepulveda et al. 2002). A population-level approach that integrates policies in these two domains is needed to ensure coherence, efficiency, and progress toward addressing disparities in access to services and outcomes (Murray et al. 2009). A population-based approach will also distil the special requirements of the burgeoning population of people with chronic life-limiting illness and how these differ from palliative and chronic care populations more generally. Surveillance measures are also needed to measure progress, including a composite of patient-reported measures (e.g., life satisfaction and well-being), healthcare system (e.g., access), and population-level measures (e.g., clinical, access, and funding policies) (Institute of Medicine 2012). Cost-effectiveness analyses are needed that compare different public health models and take into account societal costs and benefits at a population level (Dzingina and Higginson 2015).

The ICCC Framework emphasizes the need to support chronic care through policies aimed at appropriate financing and partnership building. Many of the world's health systems remain geared toward a single-disease model rather than integrated care (Bayliss et al. 2007). Funding models are needed that acknowledge multidisciplinary contributions and clinician time spent on preventive healthcare, psychosocial support, and self-management. In practice, this may mean moving remuneration away from a fee-for-service basis to the patient or population level (Oliver-Baxter et al. 2013). This approach is being adopted by a new Australian initiative called "Health Care Homes," which aims to integrate care for people with chronic and complex care needs across community and acute settings. Bundled payments, made to general practices and Aboriginal Medical Services, can be managed between services as needed and are responsive to changes in patients' needs over time, making this model especially suited to people with chronic life-limiting disease whose needs are likely to fluctuate.

Legislative frameworks presenting a barrier to outcomes for people with chronic life-limiting illness include those relating to approval and funding of new treatments. The need for these frameworks to be more responsive to emerging evidence has become an increasing focus in the popular press. Consumer advocacy is likely to be key in driving changes to policy and legislation to better align these with the needs of people with chronic life-limiting illness, as it has been in recognizing other patient populations, such as cancer survivors.

5 Conclusion and Summary

This review of the changing nature of life-limiting illness and associated healthcare needs with reference to the WHO's Framework for Innovative Care for Chronic Conditions shows the need for advocating a population-based approach aimed at harmonizing policies, systems, and services relating to chronic and palliative care. Elements of the

ICCC model requiring special support include healthcare coordination and community awareness and capacity building. More evidence and debate is needed to inform the question of optimal timing for referral to specialist palliative care services. NGOs and consumer advocacy will be expected to play an important role in advocating for appropriate resourcing and changes to policy and legislation.

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Part VI

Palliative Care in Specific Populations

Palliative Care, Frailty, and Older People

67

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_66

Abstract

This chapter provides an overview of the symptoms of frailty, the tools used to recognize and assess older people living with frailty such as the frailty phenotype and frailty index, and some of their common palliative care needs. Further, it details some of the perceived challenges of frailty to current palliative care practice, namely, recognizing dying, multiple morbidities and symptom burden, and the focus or goals of care. Palliative care for older people with frailty requires a broader disability rather than a single disease focus. Coordination and interdependencies with other care providers become as important as the discrete patient/professional clinical encounter. The centrality of the older person with frailty and their "family" living and dying over time means the social environment becomes paramount local resources; support and the interplay between services and community are vital. While evidence on the best ways to provide palliative care to this population is still developing, the chapter offers some examples of current services and suggests key elements derived from the literature and practice. The authors suggest there is a moral and clinical imperative for palliative care services to engage with older people with frailty and their caregivers, both lay and professional. This imperative brings opportunities and challenges, including revaluing living and dying rather than an overemphasis on care in the last days of life and remodeling palliative care services to focus more on need than diagnosis and the reorientation of palliative care, so that it can be integrated with older people's services.

1 Introduction

1.1 Frailty and Palliative Care

Frailty is a complex medical syndrome, combining the effects of natural aging with the outcomes of multiple long-term conditions and loss of fitness and reserve. Frailty has been termed "the most problematic expression of population ageing" (Clegg et al. 2013) and, as such, is an increasingly important consideration for palliative care. Globally, the number of people living and dying in old age is growing; by 2050 21.5% of the world's population will be aged over 60. People living into late old age are the fastest growing sector of the population (particularly in more economically developed regions),with the number of people aged over 80 growing at twice the rate of people over 60 years (McNicoll 2002). Most people who need palliative care are older adults. Increasingly, the need will be for palliative care associated with older people dying with multiple, long-term conditions and frailty (World Health Organization 2015).

Yet older people with frailty are sometimes called the "disadvantaged dying." They constitute a section of society with poorer end-of-life care experiences and less access to palliative care than other groups (Gott and Ingleton 2011). Reasons for this include siloed services related to singular diseases, perceptions that palliative care referrals relate to medical condition rather than need arising from the interplay of multiple conditions, and under-recognition of palliative care needs in older people, including from older people themselves (Hall et al. 2011). Precisely because people have lived with their symptoms for so long, older people and those around them might overlook needs,

normalizing them as part of growing old (Teunissen et al. 2006). Palliative care with the emphasis on quality of life and person-centered approaches is a vital intervention for older people with frailty; indeed Morrison et al. (2003) PX111 (Morrison et al. 2003) note "*frailty is the quintessential model for palliative care in older adults as optimal medical treatment for the frail patient typically includes preventive, life-prolonging, rehabilitative, and palliative measures in varying proportion and intensity based on the individual patient's needs*."

Older people living and dying with frailty for palliative care raise both challenges and opportunities. This chapter provides an overview of the symptom complex of frailty, the tools required to recognize and assess older people living with frailty, and the potential need for palliative care. Further, it details some of the perceived challenges of frailty to current palliative care practice, namely, recognizing dying, multiple morbidities and symptom burden, and the focus or goals of care. We argue there is a moral and clinical imperative for palliative care services to engage with older people with frailty and their caregivers, both lay and professional. Such an imperative will help to bring the realization of the WHO 2014 palliative care resolution (WHO 2014) – to be an essential healthcare service for people with chronic and life-limiting illness. Palliative care needs to move its focus from a discrete service with an overemphasis on care in the last few days of life to a service integrated with the treatment of long-term conditions and with older peoples' services.

1.2 What Is Frailty?

In practice, the term frailty is used as both a general descriptor and to signify a discrete medical syndrome. Individuals whose health status indicates they may be susceptible to decline may be described as "becoming frail." Those people who meet specific diagnostic criteria are identified as having the medical syndrome of frailty. This chapter focuses on the latter. Hence, while cognitive decline is a component of frailty (considered later in the chapter), the distinctive palliative care needs of people with severe cognitive impairment or dementia are discussed elsewhere within this publication.

Frailty is a distinctive health state related to the aging process in which multiple body systems gradually lose their inbuilt reserves, leaving a person vulnerable to dramatic, sudden changes in health triggered by seemingly small events such as a change in medication or an infection (Clegg et al. 2013). Figure 1 illustrates the reduced recovery potential of older people with frailty following a seemingly minor illness. The red line demonstrates the longer recovery time with incomplete return to levels of functional ability for a person with frailty compared to an older person without frailty.

While not all older people become frail, frailty becomes more prevalent with age. Choi et al.'s (2015) study using national population-based surveys in the UK, Europe, United States, Taiwan, and Korea found frailty prevalence was between 4.9% and 27.3% in the total population. Figures

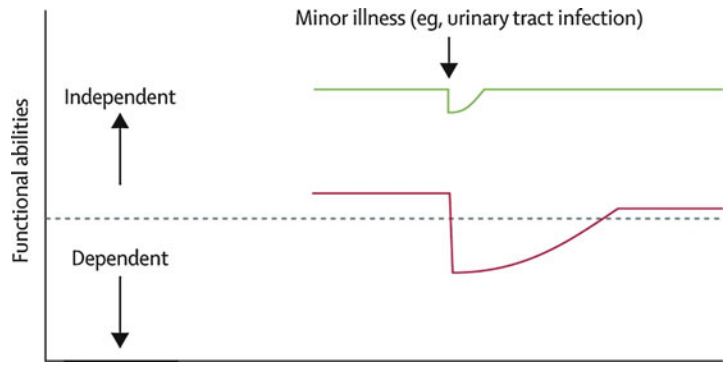

Fig. 1 Vulnerability of frail elderly people to a sudden change in health status after a minor illness (Clegg et al. 2013)

from the UK suggest frailty affects around 10% of those over 65 increasing to around 65% of those 90 and above (Clegg et al. 2013). Frailty is a dynamic state and is known to change over time, mostly worsening rather than improving (the red line in Fig. 1 does not come back to the previous level). Frailty in old age is often characterized by a progressive decline in physical, mental (Rockwood et al. 2005), and social functions (van Campen 2011), increased vulnerability to sudden deterioration (Covinsky et al. 2003), and reduced recovery potential (Turner and Clegg 2014). Typical signs and symptoms of frailty include sarcopenia, anorexia, exhaustion, and low mood. Evidence of the pathophysiology of frailty is growing, and chronic systemic inflammation leading to neurological and immunological dysfunction is a major contributor, as is cardiovascular degeneration and genetic predisposition (Fulop et al. 2010). Frailty biomarkers are being studied. Velissaris et al.'s (2017) systematic review explores the relationship between older people with frailty and systemic inflammation. C-reactive protein is an easily measurable biomarker, but not consistently associated with frailty. However, robust evidence demonstrates the association between morbidity and mortality with frailty, which increases as an older person becomes progressively more frail. Compared to fit older people, those with frailty are at greater risk of disability, nursing home admission, hospitalization, and death (Fried et al. 2001). Those with even mild frailty have almost twice the mortality risk of a fit older person; for those severely frail, the risk is almost five times higher (Clegg et al. 2016).

1.3 Identifying Frailty

It is important to identify frailty because it is predictive of adverse outcomes. While there is currently no robust evidence of the reversibility of frailty, research does demonstrate that the side effects of frailty, e.g., weakness and fatigue, can be lessened with intervention, particularly in the early stages. Frailty identification means we can deliver the most appropriate therapeutic interventions, including palliative care to those with severe frailty. The evidence on recognition, effects, and treatment for the symptom complex of frailty has grown exponentially over the last 10 years; however, it is still a concept in evolution. The two most common ways of operationally defining frailty are (1) the frailty phenotype (Fried et al. 2001) and (2) the frailty index (Rockwood et al. 2005) (see Table 1). It is useful to see the phenotype and frailty index as complementary rather than opposing approaches to identifying frailty (Cesari et al. 2013). The frailty phenotype assesses five dimensions that are hypothesized to reflect systems whose impaired regulation underlies the syndrome. These five dimensions are unintentional weight

Table 1 Comparing the frailty phenotype and frailty accumulation of deficit index approaches to identify frailty

Identifying frailty – table comparing the frailty phenotype and frailty accumulation of deficit index approaches	
Frailty phenotype	Frailty index
Frailty as a pre-disability syndrome	Frailty as an accumulation of deficits using a combination of factors including symptoms, diseases, activities of daily living, and results of holistic clinical assessments
Signs, symptoms relating to sarcopenia	
Categorical variable – five dimensions with set criteria: pre-frail meets one or two criteria, frailty requires satisfaction of three or more	Continuous variable which describes a risk profile moving from pre- to severely frail depending upon the accumulation of deficits
Five predefined dimensions with criteria: involuntary weight loss, exhaustion, slow gait speed, poor handgrip strength, and sedentary behavior	Predefined set of deficits identified over physical, psychological (including memory and cognitive problems), and social domains
Identification possible outside of a full clinical assessment	Identification part of a comprehensive clinical assessment or through an Electronic Frailty Index (EFI) (Clegg et al., 2016) calculated through routinely collected patient data in primary care

loss, exhaustion, muscle weakness, slowness while walking, and low levels of activity. Those who meet at least one or two of the criteria for these dimensions are defined as pre-frail, and those meeting three or more of the criteria are defined as frail. The frailty index is based on the concept that frailty is a consequence of interacting physical, psychological, and social factors. As deficits accumulate, people become increasingly vulnerable to adverse outcomes, moving from mild to moderate and then to severely frail. The number of deficits that are needed to indicate the presence and grade of frailty has changed with further research from the original 70 items of the earliest version of the frailty index (Rockwood et al. 2005). The Electronic Frailty Index eFI (Clegg et al. 2016) identifies 36 deficits across physical, psychological, and social domains to calculate a frailty risk value (an eFI) from data collected routinely from community-dwelling older people. The eFI is calculated by the number of deficits the patient has, divided by the number of deficits considered. Such indices can be used to identify the possible presence and grade of frailty, confirmed by a clinical assessment thus tailoring clinical services.

Clinically, there are many ways to recognize frailty. The NICE Multi-morbidity Guidelines (https://www.nice.org.uk/guidance/ng56) argue for two main approaches: (1) assessment through simple instruments based on the two main ways of identifying frailty discussed above, e.g., timed get up and go test (taking more than 10 s to get up from a chair walk 3 m and sit down again) is based on the frailty phenotype approach, or (2) through routinely collected data such as the Electronic Frailty Index which draws on the accumulation of deficits frailty index (Clegg et al. 2016). The choice of instrument is informed by purpose of identification, clinical setting, and availability. Simple tools are often a useful clinical starting point. The Clinical Frailty Scale, see Fig. 2 (The Clinical Frailty Scale), is a pictorial scale based on activities of daily living (ADLs) which

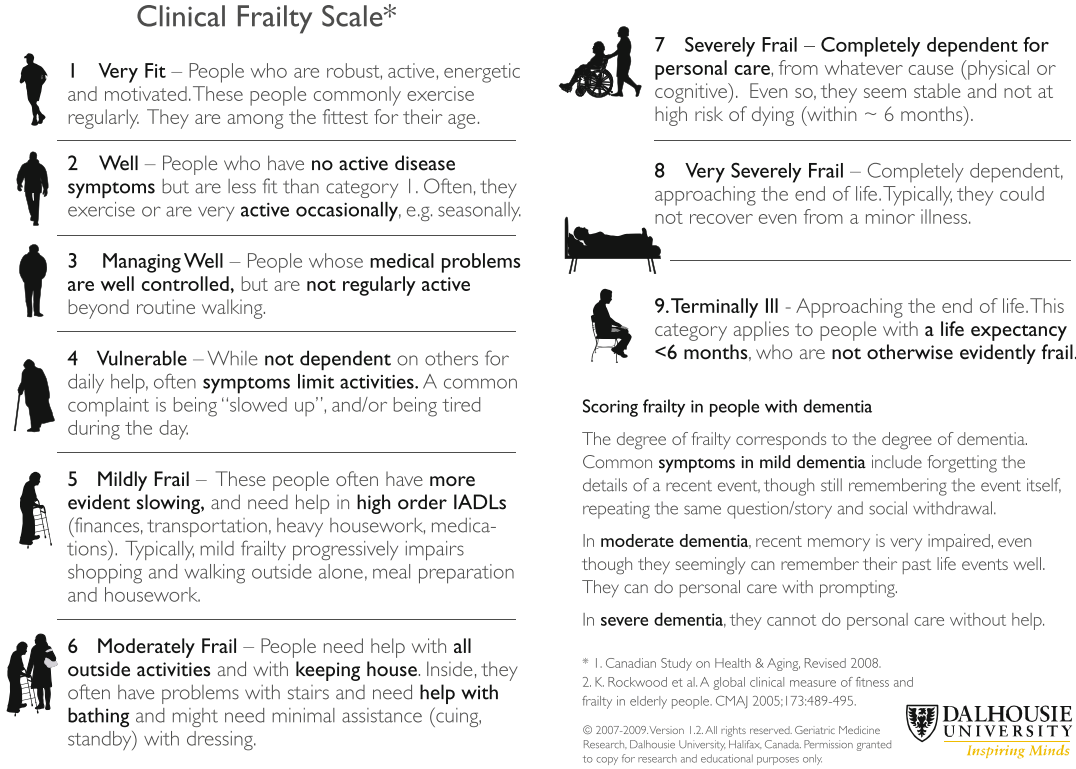

Fig. 2 The Clinical Frailty Scale. (http://camapcanada.ca/Frailtyscale.pdf)

categorizes frailty on a scale of 0–9 into mild, moderate, and severe frailty (see Fig. 2). It is a pragmatically useful tool to identify people in with frailty and appropriate therapeutic interventions, including palliative care.

2 Frailty and Multi-morbidity

While frailty might be the sole long-term condition with which an older person presents, it is often the case that it is the interplay between a combination of long-term conditions, called multi-morbidities, which are life threatening. The UK NICE guidelines (https://www.nice.org.uk/guidance/ng56) define multiple morbidity as a combination of two or more physical and mental health conditions such as diabetes or dementia, ongoing conditions such as learning disability, symptom complexes such as frailty, sensory impairment, and substance misuse. Fortin et al.'s (2012) systematic review of prevalence of multimorbidity in European and North American countries suggests there is marked variation between the prevalence of multiple morbidities due to methodological and definitional differences. However, the prevalence of multi-morbidities was associated with increased age in both general population and community-only studies. Barnett et al.'s (2012) much cited cross-sectional study across 314 community practices in Scotland suggests by age 65, 75% of the population are multimorbid, and for those 85 and over, 55% will be living with at least three long-term conditions, the number of conditions rising with age. As well as frailty, common morbidities identified by NICE from physical and mental health conditions include dementias, respiratory disease, urinary incontinence, and depression. Evidence is growing about the interplay between the frailty syndrome and cognitive decline, e.g., frailty is a risk factor for dementia (Searle and Rockwood 2015), there is a shared mechanism of pathophysiology (Sampson 2012), and cognitive decline is one of the deficits included in the frailty index accumulation of deficit approach to frailty. Pragmatically, clinicians will see many older people with frailty who have a component of cognitive decline. However, severe cognitive impairment, such as Alzheimer's disease, is a distinct condition.

The complexity of symptom burden and need over time for older adults with frailty cannot be fully captured by a biological disease model alone. This underlines the need for holistic assessment, incorporating medical, spiritual, social, and psychological care needs. Palliative care is such an approach, working with the whole person and addressing need rather than solely focusing on pathology.

3 Frailty: Moving Beyond a Biomedical Approach

Moving frailty beyond a biomedical deficit, conceptualization requires an acknowledgment of the resilience and resources of older people with frailty within the communities in which they are living and dying (Nicholson et al. 2012). An alternative conceptualization of frailty is also one where an older person is in a state of imbalance, experiencing simultaneously accumulated biopsychosocial losses while working to sustain and create new ways of connecting to their surroundings. Achieving balance between loss and continuity is crucial for the well-being of older people with frailty and is supported, or undermined, by the quality of their interactions with health and social care and the wider contexts of their lives (Nicholson et al. 2013). This approach moves beyond the dichotomies of independent/dependent or coping/requiring care to a person-centered approach, recognizing capabilities as well as potential needs, even when severely frail. It seeks to recapture McCue's (1995) insight of life naturally moving toward closure in old age. In this formulation, severe frailty is engaged with holistically and not, without careful thought, resisted biologically. However, while the case for palliative care involvement with frailty is clear, what is not so evident is robust data to describe or quantify specific palliative care needs. The following section of this chapter details some of the main issues identified to date in meeting the palliative care needs of older people with frailty.

4 Palliative Care for Older People with Frailty

4.1 Identification of Palliative Care Needs

Recognizing where a person might be in their dying trajectory is an increasingly important marker of potential care need and referral to palliative care. It also aids communication across teams and supports person-centered decision-making at end of life. Lunney et al. (2003) (ref) explores functional decline in four disease-based trajectories: sudden death, malignancy, organ failure, and frailty. The functional trajectory of frailty describes a progressive decline or prolonged dwindling over several months or years, punctuated by episodes of acute illness. This unpredictable trajectory makes it difficult to diagnose when people are nearing the end of life, and their increasing vulnerability to sudden health changes means dying might be characterized as unexpected. This is confirmed by Gill et al.'s (2010) retrospective study of disability trajectories of community-dwelling older people in the last year of life. They note considerable heterogeneity in the sample of frail older people; 25% of older people with frailty had progressive, severe disability in the last year of life, compared with 70% of people with advanced dementia. The authors conclude that the findings indicate the need for services to assist at end of life is at least as great in frailty as for those with a defined terminal condition. However recognizing this need is difficult. Pailoux et al. (2013) note that the sum of several illnesses or syndromes encompassing frailty is often looked at as separate diseases (rather than an accumulation of deficits), and thus, "practitioners have difficulty integrating the inevitably fatal nature of the situation" (p. 3). Nicholson et al. (2018) illustrate this in their work comparing patient needs and concerns of older people within an innovative new palliative care service with those of the conventional specialist palliative population (typically those with malignancy). Surprisingly similar needs were identified at first contact however Older people entered palliative care with a much lower performance status and remained in a longer period of stable deterioration than those with malignancies. Consequently, the dying phase can be very short or indeed unrecognized by clinicians. Murray et al. (2017) explore trajectories of decline with a more holistic perspective. The authors posit three main functional end-of-life trajectories: rapid, often associated with malignancy; intermittent, often associated with organ failure or multiple morbidities; and gradual, often associated with frailty or cognitive decline. For each pattern, the authors describe the likely pattern of physical, psychological, social, and spiritual decline and set out the implications for palliative care. They argue such an approach may help clinicians to identify, plan, and involve palliative care earlier.

What is clear is that in order to receive palliative care, older people with frailty need to be identified as having palliative care needs. There are a number of prognostication tools to help identify people in need of palliative care. However, evidence of reliability and validity for older people with frailty is sparse. Maas et al.'s (2013) systematic review of European and North American studies identified tools commonly used for identification of community palliative care. These include the RADPAC, Radboud Indicators for Palliative Care Need (Thoonsen et al. 2011) (which contains disease-specific assessment criteria for cancer, COPD, and heart failure); the SPICT Tool (the Supportive and Palliative Indicators Tool, a combination of general indicators, and disease-specific assessment criteria) (Highet et al. 2014), and the Gold Standards Framework Prognostic Guidance (Gold Standard Framework (GSF)) (based on three triggers that suggest that patients are nearing the end of life: the surprise question and general and specific clinical indicators for decline in organ failure, dementia, and frailty trajectories). The surprise question, "*Would I be surprised if this patient died in the next 12 months?*" has been shown to be of poor to moderate performance in specificity and sensitivity in identifying people in the last year of life (Downar et al. 2017). This is particularly the case in older people with frailty where lack of underlying pathology, and unpredictable illness

trajectories, means some doctors are less likely to use the surprise question with this patient population (Elliott and Nicholson 2017).

The SPICT Tool (Highet et al. 2014) has been validated in hospitalized geriatric patients (De Bock et al. 2017), demonstrating a significant association with 1 year mortality. The Dementia/Frailty specific section of SPICT uses functional decline, activities of daily living, and frequent falling as clinical indicators of deterioration. As such, it links well to frailty syndrome. Multiple hospitalizations (Kelley et al. 2017) and recurrent infections (Leibovici 2013) have been evidenced a marker of poor prognosis in older people with frailty. While such clusters of triggers may be helpful in identifying need for older people with frailty, they are service dependent. Studies (Campbell et al. 2004; Ávila-Funes et al. 2008) suggest it is often a complex interplay of variables that coalesce to contribute to poor prognosis. These variables might include, for example, the effect of hospital admission, multiple morbidity, as well as frailty, age, gender, cognitive function, and sociodemographic factors on baseline before admission to hospital.

4.2 Specific Palliative Care Needs of Older People with Frailty

The principles of symptom assessment remain constant, focusing on relief of discomfort and enhancing quality of life. The gold standard in geriatric care for the assessment and management of frailty in older adults is a process of care known as the comprehensive geriatric assessment (CGA) (Ellis et al. 2011). CGA has been defined as a "multidimensional and usually interdisciplinary diagnostic process designed to determine a frail older person's medical conditions, mental health, functional capacity and social circumstances" (Ellis et al. 2011). CGA has much in common with palliative care holistic assessment. The application of both geriatric and end-of-life expertise is often beneficial because of the complexity of coexisting social, psychological, and medical needs in older people with frailty.

4.3 Defining Symptoms

4.3.1 Sarcopenia, Falling, and Fatigue

Sarcopenia is the loss of skeletal muscle mass and function with old age. Frailty shares common biomedical determinants with rapid muscle aging, i.e., inflammation, malnutrition, changes in neuromuscular function, and structure, and both are closely linked with falling and exhaustion. Muscle fatigue is a common symptom associated with older people with frailty at the end of life. It can be measured through low grip strength, walking speed, or balance. The management of sarcopenia includes leucine-enriched protein and vitamin D supplements (Morley 2016). Evidence over decades suggest that exercise involving strength and balance, even those who are very frail, is the key intervention component (Cadore et al. 2013). In older people with frailty, functionality, rather than diagnosis of disease, is one of the best indicators of health status. De Labra et al. (2015) systematic review of RCTs of exercise interventions in older people with frailty noted improvement in mobility balance, strength, body composition, and falls. However, the optimal exercise program is not yet clear. A Pan-European intervention program, the VIVIfrail project, has devised a range of resources including a practical exercise guide, including those with severe frailty and at risk of falling (http://www.vivifrail.com/resources). A Cochrane systematic review of the effect of functional rehabilitation programs in older people living in long-term care showed improvements in physical function (Gold Standard Framework (GSF)) such as strength, flexibility, and balance, as well as the potential to improve mood (Crocker et al. 2013). Pulmonary rehabilitation in particular may be helpful for older people living with frailty, as it targets key frailty symptoms such as fatigue, weakness, and dyspnea and encourages physical activity (Maddocks et al. 2016).

4.3.2 Polypharmacy

An important aspect of assessment of older people with frailty is medicine optimization: there is a strong association between polypharmacy (four or more medications) and falling in old age (Ziere

et al. 2006). Palliative care clinicians need to be aware both of the medications they may prescribe and the need to optimize medications to decrease the risk of inadvertently increasing the burden of symptoms for older people with frailty including falling. Sedative hypnotics, antidepressants, cardiovascular drugs, and cardiovascular medication are of particular concern. Validated tools, e.g., the START/STOP tool (O'mahony et al. 2015), can be of use. Additionally, an important and an often underutilized expert is the pharmacist, both in the hospital and community.

4.3.3 Weight Loss

Given the interconnection between weight loss, sarcopenia, and frailty, anorexia is a powerful, independent predictor of poor quality of life, morbidity, and mortality in older persons (Morley 2003). One of the most important goals in the management of older, frail people is to optimize their nutritional status. Nutritional interventions may include smaller, more frequent meals, high caloric foods, altering consistency and referrals to speech and/or occupational therapists, and dietitians. Evidence supporting the use of nutritional supplements for older people with weight loss is mixed, in part because the underlying frailty pathology, rather than an inadequate intake, may cause the loss of weight. However, the importance of accessible nutritious food, assistance, and teeth and oral hygiene is interventions that can be overlooked. Morley (2003) notes the importance of enhancing the environment for older people and the importance of breakfast as a meal – circadian shifts in old age mean people eat more in the morning.

4.3.4 Depression

Depression is a major cause of weight loss in older people and there is a strong association between frailty and depression (Brown et al. 2014). Older adults with depressive symptoms have poorer functioning compared to those with chronic medical conditions such as lung disease, hypertension, or diabetes. Depression also increases the perception of poor health, the utilization of medical services, and healthcare costs. It is important to treat depression, as it is associated with increased mortality and risk of physical illness. Older people who attempt suicides are more likely to die than younger people, while in those who survive, prognosis is worse for older adults (Rodda et al. 2011). While not all older people with frailty who attempt suicide are depressed, treating depression is often overlooked in assessments. The British Geriatric Society (BGS) suggests medication should not be offered as a first-line treatment. Psychosocial interventions such as increasing social contact and physical exercise are first line. See http://www.bgs.org.uk/depression/cga-toolkit-category/how-cga/cga-assessment/cga-assessment-mental/cga-management-of-depression for further details. It is beyond this chapter to discuss physician-assisted suicide across differing cultures and contexts. However, it is important sensitively to addresses the fears of some older people with frailty.

5 Quality of Life and Goals of Care

Older people with frailty are frequently evidenced as having a significantly lower quality of life, compared with non-frail counterparts (Kojima et al. 2016). However, quality of life and health status are often narrowly measured, which has led to an increasing call for better measures including social, community, and psychological domains (Malley et al. 2012). Puts et al. (2007) used qualitative methods to explore the meaning of quality of life for older frail and non-frail people. Five common themes emerged, physical health, psychological well-being, social contacts, activities, and home/communities. Quality of life was derived through comparison to others, and adapted, dependent on the degree of frailty. When health was poor, there was a shift from health to social contacts as the most important factor, although poor health was not completely accepted and social goals, e.g., helping other people, checking on neighbors and friends, feelings of safety, and living conditions, became important. This adaptive shift has much in common with Knight and Emmanuel's (2007) reintegration of loss theory in palliative care. Building from literature on loss and adjustment, they describe a

conceptual framework of key adjustment processes that allow for a shift in self-concept that supports quality of life while becoming more dependent, as one approaches death.

This approach is congruent with the focus of rehabilitative palliative care (Leslie et al. 2014), an essential approach to enable goals and preferences of older people to influence quality of care. Rehabilitation aims to improve quality of life by enabling people to be as active and productive as possible with minimum dependence on others, regardless of life expectancy. In the context of palliative rehabilitation, Jennings (2013) highlights the alternative term "habilitation" to dispel any unrealistic expectations of returning to premorbid levels of function which the "re" of rehabilitation may imply. However, rehabilitation is broader than symptom management alone, focusing on enabling people with long-term conditions or a terminal diagnosis to live well, and as independently as possible, until they die. Those with long-term conditions, such as frailty, are empowered to set goals to achieve their personal priorities with the support of those important to them and with adaptations to surroundings as necessary. The centrality of such approaches for older people with frailty cannot be underestimated, the importance of independence, dignity, and continuity of personhood providing a vital counterpoint to being frail (Lloyd et al. 2014).

6 Advance Care Planning

Promoting the empowerment of older people and their surrogate decision-makers in healthcare decisions through advance care planning can also aid quality of life. Advance care planning (ACP) is an ongoing conversation between professionals and someone nearing the end of life, often with family involvement (Thomas 2011). This dialogue provides an opportunity to discuss and document what matters most about future care, including preferred care, place of care and death, unwanted treatments, and proxy decision-makers. When successful, ACP decreases inappropriate emergency admissions and invasive procedures and improves quality of life by ensuring care represents the dying person's wishes (Sudore et al. 2017). However, while ACP is reasonably embedded for diseases such as cancer and within palliative services, it is seldom used with older people with frailty, due to its complex systems and personal and family challenges (Brinkman-Stoppelenburg et al. 2014). As previously discussed, prognostication is challenging in frailty, with its repeated episodes of deterioration and subsequent recovery. It is therefore unclear when best to start ACP discussions. Further, evidence suggests older peoples' engagement with ACP is mixed, as they have a different set of preoccupations and concerns to those traditionally associated with planning future care. Older people with frailty often make decisions within their social network, a shared ecology of decision-making, which is processual and develops and changes over time (Musa et al. 2015). Decisions about preferred place of treatment and care may focus more on not wanting to be a burden to others, as well as on where the older person with frailty feels most safe and secure. This may include a preference for dying in hospital (Barclay and Arthur 2008). Further, when older people with frailty are managing well, they, and their significant others, do not always wish to discuss future planning, and there are often misunderstandings around what ACP might mean (Sharp et al. 2013).

Consequently, while ACP is particularly relevant for this population, often their priorities have not been discussed prior to a significant deterioration. This leads to crisis decision-making, for which the person may not have capacity, and often means older people with frailty are under- or overtreated and experience unnecessary hospital admissions or inappropriate, invasive procedures. Critics of ACP often relate to the process; too often ACP is defined as a stand-alone activity, with its focus frequently being only on future care decisions. However, ACP, when carried out well, should be an ongoing process, not a one-off event, a realistic and supportive conversation between professionals, the older person, and their significant others. It should focus on the persons' goals for their care, both now and in the

future, and, in that way, promotes the fundamental aim of palliative care, "*to live until you die*." Engaging in ACP does not guarantee that the dying person's wishes are realistic or possible and acknowledges that priorities may change. However, only by enabling people to make informed decisions, to articulate and record these, can we hope to deliver person-centered end-of-life care (Sudore et al. 2017). Working with older people and their significant others in partnership enables professionals to provide person-centered end-of-life care. Further, enhancing the idea of ACP as a process rather than a single event enables the focus to be on living well now, as well as planning for future terminal care needs.

7 Revaluing Living with Dying in Frailty

Frailty's dwindling trajectory fits poorly with the popular idea of a "good death in old age," in which awareness of dying, choice, communication, and control are central (Seymour et al. 2005). The idea of dying in old age with frailty as an "event" is therefore perhaps less useful than thinking of dying as a process (Martin et al. 2018). With this framing, the idea of "living as well as possible until you die" seems relevant. It is helpful to think of the concept of supportive care. This model maximizes quality of life in life-limiting illness by giving equal importance to the palliative, end-of-life approach and appropriate medical treatments, to meet patients' overall needs from diagnosis to bereavement (NICE 2004). Sometimes an open awareness of dying requires time for patients and the people, including professionals, caring for them. Supportive care can provide a bridging language and practice between curative and end-of-life discourses (Nicholson et al. 2017). Reframing language around uncertainty allows for a different praxis. Parallel planning, an approach from pediatric palliative care (Wolff and Browne 2011), acknowledges there may be numerous possibilities; some become more obvious over time, while other outcomes become less likely. Crucially, these discussions are with the family, and acknowledging honestly that this is an uncertain journey builds partnership between the clinical team, child, and family. While older people with frailty are in no way children, the degree of dependency on others for fundamentals of care and centrality of family and friends in coordinating care resonates.

A revaluation of living and dying with frailty requires a reconfiguration of partnerships and expert knowledge in palliative care. Evidence reveals that friends and family of older people with frailty are often unrecognized, unsupported, and overlooked as they care for people at the end of life (Lloyd et al. 2016). They are often coordinating a number of services, carrying out physical and emotional care over many weeks or months, and living with the uncertainty of a person dying in a protracted and often erratic way (Grande GaK 2011). While carers are often "the conductor of the orchestra" (Lowson et al. 2013), evidence (Thomas 2011; Sudore et al. 2017) highlights that their knowledge and resources are overlooked by health services. Living and dying partnerships align to health-promoting approaches to end-of-life care (Sallnow et al. 2016) in which citizens are actively engaged in their own care, drawing on partnerships between services and communities, and building on their existing strengths and skills, rather than replacing them with professional care. The focus of outcomes of care then shifts to enhancing capacity, resilience, and empowerment at an individual, social network, and wider community level, alongside more traditional palliative care outcomes.

8 Service Models to Meet the Palliative Care Needs of Older People with Frailty

Older people with frailty challenge our assumptions about who palliative care is for and where it should be delivered. Specialist of palliative care could be censured for delivering a discrete service, largely unconnected to, rather than integrated into, wider systems of health and social care. Jerant et al. (2004) criticize this model of palliative care for an emphasis on symptomatic and disease-focused treatment, resulting in a

reactive and crisis-driven approach. Older people with frailty require a focus on both living and dying well within prolonged and uncertain disease trajectories. This reorientation of palliative care models, integrating across geriatric and palliative care, supports the wider World Health Assembly (WHA) (Organization WH 2015) position for palliative care to be considered internationally as an essential health service for all people living with chronic and life-limiting conditions. Increasingly there are shared goals in geriatric and end-of-life care, to improve quality of life and to enable people to die "well" based on benefit rather than prognosis. However, what is underdeveloped is evidence on the "best" systems and models of service delivery, which and how to tailor care to meet the complex health needs associated with frailty. Sawatsky et al. (2016) argue that extending a palliative care approach to others with life-limiting and chronic conditions, such as older people with frailty, requires clear delineation of the underlying concepts of a palliative care approach. Their systematic review identified three core concepts: (1) upstream orientation toward the needs of people who have life-limiting conditions and their families, (2) adaptation of palliative care knowledge and expertise, and (3) operationalization of a palliative approach through integration into systems and models of care that do not specialize in palliative care.

The recent WHO Evans et al. (2018) scoping review of systematic reviews on service models to maximize quality of life for older people at end of life builds on Sawatzky's approach. The scoping review identified end-of-life service models as being on a continuum. At one end of the spectrum is integrated geriatric care, conceptualized as person-centered care, mainly given at an earlier trajectory of functional decline, focusing on quality of life with emphasis on strengthening and maintaining function. At the other end of the spectrum is integrated palliative care, conceptualized as person-centered care commonly accessed at a later trajectory of functional decline and dying, focusing on quality of life with emphasis on reducing symptom distress and concerns. This service continuum and the interface between integrated geriatric and palliative care balance functionality, quality of life, and quality of dying for older people with frailty and multiple morbidity. Key components across the service models reviewed were (1) multiple service providers, (2) person-centered care targeting quality of life, and (3) education of service users and providers (conceptualized in Fig. 3). However, the heterogeneity of the data within the review did not allow for detailed analysis of key components or processes to support sustainability/transferability of service models. Common outcome measures identified were quality of life, function, and impact of symptoms. However, there was insufficient data consistently to analyze outcomes and patient benefit in relation to particular service models. Health economic data was reported in less than half the reviews and results were inconclusive. Data for the review was derived mainly from high-income countries. The report argues that service delivery models must build on specific population needs, characteristics, and resources, e.g., using volunteers to deliver an end-of-life service in low- and

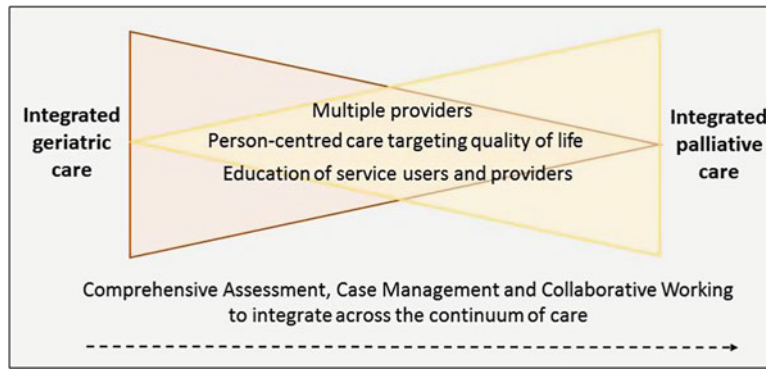

Fig. 3 Overarching integrated service delivery models and processes to maximize quality of life for older people in the last years of life (Evans et al. 2018, Adapted from Hawley 2014)

middle-income populations and consideration of the amount of primary/community palliative care available.

We consider here three examples of models of end-of-life care for older people with frailty and progressive conditions. These models seek to improve quality of life and quality of dying across the continuum of integrated palliative care and integrated geriatric care. These are as follows: first, short-term integrated palliative and supportive care, SIPScare (Bone et al. 2016); second, ongoing shared care coordination within primary care with community doctors (Bromley Care Coordination (BCC)) service via St Christopher's Hospice (Nicholson et al. 2018); and, third, skilling up the acute older adult workforce via the Assessment; Management; Best practice; Engagement and Recovery (AMBER) care bundle (Carey et al. 2014).

SIPScare (Sawatzky et al. 2016) aims to provide specialist palliative care using an approach of a consult service to assess and improve management and treatment of physical, emotional social, and other concerns and act as a catalyst to access health and social care services. Service provision is based on potential for benefit at points of actual or anticipated deterioration, with a presentation of two or more symptoms or concerns for the patient and/or their carer(s). The service is delivered "short-term" with the palliative care team providing one to three visits to assess and review concerns with expectation that the patient is discharged within 3 months. The service is integrated with the existing community services, notably GP and community nursing and other specialist nursing services (e.g., respiratory nurse). Patients/carers and practitioners re-refer at future points when care needs indicate likely benefit from palliative care services. This may be at points of anticipated or actual decline (e.g., an unplanned hospital admission), unstable symptoms, and/or concerns and care in the dying phase. The central tenets are to provide palliative care early in an individual's illness/condition based on potential for benefit and integrated professional working with the palliative care team working with the existing main provider of care. The addition of supportive care increases the emphasis on enabling individuals to live life well. Findings from the phase II trials indicate the acceptability of SIPScare for patients, families, and staff and potential for patient benefit in improving the key symptoms identified as the respective main outcome and evidence of cost saving.

Bromley Care Coordination (Nicholson et al. 2018) was commissioned by a community care-commissioning group in December 2013 to enable patients with progressive and advanced illness or frailty, thought to be in the last year of life, to receive timely and coordinated end-of-life care. The majority of patients are older and would not have met the referral criteria for "specialist palliative care" services. The service aims to address the inequalities of access to services for dying patients to prevent unnecessary hospital admissions, to help people die with dignity in their place of choice, and to provide support for their families and carers. BCC is a nursing-led service, with the community doctor taking medical responsibility for the patient. The team consists of clinical nurse specialists, community staff nurses, and administrators. Other hospice services are available as necessary to meet patient needs. Those using the service can access advice and help around the clock, 365 days a year. The service averages 280 people on the caseload at any 1 time, of which 85% have a non-cancer diagnosis and 63% are over 85 years of age. To date, outcomes include reduction of deaths in hospital (76% of patients have died at home, compared with the average in the borough of 23%) and reduction in inappropriate hospital admissions. It also increased patient and family satisfaction and anticipatory care planning. Resource implications to the proposed model include an increase in key working some patients, rather than the original plan to assess and refer onto other services. This is in part due to the lack of services for some patient groups, e.g., people with dementia and long-term neurological disorders who have high levels of dependency and uncertainty around deterioration. In part, the nonexistent or fragile social networks of people living on their own make the ongoing connection or "watchful waiting" aspect of hospice care of extra importance.

The AMBER care bundle was developed and piloted in the UK for patients in hospital whose clinical situation was uncertain in terms of recovery or continued decline, increasing risk to end of life. The model of care was in response to inconsistencies in the quality of care for patients presenting with decline and clinical uncertainty as to recovery and risk to end of life. Typically, these were older patients with frailty and multi-morbidities presenting with signs and symptoms not defined by a chronic illness. The AMBER care bundle follows an algorithmic approach to encourage clinical teams to develop and document a clear medical plan, considering anticipated outcomes and resuscitation and escalation status and revisiting the plan daily. The AMBER care bundle encourages staff, patients, and families to continue with treatment in the hope of a recovery while talking openly about preferences and priorities for end-of-life care and increasing nearness to end of life. It aims to increase and improve communication, support shared decision-making, reduce patient and family anxiety and distress, and increase attainment of preferences for end-of-life care and reduced unplanned hospital admission. Evaluation of a single site demonstrated increased communication between clinical staff and patients on prognosis and reduced length of hospital stay. However, the quality of the communication was not assessed, and relatives of patients supported by AMBER reported more unresolved concerns about providing care at home. A cluster feasibility trial is underway.

Key features of palliative care provision for older people with frailty exemplified in these models are summarized as follows:

1. Partnership with the older person and their family to enable hopeful and realistic conversations about living and dying with frailty. There is a delicate balance between perseverance/continuity and adaption to loss/dying in old age.
2. The importance of goals of care which maintain function and center on the quality of everyday life of the older person in their community as well as future planning for the last few days of life.
3. Early introduction and revisiting of advance care planning during an unpredictable and possible prolonged dying trajectory.
4. Integration and interdependencies with other care providers is an essential component as assessment and care focus on living and dying with frailty.
5. Early identification and involvement of palliative care which requires close collaboration and discussion.
6. A dynamic model which involves palliative, older person and their family, voluntary, health, and social care providers. With shifting service provision aligned to a person's needs and goals of care.
7. Proactive care – Health service care tends to manage points of decompensation on the frailty trajectory as "event-based care" by treating and managing the cause of the decline, e.g., an infection (see Fig. 1). Equal attentiveness is required to the older person's gradual deterioration with each event increasing their risk to unplanned hospital attendance, and requirement for long-term care and end of life. Regular planned assessment and use of identification tools, e.g., Electronic Frailty Index (Clegg et al. 2016)

This chapter has argued that person-centered palliative care demands a meaningful engagement with the older person with frailty within the social networks in which they are both living and dying. An understanding and valuing of capacity and strategies of continuity, alongside older people's potential and actual vulnerability, is crucial as older people with frailty reach the end of their life. However, living and dying with frailty does not always fit well within current palliative care policy and practice. This chapter argues for a flexible practice that works with uncertainty, transitions, and need, rather than a defined prognosis. The invitation to palliative care with the rise and need of older people living and dying with frailty can be framed within the potential to flourish within dying. Illes (2016) suggests that dying is the most grown up thing we will ever do, moving the focus away from productivity, external validation of worth, and the future to a more conscious

habitation of the present. Such flourishing requires an integration of palliative and older people's care crucially working with older people and the communities in which most older people will live and die.

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Palliative Care of Pediatric Populations

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Ross Drake and Emily Chang

Contents

Abstract

Pediatric palliative care clinicians care for children with life-limiting illnesses – ranging from the unborn child through to young adulthood. It is a unique specialty that shares some concepts with adult palliative care but also

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_67

important differences. The range of diagnoses, illness trajectories, and prognoses are very different to the diseases of adults. In addition, children are developing with changes in cognition, psychological and emotional maturity, spiritual and cultural influences, and behavior. The evolving roles of the child and family through illness, end-of-life care, death, and bereavement also influence palliative care provision.

Multidisciplinary pediatric teams provide family-centered care, in the setting of the child and family's choice. Core responsibilities include symptom management, psychological and emotional care, advocacy, and spiritual and cultural care. Advance care planning and decision-making are fluid processes that require attention to the child's level of understanding, capacity to make decision, his/her role in the family, parental views, and the child's condition.

Due to a low prevalence compared with adult patients, geographical distance, and resourcing limitations, not all children with palliative care needs will have access to a specialist pediatric palliative care team. Care can be provided by general pediatric and adult palliative care teams working together and complimenting each other's skill sets where there is an absence of a specialist pediatric palliative care team.

Research in this area is in a phase of development. Ethical considerations of conducting research in children and with families who are considered vulnerable make study design and recruiting challenging. However, there is a great need for evidence to enable high-quality palliative care provision in this population.

1 Introduction

Providing palliative care to children and young people with life-limiting illnesses has similarities with adult palliative care, but also significant differences (Hynson et al. 2003; Dingfield et al. 2015), enough to make it a related but separate discipline. Shared principles of care include attention to quality of life, symptom management, and psychosocial and spiritual care. However, delivery of care is greatly affected by the diagnosis, illness trajectory, developmental needs of the child, and his/her place within the family and wider community.

Children requiring palliative care have a wide range of diagnoses, each with a different and sometimes very uncertain prognosis (Serwint and Nellis 2005; Brook and Hain 2008). The illness trajectory and palliative care needs of a child with acute lymphoblastic leukemia or neuroblastoma, for example, are very different to those with neurological disability arising from rare genetic or metabolic disorders.

In addition, the child is continuously developing, undergoing remarkable physical, social, and cognitive changes throughout childhood. He/she starts life as an unborn baby and progresses through infancy, childhood, and eventually to being a self-aware, autonomous young adult. His/her perception and understanding of life, illness, and death are, through this time, formative and malleable. At the same time, his/her role and relationships within the family and wider community is shaped by the culture of the family and society and evolves over time. In contrast, a significant proportion of children accessing palliative care services have varying degrees of neurological disability and cognitive impairment. This affects the degree of dependence on caregivers, their role within the family and community, and his/her awareness and understanding of illness and death.

Diagnosis of a life-limiting condition has far-reaching physical, psychosocial, emotional and spiritual, and cultural ramifications on the child, parents, siblings, grandparents, and other members of the extended family and community. Children and young people are dependent to varying degrees on their caregivers to provide the essentials of life, love, security, and increasingly, complex medical and nursing interventions.

This chapter outlines the principles and practicalities of pediatric palliative care provision and the epidemiology, special considerations, and challenges of research in this population.

2 Principles of Pediatric Palliative Care Provision

The World Health Organization (WHO) defines pediatric palliative care as:

"the total active care of the child's body, mind and spirit, and also involves giving support to the family.

- It begins when the illness is diagnosed and continues regardless of whether or not a child receives treatment directed at the disease.
- Health providers must evaluate and alleviate a child's physical, psychological and social distress.
- It makes use of available community resources; it can be successfully implemented even if resources are limited.
- It can be provided in tertiary care facilities, in community health centres and even in children's homes" (Sepúlveda et al. 2002).

Another frequently quoted definition from the Association for Children with Life-Threatening or Terminal Conditions and Their Families (ACT, now known as Together for Short Lives) and the Royal College of Paediatrics and Child Health (RCPCH) is given below:

"Palliative care for children and young people with life-limiting conditions is an active and total approach to care, embracing physical, emotional, social and spiritual elements. It focuses on quality of life for the child and support for the family and includes the management of distressing symptoms, provision of respite and care through death and bereavement" (Association for Children with Life-threatening or Terminal Conditions and their Families and Baum 1997).

Both these definitions acknowledge the importance of multidimensional care and the need to support both the child and family.

3 Referring to Palliative Care

In general, pediatric palliative care services will take referrals for children from before they are born through to late adolescence and increasingly young adulthood. Both the WHO and the American Academy of Pediatrics support the introduction of components of palliative care at diagnosis of a life-limiting illness (American Academy of Pediatrics Committee on Bioethics 2000; Feudtner 2007).

In 1997, the Association for Children's Palliative Care (ACT) and the Royal College of Paediatrics and Child Health (RCPCH) published a system identifying life-limiting illness in childhood. Four distinct categories (groups) were identified (Association for Children with Life-threatening or Terminal Conditions and their Families and Baum 1997). These categories were found to apply well to the pediatric palliative care population (Wood et al. 2010).

Group 1
Life-threatening conditions for which curative treatment may be feasible but can fail. Palliative care may be necessary during periods of prognostic uncertainty and when treatment fails. Children in long-term remission or following successful curative treatment are not included.

Examples include cancer and severe organ failure: heart, liver, or kidneys. Case 1 illustrates this concept.

Case 1
J, a previously healthy 11-year-old Maori (New Zealand indigenous peoples) boy presented with a 2-week history of abdominal pain and jaundice. An ultrasound and endoscopic retrograde cholangiopancreatography (ERCP) showed dilated bile ducts and polyps in the stomach and duodenum. A mediastinal mass and pleural and pericardial effusions were found on computed tomography (CT) imaging. A full blood count showed circulating blast cells and he was diagnosed with high-risk acute myeloblastic leukemia.

He was started on chemotherapy with curative intent and disease remission was achieved. He proceeded to a matched

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unrelated bone marrow transplant but relapsed 46 days after transplant. A referral to the palliative care team was made.

J's disease progressed rapidly. He developed breathlessness from leukemic infiltration of his lungs and bone pain in his legs. Both of these problems responded well to opioid medications. The palliative care team met with his parents and extended family who expressed a desire to take him home for end-of-life care. An advance care plan was created with his parents. He was discharged home with palliative care and pediatric community nursing support for end-of-life care. His pain and breathlessness escalated rapidly requiring frequent morphine and midazolam boluses and continuous subcutaneous infusions. He died 1 day after discharge surrounded by his family.

Group 2

Conditions where there may be long periods of intensive treatment aimed at prolonging life and allowing participation in normal childhood activities, but premature death is still possible.

Muscular dystrophy and other neuropathies causing respiratory failure fall into this category. Attention to nutrition and noninvasive ventilation have led to longer life expectancy but premature death is still likely.

Case 2

H, a 10-month-old New Zealand European girl was referred to the pediatric neurology service for delayed gross motor development. She was not able to hold her head up in the prone position consistently (a milestone normally attained at 3 months old) or roll over (usually 4 months old). Her social and language development were normal. She was profoundly weak and hypotonic on examination.

Genetic testing showed she had a homozygous deletion of the SMN1 gene, giving a diagnosis of spinal muscular atrophy (SMA) Type 1. This is an autonomic recessively inherited disease resulting in death of the anterior horn cells in the spinal cord. Life expectancy is limited by respiratory failure from muscle weakness. Impaired cough, hypoventilation, and chest and lung underdevelopment contribute to recurrent life-threatening respiratory tract infections. Prognosis is poor with a natural age of death younger than 2 years. Noninvasive ventilation and enteral nutrition can prolong life but premature death is still likely (Wang et al. 2007).

H was referred to respiratory, neurodevelopmental therapy and disability services as well as the pediatric palliative care team.

H's respiratory function and oral intake began to decline after diagnosis. At 12 months of age, she developed respiratory failure and started nocturnal noninvasive ventilation. Soon afterwards, she required a nasogastric tube to support her growth and nutrition. At 22 months old, she suffered her first life-threatening respiratory tract infection with admission to the intensive care unit, intubation, and mechanical ventilation. She developed several more serious lower respiratory tract infections over the next 2 months requiring long hospital admissions, without full recovery in between.

Just before her 2nd birthday, H suffered a series of life-threatening respiratory tract infections. She did not improve with maximal therapy on the ward. With the support of the palliative care team and the respiratory team, her parents made an advance care plan that avoided further intensive care admissions, intubation, mechanical ventilation or cardiopulmonary resuscitation. Her noninvasive ventilation was stopped and replaced with low flow oxygen. A continuous

(*continued*)

subcutaneous morphine infusion was started with provision for frequent morphine boluses for breathlessness.

Surprisingly, her symptoms improved dramatically on this regimen, from being obtunded to being able to play and interact. She steadily improved and was discharged home.

She is now 4 years old, relatively stable and well with excellent quality of life. Her advance care plan was changed at the age of 32 months to include full resuscitation and intensive care admission.

Group 3
Progressive conditions without curative treatment options, where treatment is exclusively palliative and may commonly extend over many years.

Some metabolic disorders such as Batten's disease fall into this group. Batten's disease is an autosomal recessive disorder affecting the lysosome. Progressive neurological disability results from a buildup of lipofuscins, causing developmental regression, seizures, and death. Palliative care can involve treating pain, muscle spasms, seizures, nutrition, and other disability-related problems. Care of these children and their families often involves several pediatric multidisciplinary teams, including neurology, rehabilitation, and general pediatric community teams, with whom palliative care work closely in a coordinated fashion. Prognosis and illness trajectory can be uncertain with plateaus and acute or more gradual episodes of decline.

Incurable cancers such as some childhood brain tumors also fall into this category. Tumor-directed therapy including debulking surgery, chemotherapy, and radiotherapy can control pain and other symptoms and prolong life expectancy.

Case 3
B was diagnosed at 6 months of age with a peroxisomal biogenesis disorder. She had been hypotonic since birth with difficulty feeding. Previously showing signs of having intact vision and hearing, both of these abilities had declined over the preceding 2 months. Her gross motor and language development had both regressed over the same time course. Her liver function tests were abnormal, putting her at risk for coagulopathy.

There is no known treatment for her condition. Her prognosis is uncertain but she could develop progressive degeneration of the white matter with increasing disability and shortened life expectancy. A referral to the palliative care was made to support her family with grief and loss issues, advocacy obtaining respite and suitable housing and advance care planning.

Over the next 4 years, B developed a series of neurological, respiratory, and gastrointestinal complications. She developed recurrent life-threatening respiratory tract infections and compromised liver function. Her vision and development regressed. Distressingly she developed severe muscle spasms, intractable irritability, gastrointestinal pseudo-obstruction, and gastric bleeding of unknown cause.

B's family had moved to another town and her care was transferred to the local pediatric team. However her parents brought her back to the metabolic team at the children's tertiary hospital where she had been cared for previously.

During her prolonged admission, she was cared for by the pediatric metabolic team, pediatric palliative care team, pediatric neurology team and pediatric gastroenterology teams, and child liaison psychiatry and ward nursing teams. She had a team of allied health practitioners including a physiotherapist, occupational therapist, and dietician to help support her development, seating aids, and nutrition. They did not have suitable housing or adequate respite

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care in their hometown, and the palliative care social worker advocated for access to these during her admission.

When she was ready for discharge, several videoconferences were held with the local general pediatric and palliative care teams to ensure a smooth coordinated handover of care. A detailed symptom management plan was drawn up by the palliative care and metabolic teams. A contact and communication system was set up so her parents knew who to call and where to get help.

Group 4

Conditions with severe neurological disability which may cause weakness and susceptibility to health complications and may deteriorate unpredictably, but are not usually considered progressive.

Children with severe cerebral palsy or have multiple disabilities from head or spinal cord injury fall into this group. Although the neurological lesion itself is nonprogressive, the child may suffer from frequent, worsening respiratory tract infections or seizure disorders which can cause premature death.

Case 4

E was born by emergency cesarean section at term after placental abruption. She required extensive resuscitation at birth and mechanical ventilation for 6 days. Magnetic resonance imaging (MRI) showed severe cerebral edema, consistent with severe hypoxic ischemic encephalopathy. She developed seizures and her EEG was profoundly abnormal. In discussion with her parents, mechanical ventilation was withdrawn with the expectation that she would not survive. However, surprisingly, she established spontaneous respirations and some oral feeding skills and was discharged home with palliative care and general pediatric support.

Shortly before discharge, E developed moderate irritability. This escalated sharply after she went home. Her high-pitched screaming cry lasted 20 h a day, causing much distress and fatigue for her parents and extended family members. She lost the ability to bottle-feed and became fully nasogastrically fed. Several full pediatric assessments failed to reveal any cause. Treatments for infantile colic and gastroesophageal reflux disease were not effective.

A diagnosis of cerebral irritability following hypoxic ischemic encephalopathy was made. Gabapentin was titrated up with initial improvement but irritability increased again.

Her parents were sleep deprived, exhausted, and distressed. Respite was slow to become available and was far from adequate. The palliative care social worker obtained some short-term night nursing and advocated for the parents with the local needs assessment agency for an increase in respite hours.

Several more possible causes of pain and irritability emerged over several months, prolonged oral candidiasis, projectile vomiting, seizure activity, dystonic posturing, and muscle spasms. Each of these were investigated and treated with varying levels of effectiveness on her irritability.

Agents trialed include gabapentin and morphine for cerebral irritability and central pain; diazepam, clonazepam, baclofen, and midazolam for dystonia and spasms; ranitidine, omeprazole, and gaviscon antacid liquid for reflux oesophagitis; a change of enteral feed to elemental formula for milk protein intolerance; carbamazepine, sodium valproate, and topiramate for seizures; and fluconazole for oral candidiasis.

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Her parents and grandparents became exhausted and experienced feelings of helplessness, despair, and anger. The healthcare professionals also felt frustrated and helpless.

After 3 months, her irritability slowly settled but continued to fluctuate for the first year of her life causing much distress.

4 Epidemiology

4.1 Prevalence

There is evidence that the prevalence of children needing palliative care is increasing. In England, the prevalence was estimated at 10 per 10,000 children in 1997 (Association for Children with Life-threatening or Terminal Conditions and their Families and Baum 1997). This figure had risen to 25 per 10,000 in the year 2000, then increased again by 33% to 32 per 10,000 by 2010 (Fraser et al. 2012). The groups with the highest prevalence were those less than 1 year old. However, the 16–19-year-old age group showed the greatest increase, rising by 45% over the 10-year period between 2000 and 2010. This suggests that increasing survival times, possibly from medical interventions, accounts for at least some of the increase in overall prevalence.

Exploring the young adult group in more detail, a study from the University of York, England, demonstrated a linear relationship between prevalence and deprivation. Those who were most deprived had the highest rates of life-limiting illness. Variation between ethnic groups was also found, with those of black or South East Asian descent having significantly higher rates of life-limiting illness (Fraser et al. 2014).

4.2 Diagnosis

The majority of referrals consist of children with non-cancer diagnoses, a departure from the traditional adult palliative care population. In a prospective observational cohort study (Feudtner et al. 2011) of children served by 6 hospital-based services in the United States and Canada, 515 new (35.7%) or established (64.3%) patients were identified over a 3-month period. Of these, the predominant primary clinical conditions were genetic/congenital (40.8%), neuromuscular (39.2%), cancer (19.8%), respiratory (12.8%), and gastrointestinal (10.7%). Similar patterns have been recorded in England (Fraser et al. 2012). Most patients were reliant on some form of medical technology, with gastrostomy tubes (48.5%) being the most common, and 47.2% of the children had cognitive impairment.

Similarly, children with non-cancer diagnoses accounted for over 70% of deaths in a New Zealand study (Chang et al. 2013). Children with non-cancer diagnoses often have a less predictable illness trajectory and prognosis, resulting in greater uncertainty and often require palliative care for a number of years (Brook and Hain 2008). More detailed discussion of the challenges of working with this group is covered in following sections of this chapter.

5 Illness Trajectories

How children progress from health, through illness, and finally death can be roughly divided into 4 patterns – sudden death, steady decline, fluctuating decline, and fragile with repeated risk of decline and death (Feudtner 2007). These do not completely correlate with the four diagnostic categories outlined by the ACT/RCPCH. There are some common elements of disease trajectory which cross all categories as well as some distinct to certain categories (Wood et al. 2010).

5.1 Sudden Death

A previously healthy child experiences a sudden event, such as an accident or previously asymptomatic undiagnosed medical illness such as hypertrophic cardiomyopathy. Other than

bereavement care, there is no opportunity to benefit from palliative care.

5.2 Steady Decline

A previously healthy child is diagnosed with a life-limiting illness such as a cancer with poor prognosis. There may be some decline in quality of life and health status before diagnosis and some improvement with treatments such as chemotherapy, radiotherapy, and surgery. However, once there are no further treatments that can modify disease progression, the child's condition declines until the child dies.

Case 1, J with acute myelocytic leukemia from Group 1 (above) followed this type of course.

5.3 Fluctuating Decline

Children from Groups 2 and 3 (above) often have a turbulent course with periods of acute illness and decline followed by recovery. After each episode of illness, however, the recovery is incomplete and the child may not return to his/her previous health status or quality of life. This is common in children with non-cancer conditions, but increasingly, with development of novel cancer therapies, children who die from cancer can also follow such a course. Diagnosis is followed by chemotherapy, radiotherapy, and sometimes surgery resulting in periods of recovery followed by relapse. Second-line treatments can be introduced to prolong life or enhance quality of life for a limited time before the child's condition declines and eventually they die.

5.4 Fragile

Children from Group 4 often experience a compromised level of quality of life and health status from the start due to disability and can plateau for long periods of time. Events such as aspiration pneumonia, intractable seizures, cerebral irritability, and spasticity can lead to acute decline in quality of life. If these are treated, the child can recover to some extent and plateau but is always vulnerable to further complications.

6 Settings

Palliative and end-of-life care can be provided wherever the child is. The three main settings are the child's home, in hospital, or in a children's hospice. Rates of death in these settings vary internationally. This may be influenced by availability of services and facilities, e.g., children's hospice, community outreach teams, etc. Cultural beliefs about the place of death may also influence where children are cared for at the end of life.

In a large multicenter trial looking at place of death of children referred to pediatric palliative care services in Canada, Australia, and the United Kingdom, the numbers of children dying at home, in hospital, and in a children's hospice were equally divided between the three settings (Siden et al. 2008). Rates of death in hospital have been shown to vary by age, diagnosis, and ethnic group (Feudtner et al. 2002; Cochrane et al. 2007; Chang et al. 2013). Infants (children under 1 year old) have higher odds of dying in hospital as do children with non-cancer diagnoses. Referral to a pediatric palliative care team has been shown to decrease the odds of dying in hospital (Chang et al. 2013).

7 The Palliative Care Team

The World Health Organization, as mentioned before, refers to palliative care of children as the "total active care of the child's body, mind and spirit" and "health providers must evaluate and alleviate a child's physical, psychological and social distress" (Sepúlveda et al. 2002). Caring for the child also means caring for the family, consisting of parents, siblings of varying ages, grandparents, and other significant members. Providing effective, quality palliative care to the child therefore means providing family-centered care. This approach equips families to care for their children through diagnosis and

palliative and end-of-life care and provides support into bereavement. Not included in the WHO definition, but of increasing importance with globalization and immigration, is providing care that meets the cultural needs of each family.

Such an all-encompassing job description means that no single practitioner or discipline is able to acquire all the skills needed. An interdisciplinary team working closely in a coordinated fashion is most likely to provide quality palliative care. This team can then be truly responsive to the requirements of the individual child and their family by effectively communicating with the family unit about anxieties, fears, and misconceptions and, in so doing, openly discuss treatment strategies.

Team members in pediatric palliative care services around the world vary according to training and resources. In general, however, most teams will have, as a minimum, pediatric nurses and pediatricians with some expertise in children's palliative care. Psychologists, social workers, psychotherapists, psychiatrists, play specialists, physiotherapists, and occupational therapists are among the other members of the interdisciplinary team (Knapp et al. 2012).

In conjunction with the palliative care team, children and their families are cared for by other pediatric teams, disability support services, and cultural and spiritual support services. General and/or subspecialty multidisciplinary teams may have cared for them since diagnosis and can remain involved through palliative and end-of-life care.

Often, one member of the palliative care team acts as a key or link worker. This strategy gives the family a point of contact to assist with coordination and planning of care, particularly as this group of children often have a large number of care providers and agencies involved across a range of care settings (Hynson et al. 2003). Case 3, the child with a peroxisomal biogenesis disorder illustrates the large number of teams and healthcare professionals that are typically involved with pediatric palliative care patients and now care needs to be carefully coordinated.

8 Special Considerations in Children

8.1 Developmental Issues

The most obvious difference between children and adults is the considerable physical, cognitive, and emotional change that occurs as a child moves from infancy through childhood then into adolescence. This is by no means a linear process and neither is it determined by the age of the child. Rather "milestones" are achieved within a likely age range and developmental gains are followed by periods of plateau whether that is physical, cognitive, or emotional. This is seen in full clarity during the adolescent years, internationally recognized as ranging from 10 to 25 years, when adult physical attributes are gained relatively quickly compared to the staggered and slower cognitive and emotional changes with connection of the executive functioning of the frontal lobes to the deeper emotional centers of the limbic system.

This then requires the pediatric healthcare clinician to be able to determine the child's developmental level at the time of assessment. This is not a skill gained by having your own children but gained by years of interaction with acutely and chronically ill children of all ages where age-appropriate development is the norm and through this experiential foundation being able to determine when a child is outside the expected. The additional nuance brought to the table by working with seriously ill children is when development out of keeping for the child's age is acceptable. For example, the 7-year-old child with intestinal failure from birth who appears physically frail but through years of interaction with the medical system has advanced cognitive and emotional skills, or the 15-year-old physically well-developed adolescent with cancer shows regression in behavior consistent with a 10-year-old at a time of an acute deterioration requiring hospitalization for further evaluation.

This means assessing children across the age range requires a large array of approaches to allow a therapeutic relationship to be established with not only the child but their family as well. This raises the fundamental need to see the child not

only as an individual but a unit involving their parents (and not uncommonly in today's Western society separated but equally concerned parent's), their siblings, and, in many cultural settings, the wider family unit of grandparents, aunts, uncles, etc. who may also be the main point of communication or decision-making rather than the parents (Craig et al. 2007; Bradford et al. 2014).

8.2 Symptom Management

As in adult palliative care, management of physical symptoms is a core part of providing quality care. However, the range of symptoms faced by children is very much determined by the mix of conditions cared for by pediatric palliative care specialist services. Children often present with multiple symptoms. The most common symptoms identified were cognitive impairment, speech impairment, fatigue and sleep problems, low enteral intake, and seizures (Feudtner et al. 2011).

Pain was less common with approximately 20% presenting with somatic pain, 10% visceral pain, and another 10% with neuropathic pain. The assessment and management of pain in children is a good example of the specialized skills and knowledge required in this field (Feudtner et al. 2011).

8.2.1 Pain

Even though a relatively small proportion of children present with pain, it is consistently the most concerning for children and their families during palliative and end-of-life care. Good pain management plays a central role in maintaining a satisfactory quality of life. It also exemplifies many of the issues involved in working with children during palliation and provides a good window onto managing any symptom a child may experience.

The clinician requires a sound knowledge of pathophysiology, child development and behavior, pain responses and family dynamics, children's spirituality, and cultural influences to elicit and interpret a history given by the child and caregivers. Case 4, the newborn with hypoxic brain injury during birth, illustrates some of the complexity involved in assessing pain and irritability in an infant.

Pain is subjective; it is "what the child says it is," but it is not uncommon for children to underreport pain. The reasons for this can be simple or more complex. A simple explanation being the child underreports pain to avoid a possible or perceived painful experience as they fear this will lead to an injection. An example of a more complex issue is seen when the child plays their part in "mutual pretense" (Bluebond-Langner et al. 2005); a situation where the child and parent(s) guard against the disclosure to each other that the child will eventually die to avoid distressing the other party with this extending to the child underreporting pain.

The assessment of pain needs to be thorough and, if suspected but not revealed, specifically asked about. This can be particularly challenging when the child is not fully able to express themselves. However, the lack of verbal ability does not preclude assessment as several validated, observational pain assessment tools are available. The FLACC Behavioral Pain Assessment Tool is suitable for infants and toddlers (Voepel-Lewis et al. 1997), the Premature Infant Pain Profile for preterm neonates (Stevens et al. 1996; Voepel-Lewis et al. 1997), and the Non-Communicating Children's Checklist, the Paediatric Pain Profile, and the revised FLACC for children with disability (Breau et al. 2002; Hunt et al. 2004; Malviya et al. 2006). These tools can be applied in any setting by the child's caregiver or health professional and, for most, only take a few minutes. The child is observed for signs and behaviors that indicate pain and a score is generated which indicates the likely level of pain the child is experiencing. Pain behaviors in children with cognitive impairment can differ from those of other children and not easily recognized. For example, a sign of moderate pain could be "tense or guarded movements; mild agitation (e.g. head moved back and forth, aggression); shallow splinting respirations and intermittent sighs." Another example could be an "increase in spasticity, constant tremors or jerking of the legs" (Voepel-Lewis et al. 1997). The use of a validated pain tool is a prerequisite to effective pain assessment and management and

the onus is on clinicians to be aware of, and use these tools, appropriately.

In addition, if pain is seen purely as a physical phenomenon, then the ramifications and impact on the child's emotional, psychosocial, and existential or spiritual domains will be missed. Furthermore, this Cartesian view, where the mind is separate from the body, also overlooks the likelihood that a disease in any one of these domains can influence pain. This reinforces the need for a holistic approach to symptom assessment and for these to be pitched at a level of understanding harmonious with the individual child. This requires therapeutic actions to employ a combination of pharmacological and nonpharmacological approaches and any endeavors failing to take this into account are less likely to be successful (McGrath 1996).

The value of any chosen therapy should be carefully considered by weighing up potential benefits against burdens. This requires the clinician to have knowledge about the disease process, pathophysiology of pain (or symptom being addressed), and the pharmacolical and nonpharmacological methods used to treat it. As always, basing this on published evidence is the ideal. The problem is children are "therapeutic orphans" where investigation of treatment options to base management decisions is generally lacking. This does not mean medications should be denied because of absent published studies or the availability of poor data. What it does mean is use can be informed by inference from adult data and moderated by clinical experience of tolerability and effectiveness in children.

8.3 Prescribing in Children

The key distinction of growth and development as linked processes between working with children and adults is illustrated by prescribing medication. Historically, dosing has been based on body weight or the use of body surface area for drugs with a low therapeutic index. The problem with these methods is body weight can underestimate while surface area overestimate dosing in children. However, there are many formularies that offer suitable instructions based on the supposition that the volume of distribution per kilogram is the same in children as for adults. These "per kilogram of weight" dosing recommendations, while approximations, work reasonably well (Hain 1999; Hunt et al. 1999). However, there is a third, more complicated model, **allometric power model**, which has been found useful in normalizing a large number of physiological and pharmacokinetic variables. Essentially, this model uses an exponent of weight to derive a potentially more appropriate dose of a drug for children (Anderson and Meakin 2002).

8.4 Communication and Decision-Making

One specific difference to adult care is how the healthcare professional communicates with the child and family. Primary communication is not always going to be with the child, regardless of age, it is going to be with their caregivers. This requires the child health worker to be able to change their style of communication to not only talk at a level consistent with child's cognitive ability, which is not necessarily the same as their chronological age, but to connect with and inform parents, grandparents, and siblings alike. This may raise concern about the child's autonomy (right to self-determination) which means one must act with intention, with understanding, and without controlling influences. Children requiring palliative care may not be able to fulfill these requirements because of the effects of the illness, or they may not wish to have the additional burden of decision-maker on their shoulders, even if able to do so, making them reliant on their caregivers as surrogate decision-makers.

No one would dispute that the infant is fully dependent on its caregivers, particularly their mother, for food, warmth, shelter, and safety. This requires the health worker in children's palliative care to work with, at least, the mother to ascertain the needs of the baby and, in many ways, the parent(s) becomes a vital interpreter of the baby's welfare, for example, interpreting

mannerisms that are out-of-keeping for their baby and indicative of troublesome symptoms or changes in behavior that are more reflective of emotional or psychological distress. In some cases, such changes may not be related to the disease process at all; rather they are consistent with a known developmental phenomenon such as colic vs. pain from a disease entity or movements at night being a normal part of the sleep cycle vs. movements associated with age-related reflux vs. seizures or dystonia associated with the child's disease state.

Switch to the other end of the developmental trajectory and you could be confronted by the reticent, if not patently disrespectful, adolescent who in the face of distressing symptoms ignores effective medications out of a need to have, at least, some form of control and independence in a situation that is trying to rob them of this desired goal attainment. Yet, the adolescent in this situation is not fully equipped to be truly autonomous as they are not free of influences such as undertreated symptoms that can affect their ability to make decisions. However, within the context of children's palliative care, experience indicates that even older adolescents do not necessarily wish to be the sole architect of their fate, preferring to defer to their parents for decisions about their care. This can lead to a harmful misinterpretation by the healthcare worker that the parents are controlling the young person's decision-making against their will unless time is taken to determine the actual circumstances.

In the medical context, respect for autonomy involves allowing a person to make informed choices, a nebulous concept, about their care. The Royal College of Paediatrics and Child Health among others (Royal College of Paediatrics and Child Health London 2004; Jacobs et al. 2015; Xafis et al. 2015; Day et al. 2016) advocate strongly for participation of children in decision-making to the extent their ability allows, and they identify four levels of decision-making in pediatric care:

1. The child being informed
2. The child being consulted
3. The child's views being taken into account
4. The child being respected as the main person in decision-making (Royal College of Paediatrics and Child Health London 2004)

This translates to even young children having the right to be informed about decisions affecting their future with this communicated in a way that is appropriate to their level of understanding. It is also important that no matter what the child's ability or inability to communicate or participate is, it does not mean their suffering should be excluded from benefit vs. burden considerations. Facilitation of information also requires the child and their family to be free of conditions such as fear, pain, and depression which may compromise their capacity to make truly autonomous decisions. The obligation on the pediatric palliative care worker is to ascertain if they are free of such encumbrances.

The other important concept in palliative care for children as compared to adult care with respect to decision-making capacity is competence. Assessing a child's competence requires the ability to ascertain the child's cognitive ability. At its simplest, this can be determined by their ability to provide a clinical history, understand their condition and treatment options, and have an appreciation of the consequences of choosing one treatment approach over another. These factors then need to be considered in the context of their level of education, verbal skills, and previous demonstrations of their capacity to make decisions. All in the presence or absence of disturbed thinking that could be part of a psychiatric disorder or psychological diagnosis.

To this point, an attempt has been made to downplay age as a determining factor, but this is the very thing turned to if a legal perspective is sought. At least in the United Kingdom and in its legal system, the following concept has some influence.

There is an assumption that children <14 years of age are not competent to make decisions while young adults, 18 years and over, are considered adult with full decision-making capacity. Between these bookends of age, a gray zone exists where children between 16 and 18 years are known as mature minors and legally considered able to

consent to treatment but not able to consent to withdrawal of life-sustaining treatment against their parents' wishes, while children aged between 14 and 16 years require careful assessment as to what level of decision-making they fulfill. However, this viewpoint is not universally accepted. Cultural views on childhood and coming of age vary around the world. For example, an Islamic perspective of adulthood is tied to the ability to reproduce. Thus, menarche in girls and first ejaculation in boys signals the onset of adulthood, a view not commonly accepted in Western societies (Gatrad and Sheikh 2001).

In practice though, the majority of children and their parents agree about the most appropriate way to make decisions. A young adult may wish to make some or all decisions during palliation and end-of-life care but may also wish for his/her parents to do this on their behalf.

8.4.1 Advance Care Planning and Illness Trajectories

Illness trajectories seen in pediatrics lead to further challenges in decision-making. For many children, their clinical course and rate of decline is uncertain and unpredictable. He/she may suffer several life-threatening episodes where end-of-life care is started, only to survive and recover. Advance care plans need to factor in this unpredictability and encompass the hope for recovery and longer survival as well as symptom management, emotional, psychosocial, spiritual, and cultural support for the end of life. One scenario in which the advance care plan needs to encompass a range of possibilities is when a fetus is diagnosed with a life-limiting condition.

Case 2, the child with spinal muscular atrophy, shows how advance care plans need to be changed according to the child's condition and the hopes of the child and family.

9 Collaboration Between Adult and Pediatric Services

Although pediatric palliative care is distinct from adult palliative care, the number of specialist clinicians in pediatric palliative care, medical and nonmedical, is limited. Children often live geographically distant from specialist pediatric palliative care services as teams are mostly based in larger towns and cities. Currently and in the near future, the pediatric palliative care workforce is unlikely to reach a number sufficient to care for, in any country, every child eligible for palliative care support (Knapp et al. 2012).

This requires a pragmatic approach to providing an alternative model of care. It is not entirely surprising that a reasonably consistent attitude has developed where specialist services promote supporting health professionals in the pediatric healthcare and adult palliative care sectors.

Ideally, these two groups will collaborate to ensure their particular skills and knowledge are used to complement each other. The pediatrician and pediatric multidisciplinary team have in-depth knowledge of the child's disease, prognosis, likely complications, and management strategies. This knowledge is essential for good symptom management and decision-making. He/she may have established a significant relationship with the family from many years of involvement. This enhances communication and provision of psychological and emotional support. The adult palliative care physician and team have experience in symptom management and end-of-life care and regularly provide psychological, emotional, and spiritual support to family members through grief and bereavement. A combination of these two skill sets can result in good quality palliative, end-of-life care, and bereavement care.

For the reasons outlined in this chapter, it cannot be recommended that the adult palliative care workers operate in isolation to pediatric teams. Lack of expertise in normal child development, pediatric pathophysiology, and assessment of symptoms in children can mean misdiagnosis and incorrect treatment with consequent suffering. Practicing without experience and understanding of cognitive and emotional development and family dynamics can lead to miscommunication, anger, and a compromised therapeutic relationship with long-lasting effects in bereavement.

If you work in isolation by choice, no matter your profession, training, or experience, then consider Alexander Pope's quote in "An Essay on

Criticism." "Of all the causes which conspire to blind man's erring judgment and misguide the mind, what the weak head with strongest bias rules, is pride, the never-failing vice of fools."

10 Research

As a relatively new specialty, pediatric palliative care research is still developing. Currently, much of the literature comprises of case series and descriptive studies with small numbers of participants (Ullrich et al. 2013). Clinical guidelines rely strongly on expert opinion and experience and studies on the adult population which have been extrapolated to children, which for various reasons are of limited use. The evidence base is weak and this is well recognized. Why then is research so underdeveloped?

The patient population itself presents a hurdle to high-quality research. Children with palliative care needs have a diverse range of diagnoses, illness trajectories, and potential symptoms, making it difficult to compare one group of children with another (Ullrich et al. 2013). Rarity of diagnoses with small numbers of potential participants can mean that studies are underpowered to look for desired outcomes. The emotionally charged nature of this field and ethical considerations pose an additional challenge.

One barrier to research is difficulty recruiting children and families (Ullrich et al. 2013). Fear of causing distress and adversely affecting a family's journey through grief and bereavement is a valid concern. Selection of potential participants is often done via palliative care team members who have cared for the patient and family. This can lead to "gatekeeping" where eligible children and families are not approached to participate out of concern for the distress this is perceived to cause. For example, in a recent study looking at parents' experiences of advance care planning, only 5% of eligible families currently receiving palliative care were invited to participate. The rate was a little higher with recently bereaved families with 29% invited to participate (Crocker et al. 2014).

Looking at clinician's field notes of how they chose families to approach, several factors were identified. The perceived well-being of the family, how they may react to being approached, and their previous engagement with healthcare professionals were important. How likely they were to contribute to the study, e.g., communication abilities and relevant experience, is also featured.

Recruitment was affected by the relationship between family and clinician. Clinicians felt they could invite families with whom they had a good established relationship. Concern that the relationship could be adversely affected by recruitment led to non-recruitment. As a result, families who had had more contact with clinicians and in particular out of hours contact were more likely to be invited. (Crocker et al. 2014) This leads to potential bias, with those considered well adjusted, articulate, and able to engage clinicians more likely to be selected. Therefore, the needs of families who have been less able to access palliative care services are not well identified, and little is written about how to engage this population.

How well founded are the concerns of clinicians and researchers? A survey of parents looking at the effect of participation from the Dana Farber Cancer Institute suggests that this is not as great an issue as feared. One hundred and ninety-four parents (70% response rate) who had taken part in a study about discussion of their child's prognosis were asked about the positive and negative effects of participating (Olcese and Mack 2012).

Only 1% found research participation very distressing. Sixty-two percent indicated that they were not at all distressed and 69% felt it was useful to them personally to have participated. Overall, 18% of parents gave higher ratings for distress than utility. Parents were more likely to have found it distressing if the research was done less than 100 days since the child's diagnosis and less likely if they felt a sense of peace about the child's illness. This suggests that a lower than anticipated number of parents would find participation distressing. The majority also found participation useful even if it caused distress. Paying attention to factors such as the timing of the research could help lower distress.

So what is the future for pediatric palliative care research? A Delphi study involving clinicians and

researchers identified family experiences, pain and symptom management, bereavement, and suffering at the end of life as priority topics (Steele et al. 2008). More recently, an editorial from the *Journal of Palliative Medicine* further clarifies these priorities. Research should focus either on child-specific issues or areas in palliative care for children that would contribute to palliative care provision for children as well as adults. In addition, the needs of the very young (perinatal palliative care) and the young adult need to be highlighted. Lastly, adequate funding, research training, and expertise are essential for these priorities to result in quality pediatric palliative care research (Ullrich et al. 2013).

11 Summary

Children with life-limiting illnesses have unique palliative care needs that are distinct from adults. Pediatric palliative care services care for children with life-limiting illnesses, from the unborn baby through to the young adult. A wide range of conditions, some rare with unpredictable and changing illness trajectories, require expert knowledge in childhood conditions and a flexible approach to symptom management, goals of care, and advance care planning. The child's developmental needs and his/her place in the family and society change through the lifespan and must be considered at all times when assessing and communicating with the child and family. The child or young person's ability and willingness to participate in their own care and in advance care planning can vary widely depending on age, intellectual ability, cultural influences, family dynamics, and past experiences. Care of the child and the whole family through illness, end of life, and bereavement is essential when delivering quality pediatric palliative care.

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Palliative Care and Intellectual Disability

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Irene Tuffrey-Wijne

Contents

Abstract

People with intellectual disabilities make up an estimated 1–3% of the population. This is an aging population, with an associated increasing need for palliative care provision.

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_69

However, many do not have equitable access to palliative care services, for a variety of reasons. They often have issues, challenges, and circumstances that make it particularly difficult to meet their palliative care needs. This includes communication difficulties which affect all the aspects of palliative care provision; difficulties around insight and the ability to participate in decision making; unconventional ways of expressing signs and symptoms of ill health and distress; multiple comorbidities; complex family and social circumstances; and higher levels of behavioral or psychiatric problems.

This chapter describes the unique challenges in meeting the needs of people with intellectual disabilities at the end of life. It is based on the White Paper on Intellectual Disabilities, published by the European Association of Palliative Care in 2015. It addresses the following key areas: equity of access; communication; recognizing the need for palliative care; assessment of total needs; symptom management; end of life decision-making; involving those who matter; collaboration; support for families and carers; preparing for death; bereavement support; education and training; developing and managing services. This provides a comprehensive overview of the current state of the art.

1 Introduction

There has been a growing recognition in recent years of the importance of focusing attention on the palliative care needs of people with intellectual disabilities. The life expectancy of people with intellectual disabilities has increased significantly over the past 50 years (Patja et al. 2000). The increase in life expectancy for people with Down syndrome has been particularly marked, from 12 in 1949 to nearly 60 in 2004 (Bittles and Glasson 2004). This dramatic shift has been attributed to reduced childhood mortality and to better knowledge, healthcare, advocacy, and services (Yang et al. 2002; Haveman et al. 2009).

As people with intellectual disabilities are living longer, they are more likely to die of illnesses usually associated with old age, and they more likely to need a period of palliative care (Tuffrey-Wijne 2003). The aim of this chapter is to describe the unique challenges in meeting the needs of people with intellectual disabilities who require palliative care, as well as important considerations in addressing those challenges. It is based on the White Paper published by the European Association for Palliative Care (EAPC) in 2015, which sets out aspirational norms in 13 areas of practice. These norms were reached through using the Delphi method to reach consensus, involving 92 professionals in 15 countries who had expertise in the fields of palliative care, intellectual disabilities, or both. The full methods and detailed norms can be found in the White Paper itself (Tuffrey-Wijne and McLaughlin 2015) and an accompanying open access paper (Tuffrey-Wijne et al. 2015). Here, the focus is on describing the relevant issues under the following headings, in line with the 13 norms:

1. Equity of access
2. Communication
3. Recognizing the need for palliative care
4. Assessment of total needs
5. Symptom management
6. End-of-life decision making
7. Involving those who matter: families, friends, and carers
8. Collaboration
9. Support for families and carers
10. Preparing for death
11. Bereavement support
12. Education and training
13. Developing and managing services

First, the context of these issues will be set out through describing the prevalence of intellectual disabilities and the profile of illness and dying among this population.

2 Background

2.1 Definition

Intellectual disability is characterized by significantly impaired intellectual and adaptive functioning. Someone has intellectual disabilities if the following three aspects are present simultaneously: (1) a significantly reduced ability to understand

new or complex information and to learn and apply new skills (impaired intelligence); (2) a significantly reduced ability to cope independently, expressed in conceptual, social, and practical adaptive skills (impaired adaptive functioning); and (3) onset before the age of 18, with a lasting effect on development (American Association on Intellectual and Developmental Disabilities 2013a).

This definition covers a large and heterogeneous group of people with a wide range of skills and limitations. On one end of the spectrum, it includes people with mild intellectual disabilities who may be able to function in society with little or no support and may have good communication skills. Sometimes, it is only when the equilibrium of life is disturbed (e.g., when their health fails) that their independent coping is challenged. On the other end of the spectrum, people with profound intellectual disabilities have significant and multiple impairments, usually including physical impairments; they will need 24 h support.

The term "intellectual disability" is currently most widely accepted across the world, replacing earlier terms including "mental retardation" (Schalock et al. 2010). In the UK, the term "learning disabilities" is used synonymously with "intellectual disabilities," but this can be confusing internationally. In the USA, for example, "learning disabilities" refers simply to weaknesses in certain academic skills, such as reading or writing. "Developmental disabilities" is an umbrella term that includes intellectual disabilities but also includes other disabilities that are apparent during childhood, such as cerebral palsy or epilepsy; they are severe chronic disabilities that can be physical, cognitive, or both (American Association on Intellectual and Developmental Disabilities 2013b).

An estimated 20–30% of adults with intellectual disabilities also have an autistic spectrum disorder (ASD). ASD is a lifelong condition that affects how a person communicates with, and relates to, other people. It is characterized by difficulties with social communication, social interaction, and social imagination (Emerson and Baines 2010). Not all people with ASD have intellectual disabilities. For example, people with Asperger's syndrome (a form of autism) have average or above-average intelligence, and therefore do not have intellectual disabilities.

2.2 Prevalence

Intellectual disability affects an estimated 1–3% of the population (Mash and Wolfe 2004). The exact prevalence is unknown, as there is little standardization of definitions or methods of data collection and there is a general lack of statistical information.

People with mild intellectual disabilities make up around 85% of the total population of people with intellectual disabilities (Department of Health 2001). There is a higher incidence of mild to moderate intellectual disabilities in deprived areas. It is difficult to establish causal effects with certainty. Exposure to socioeconomic adversity prenatally and in the early years of development is likely to increase the incidence of intellectual disability. It is also possible that the heritability of intellectual ability, and the link between low intellectual ability and social position, contributes to a higher incidence of intellectual disabilities in the areas of social and economic deprivation (Emerson 2012).

Many people with intellectual disabilities, especially those with mild and moderate intellectual disabilities, are not known to specialist services and may never have been diagnosed as having intellectual disabilities (Learning Disabilities Observatory 2016). This is therefore a largely hidden population. The fact that people's disabilities may not be recorded, supported, or even recognized creates particular challenges for services trying to meet their needs at the end of life. Some risk being labelled as "difficult" or "uncooperative," whereas their behavior or coping strategies may simply be due to undiagnosed intellectual disabilities.

2.3 Death and People with Intellectual Disabilities

2.3.1 Life Expectancy

Although life expectancy for people with intellectual disabilities has increased dramatically over

the past century, it is still significantly below that of the general population. A recent government inquiry in England investigated the deaths of 247 people with intellectual disabilities between 2010 and 2012 (the CIPOLD study: Heslop et al. 2013). This important study, which was comprehensive and methodologically sound, has informed several parts of the EAPC White Paper and this chapter. A key finding was that the median age of death for people with intellectual disabilities (65 years for men; 63 years for women) was, on average, 16 years younger than the general population. Similar statistics have been found in the USA, where there have been mortality reviews for people with intellectual disabilities since 2004. The average age of death in 2014 was 59 (Connecticut State Department of Developmental Services 2015).

This shorter life expectancy may be partly due to factors related to the intellectual disability itself. For example, some conditions that cause intellectual disabilities can also cause significant physical health issues, which may be life-shortening. Some are related to the premature birth of babies that would not have survived in the past, but are now living into childhood or beyond. A significant proportion of the population of people with intellectual disabilities have a specific syndrome, which can be genetic (Down syndrome is the most common chromosomal disorder) or caused by toxins, injuries, infections, and genetic/metabolic disorders which can affect the central nervous system or other organ systems during the developmental period. These effects can become evident during the person's life (Evenhuis et al. 2001). For example, there are high rates of cardiovascular disease and diabetes among adults with Prader-Willi syndrome, arising from morbid obesity (Greenswag 1987).

However, there is sound evidence that the shorter life expectancy of people with intellectual disabilities is not just related to factors inherent in the presence of intellectual disabilities itself. This population experiences substantial health inequalities, leading to poorer outcomes (Emerson and Hatton 2013). There are inequalities in healthcare provision, including poorer access to palliative care services. People with intellectual disabilities, therefore, are at risk of premature death that could be amenable to better healthcare provision (Heslop et al. 2013).

2.3.2 Causes of Death

Leading causes of death among people with intellectual disabilities are respiratory disease, heart disease, and cancer. International data on cancer deaths among people with intellectual disabilities are lacking. In the CIPOLD study, cancer accounted for 20% of deaths among people with intellectual disabilities. The cancer profile is slightly different from the general population, with a higher than average incidence of gastrointestinal cancers (Hogg and Tuffrey-Wijne 2008). People with Down syndrome have a significantly increased risk of leukemia and a lower risk of many solid tumors (Satgé and Vekemans 2011).

The incidence of dementia is higher among people with intellectual disabilities (Strydom et al. 2010). In particular, the incidence of Alzheimer's disease is high among people with Down syndrome, with incidence rising sharply between the ages of 40 and 60. Around 40% of people with Down syndrome aged 60 and over suffer from the condition (although exact prevalence estimates vary). It is thought that there is an association between the presence of the third chromosome 21 and the production of the beta-amyloid protein which is involved in Alzheimer's disease.

3 Palliative Care for People with Intellectual Disabilities

Palliative care sets out to preserve the best possible quality of life until death. This involves management of pain and other symptoms, and of social, psychological, and spiritual problems. It requires an approach that encompasses the patient, the family, and the community in its scope (European Association for Palliative Care 1998).

The palliative care needs of people with intellectual disabilities are, on the face of it, no different from those of the general population. However, they often present with unique issues,

challenges, and circumstances that make it much more difficult to meet those needs. This includes, for example: communication difficulties which affect all aspects of palliative care provision; difficulties around insight and the ability to participate in decision-making; unconventional ways of expressing signs and symptoms of ill health and distress; multiple comorbidities; complex family and social circumstances; and higher levels of behavioral or psychiatric problems.

In order to promote best practice, it is worth considering the 13 areas of practice and service delivery that are set out below.

The scope of the White Paper on which this chapter is based includes patients who are *adults* (children require a particular and additional focus); across *the entire spectrum of intellectual disabilities* (ranging from mild to profound); and *in a wide range of settings*, including the family home, independent living arrangements, residential care settings, nursing homes, hospitals, and specialist palliative care settings.

3.1 Equity of Access

3.1.1 Barriers

The barriers people with intellectual disabilities face in accessing health services, including palliative care services, arise from a number of different sources (Emerson and Hatton 2013). Some of these are related to late diagnosis of life-limiting illness such as cancer. People with intellectual disabilities themselves may not recognize the signs and symptoms of ill health, or they may be less able to communicate these signs effectively to others. They may also not appreciate the importance of taking up health screening.

It has often been asserted that late diagnosis is due, in large part, to family members or paid caregivers not realizing that something was wrong (Tuffrey-Wijne et al. 2007b). However, the CIPOLD study found that the majority of people with intellectual disabilities who died had been identified as being unwell prior to the diagnosis and treatment of their final illness, either by themselves, a family member or a paid carer; in most cases, medical attention had been sought in a timely way. However, there were significant problems with making a correct diagnosis. Frequently, the investigations that were needed to diagnose the problem were not done or posed difficulties. Physicians were more likely to take a "wait and see" approach. In a quarter of those identified as being unwell and who responded appropriately, the concerns of the person with intellectual disabilities, their family, or paid care staff were reportedly not taken seriously enough by medical professionals. Families of people with intellectual disabilities were significantly more likely than those of people without intellectual disabilities to not feel listened to; this finding echoed previous reports (Michael 2008).

Barriers can be created by attitudes and a lack of knowledge of clinicians and carers. Those working in generic health or social care settings may lack training and knowledge of intellectual disabilities. There is a risk of professionals attributing the signs and symptoms of ill health (which may take uncharacteristic forms of expression) to the intellectual disability itself rather than to the underlying illness – a phenomenon known as "diagnostic overshadowing" (Reiss and Syzszko 1983).

Another barrier may simply be that those working in palliative care services do not know the population of people with intellectual disabilities in their catchment areas and are therefore unlikely to reach out to them. Among those working with people with intellectual disabilities, there may be a misconception about hospice and palliative care services as being concerned only with the final stages of dying, rather than with helping people to live and cope with the life they have left. It may not be known to families and support staff that palliative care can be provided within people's own homes.

3.1.2 Reasonable Adjustments

Equitable access to health care is an internationally recognized human right (United Nations 2006). In Great Britain, the requirement to make "reasonable adjustments" to healthcare services, in order to make them accessible to people with disabilities, is enshrined in law (Disability Discrimination Act 2005). The underlying principle

of equality is not usually disputed, but it can be difficult for palliative care services to know what changes they have to make in order to provide equal access to all patients. The need to remove physical barriers (such as providing lifts and ramps) may be easily understood, but it is important also to include changes to the ways in which services are delivered, so they work well for people with intellectual disabilities. In order to do so, services will have to recognize the specific additional needs of people with intellectual disabilities. Examples of reasonable adjustments for people with intellectual disabilities, which can be made by generic healthcare services or specialist palliative care services, include:

- Giving people information that is tailored to their communication needs (e.g., providing easy-read materials and pictures, or opportunities to see clinical areas or equipment beforehand)
- Allowing more time
- Involving family and other care givers
- Providing staff training about the needs of people with intellectual disabilities
- Accessing expertise about intellectual disability when needed (e.g., by engaging with intellectual disability nurses)

It is important to acknowledge that different countries have different ways in which health services are delivered to people with intellectual disabilities, which may affect the kinds of adjustments that may be needed. In the UK, Public Health England (2016) has an online database of reasonable adjustments provided by healthcare services, including tools and resources (Public Health England 2016).

3.2 Communication

Most people with intellectual disabilities, even at the mild or moderate end of the spectrum, will have some difficulty with communication. This can include any or a combination of the following (Iacono and Johnson 2004):

- Speech that is difficult to understand
- Problems in understanding what is said
- Problems in expressing themselves because of limited (or even absent) vocabulary and sentence formulation skills

These problems need to be recognized and taken into consideration. It is not surprising that difficulties with communication are often highlighted as one of the main reasons why palliative care provision for people with intellectual disabilities is so difficult (Tuffrey-Wijne and McEnhill 2008). It affects assessment of pain and other symptoms; the provision of emotional, social, and spiritual support; truth disclosure; and issues around consent and decision making.

Many people with intellectual disabilities benefit from communication aids to augment their spoken language, such as *objects of reference* (e.g., being shown a cup to signify drinks), *signs* (there are some specific sign languages used by people with intellectual disabilities, such as Makaton and Signalong), or *symbol-based systems* (including photograph and line drawings). Picture books, such as *Am I Going To Die?* from the *Books Beyond Words* series (books designed to help adults with intellectual disabilities understand and talk about difficult issues, see www.booksbeyondwords.org) can be useful.

However, some people with intellectual disabilities, especially those at the severe and profound end of the spectrum, do not easily understand either words or pictures. They have high individual communication needs, and it is imperative to involve family and other care givers in interpreting their behavior. As Thurman et al. (2005) describe:

> They may be unable to ask for things that are not actually present and are dependent on others to present them with the real tangible items... [they] can only react to situations as they arise. Such reactive communicative behaviour is often interpreted as challenging (for example, "He spits his food out on purpose").

It is important, therefore, to see any unconventional or "challenging" behavior as a possible message that the person is trying to communicate

– and to become a "detective," trying to interpret this unconventional communication correctly, together with those who know the person well.

3.2.1 Truth Disclosure

Many people with intellectual disabilities are being protected from knowing that their illness is expected to lead to their death. In one study, staff and families gave the following reasons for non-disclosure: "He will get upset"; "I will get upset"; "He can't understand"; "He has no concept of time"; and "Others don't want him told." Reasons for disclosure were related to the person's rights ("He has a right to know"), their coping ("Understanding will help him cope"), and involvement ("He needs to be able to plan and make decisions") (Tuffrey-Wijne et al. 2013). Similarly, people with intellectual disabilities are often not prepared for the death of someone close to them. Staff who work with people with intellectual disabilities usually talk to them about death *after* the death of someone close to them has occurred, but not beforehand (Ryan et al. 2011). This is especially poignant for people with intellectual disabilities who are themselves dying; they are not offered opportunities to engage with the topic of death unless they themselves initiate the conversation (Wiese et al. 2013).

It is important to make no assumptions about how much someone has understood. It is important to take people's life experiences into account, which will affect how someone makes sense of new information. This is illustrated by the following example:

> Dale, living with and caring for his remaining terminally ill parent told me in response to the question 'What is cancer?' that he had learned about it at school and that it was 'a disease the grows in your body, in your lungs and other places'. When I asked him whether it a serious illness he said 'Yes, very serious' but when I asked him whether he had then expected that his father would die of the disease, he said 'No I never expected that, no one told me'. Now faced with his mother's illness I asked him what he had thought when he had been told that she had cancer, he said 'I just froze, I thought, I am going to be on my own'. (McEnhill 2008).

There is little evidence within the literature that truth disclosure can be harmful for people with intellectual disabilities who are at the end of life, but research in this area is very limited. One study has suggested that for some people, full knowledge of what will happen in the future could be overwhelming, particularly if they are unable to put the information into the perspective of a time frame. The concepts of illness, treatments, and deaths might be too abstract to understand, which could cause severe distress for some people. Some people have high levels of anxiety, which makes it difficult to cope with distressing information. Any decision *not* to disclose the truth needs to be taken in the person's best interest, after careful consideration by everyone involved (especially those who know the person well), and reviewed regularly (Tuffrey-Wijne et al. 2013).

In recent years, a new model has been developed for breaking bad news to people with intellectual disabilities (Tuffrey-Wijne et al. 2012; www.breakingbadnews.org). This is based on evidence that the widely taught step-by-step approach to breaking bad news (Kaye 1996; Baile et al. 2000) doesn't work well for people with intellectual disabilities. For example, "finding out how much the patient already knows" can be difficult. "Warning shots" preceding disclosure of bad news can be confusing or even alarming for people with intellectual disabilities. Traditional models for breaking bad news do not take into consideration that people with intellectual disabilities usually begin to make sense of their situation (and the bad news) in their own environment, rather than in a doctor's office. Families and other care givers are often involved in disclosure of bad news, and they may find this particularly challenging. The new model takes account of the person's understanding and capacity, the people involved in the situation, and everyone's support needs. It is based on the premise that news needs to be broken down in very small chunks and added gradually, in order to build someone's understanding. This is different from "warning shots," even if it looks similar. Warning shots tend to be given in order to make the person aware that the news is bad. Telling someone "Dad is not going to get better" as a way of getting someone to ask or understand "Dad is going to die" is a warning shot – it's much better, in that

case, simply to say "Dad is going to die." However, "Dad is not going to get better" could also be used in order to help someone understand what is happening with Dad's illness. It may be too early to tell someone "Dad is going to die" (especially if they have a poor sense of time), but when that time comes, this earlier bit of information will help the person to make sense of the situation.

3.3 Recognizing the Need for Palliative Care

Poor access to palliative care services may be due to a lack of recognition by those that support people with intellectual disabilities that palliative care is needed – or even, that palliative care services exist.

Predicting a need for palliative care can be particularly difficult when someone has intellectual disabilities (Vrijmoeth et al. 2016). This is complicated by the fact that prognostication can be challenging, as many people with intellectual disabilities have a range of comorbidities, such as epilepsy. Those with congenital conditions may have had complex health problems throughout their lives, so it can be hard to know when lifelong and ongoing management of these problems turns into a need for palliative and end-of-life care.

It may be much more important, therefore, to take an approach that does not rely too heavily on prognostic indicators. Commonly used indicators for identifying those in need of palliative care can still be very useful in predicting mortality, including the "Surprise Question" ("Would you be surprised if this person were to die in the next 6–12 months?" (Moss et al. 2010). General and specific indicators can all lead to the answer being "No, I wouldn't be surprised": general physical decline, decreasing activity, progressive weight loss, repeated hospital admissions; cancer, organ failure, dementia). But more important is the anticipation and meeting of likely needs, "hoping for the best but preparing for the worst." There should be a proactive, even instinctive prediction of the rate and course of decline, and a regular review of the situation (Thomas et al. 2011).

3.4 Assessment of Total Needs

The unconventional way in which many people with intellectual disabilities express their emotional, social, spiritual, and physical needs means that their needs can be easily overlooked. In addition, their emotional capacities – including the capacity to cope with illness, death, and loss – are often underestimated.

In assessing someone's needs, it is essential to have an understanding of that person's experience of life. Here are some examples of relevant past life experience:

- Many people with intellectual disabilities have a life-long experience of being dependent on others. For some, this can lead to resilience and an ability to accept the need for increased care. Others, particularly those on the autistic spectrum, may find a change of circumstances and routines much more difficult to cope with.
- Many people with intellectual disabilities have not had extensive opportunities to make even the most basic of choices. Discussing different care or treatment options may not make much sense to people who have never been involved in deciding what to have for dinner.

There is evidence that spirituality plays a significant role in the lives of people with intellectual disabilities (Swinton 2001) and, therefore, they may need to be facilitated in expressing their spiritual needs at the end of life, like anyone else.

It is always worth remembering that challenging behavior in someone with intellectual disabilities may be a way of communicating pain. It is also worth paying attention to comorbidities that may be painful, especially if these are long-standing (e.g., contractures, sensory or motor impairments and postural problems). People who have experienced persistent and chronic pain throughout their lives may have been conditioned not to express their pain, or may express pain in unconventional ways.

There are some specific tools available. The Disability Assessment and Distress Tool (DisDAT) (Regnard et al. 2007) is particularly

useful for people with intellectual disabilities, including those with severe and profound disabilities. The DisDAT is intended to help identify distress cues people who have severely limited communication. It is designed to describe a person's usual content cues, thus enabling distress cues to be identified more clearly. For example, a hospice nurse may not realize that someone who sits calmly and quietly in her chair is actually severely distressed; but her carers will know that this person usually rocks backward and forward, and therefore carers will realize her stillness is a cause for concern. Documenting this will help all professionals. Identification of the distress is only the beginning of the assessment; unless the person is able to tell you clearly what is causing the distress, this still needs to be determined and can often be no more than an "educated guess" (See also Sect. 3.5).

3.4.1 Tips for Effective Assessment

The following may be useful in assessing the needs of someone with intellectual disabilities (see also Tuffrey-Wijne and McEnhill 2008).

- Get to know the person. The earlier palliative care professionals can be involved, the better, as this provides opportunities to build a relationship of trust, which will be crucial in future needs assessment.
- Involve families and others who know the person well. They can be effective "interpreters" of the person's verbal and nonverbal communication, and should be part of your team.
- Take plenty of time, and accept that this is an ongoing process, to be refined over the coming days, weeks, or even months.
- Always speak to the person with intellectual disabilities first (even if they don't use verbal communication), and only then refer to the person's carer. Even if most of the assessment will need to be through the carer (e.g., if the person's communication is only understood by the carer, or if the person is too anxious to speak to those they don't know well), refer to the person frequently. This will build trust and confidence, not only for the person with intellectual disabilities but also for their carer.
- Use simple and straightforward questions. Never use more than one concept per sentence. Don't ask: "How are you, do you have pain today?", but rather, "How are you?" (wait for response), "Do you have pain today?" (wait for response).
- Allow the person plenty of time to respond. Do not fill necessary silence with another question.
- Many people with intellectual disabilities are eager to please and will tell you what they think you want to hear.
  - It is not unusual for people with intellectual disabilities to answer "yes" regardless of the question. Closed questions ("Do you have pain today?") may be important in assessments, but should be used with care. It is worth asking the opposite question as well, to see if you get a similar response ("Has the pain gone away?")
  - When presented with different options, some people with intellectual disabilities tend to repeat the final option ("Is the pain there all the time or only sometimes?" "Sometimes," so try repeating the question with the options the other way round, to see if you get the same response.
- Abstract concepts are much more difficult to understand than concrete ones. Concepts of time can be particularly difficult. Therefore, try to be as specific and concrete as you can. Instead of "How long have you had the pain," you could ask, "Did you have the pain when you went to church?"
- Do not assume that the person understands the connection between the symptoms and the illness.

3.5 Symptom Management

Pain and symptom management can be particularly complex in people with intellectual disabilities, many of whom have a range of chronic medical conditions and comorbidities; multipharmacy is not uncommon (Symons et al. 2008).

Pain is often not recognized, validated, or treated in people with intellectual disabilities. The CIPOLD study (Heslop et al. 2013) found

that they receive less opioid analgesia in their final illness than the general population. The belief still exists that people with intellectual disabilities feel less pain than the general population. Pain assessment is complicated by the fact that self-reporting of pain can be difficult, and conventional pain assessment tools may not work well for this population.

It is important to try and determine the most likely cause of someone's distress. This is an imprecise art, but it is unacceptable to leave pain and other symptoms untreated because of uncertainty. Professionals need to use their clinical expertise and judgement to make an "educated guess" about the most likely cause. For example, is the symptom or the distress cue caused by the disease itself? The treatment of the disease? Debility or comorbidities? The impact of the symptom or illness on the person's life?

Treatment should be instigated accordingly and the result should be monitored, to see if the distress signs diminish over time. If they don't, then the situation needs to be reconsidered and another possible cause may be treated or managed. Consider both pharmacological and nonpharmacological treatments, including complementary therapies, emotional and spiritual support, the use of life stories and reminiscence therapy, relaxation exercises, etc.

The DisDAT assessment tool (See Sect. 3.4) includes a useful clinical decision checklist to help decide the cause of the distress. This is not an exhaustive list, and there is a strong emphasis on physical causes of distress; but it is important to exclude underlying physical causes, especially in this group where there is a risk of "diagnostic overshadowing."

IS THE NEW SIGN OR BEHAVIOR. . ..

• **Repeated rapidly?**

Consider pleuritic pain (in time with breathing); colic (comes and goes every few minutes); repetitive movement due to boredom or fear.

• **Associated with breathing?**

Consider: infection, COPD, pleural effusion, tumor.

• **Worsened or precipitated by movement?**

Consider: movement-related pains.

• **Related to eating?**

Consider: food refusal through illness, fear or depression; food refusal because of swallowing problems; upper GI problems (oral hygiene, peptic ulcer, dyspepsia) or abdominal problems.

• **Related to a specific situation?**

Consider: frightening or painful situations.

• **Associated with vomiting?**

Consider: causes of nausea and vomiting.

• **Associated with elimination (urine or fecal)?**

Consider: urinary problems (infection, retention); GI problems (diarrhea, constipation).

• **Present in a normally comfortable position or situation?**

Consider: anxiety, depression, pains at rest (e.g., colic, neuralgia), infection, nausea.

Taken from **DisDAT** © 2006 Northumberland Tyne & Wear NHS Trust and St. Oswald's Hospice.

3.6 End of Life Decision-Making

People with intellectual disabilities have a right to be facilitated in making choices about care and treatment, where possible. People with intellectual disabilities are particularly vulnerable and can be excluded from conversations that they may be able to have which could help plan the palliative and end-of-life care that they wish to receive. There is evidence that medical decision making is sometimes based on misguided assumptions about the quality of life of people with intellectual disabilities, their ability to comply and cope with treatments, or their ability to consent to treatment and be involved in the decision making process. This can lead to people with intellectual disabilities not receiving potentially lifesaving treatment (Mencap 2007; Michael 2008; Wagemans et al. 2010). There should be no assumptions about their capacity to make decisions due to the label "intellectual disability" (Johnson 2010).

Professionals should be aware of the fact that capacity may be an issue and needs to be assessed. They should also be aware of, and adhere to, national and local laws and regulations around capacity, consent, and advance decision making.

3.6.1 Assessing Capacity

With the right support, many people with intellectual disabilities are able to make at least some decisions. A person's capacity needs to be

assessed for each situation. Capacity is "decision specific," and some decisions are easier than others. A decision to start on opioid analgesia for pain may be easier than a decision to start (or continue with) chemotherapy for an invisible cancer. In the UK, a person is deemed to lack capacity if he or she is unable to do at least one of the following:

(a) Understand the information relevant to the decision
(b) Retain the information (for long enough to be able to make the decision)
(c) Balance the information (in other words, use the information to weigh up the options)
(d) Communicate the decision

It is important that people are given relevant information in a format that they can understand. Professionals must consider, therefore, what information is needed to enable informed decision making. It may be necessary to restrict information to the most essential. It is also important to remember that people have a right to make a decision that others may perceive as "unwise." In order to assess whether the person has been able to use the information to weigh up the options, it can be useful to ask them how they have come to their decision. This could show that someone does indeed have capacity to make the decision, but it could also demonstrate that someone who makes a seemingly clear decision has not, in fact, understood the full implications of the decision. It is not unusual for someone to be clear that he doesn't want surgery, and for this choice to be respected; but it may be that he has not understood that surgery could be life-saving and not having the surgery will eventually lead to his death – and therefore, he either has not been adequately informed, or he did not have the capacity to make this decision due to an inability to weigh up the information.

If someone lacks capacity, then someone else needs to make the decision for them. Who the surrogate decision maker is will depend on national laws, but an important general principle is that decisions are made *in the person's best interest*. All relevant circumstances, as wells as the person's wishes, feelings and values, must be taken into consideration. Even if it is decided that complying with their wishes is not in their best interest, people's wishes clearly matter. The important question to ask is: "If this person had capacity, and could understand all the relevant issues, what do we think he or she would choose?"

3.7 Involving those Who Matter: Families, Friends, and Carers

Involving families, friends, and carers is particularly important for people with intellectual disabilities. Families and carers are often effective advocates and can play an important role in reassuring the person, providing communication support, contributing expert knowledge, and participating in decision-making. Studies that have included the voices of people with intellectual disabilities themselves, ascertaining their views on support at the end of life, have shown how important it is for them to have familiar people around (Tuffrey-Wijne et al. 2007a; McLaughlin et al. 2015). Furthermore, it has been shown that a lack of effective carer involvement leads to poorer outcomes for people with intellectual disabilities (Heslop et al. 2013; Tuffrey-Wijne et al. 2016b).

The important relationships of people with intellectual disabilities ("significant others") should therefore be identified, with the help of the people themselves if at all possible. This could include family, partners, friends, informal (unpaid) carers, paid support staff, and professionals. The profile of this social network is likely to be different from that of the general population. Those in the general population often rely on the support of partners and children when they develop a serious illness, but for people with intellectual disabilities, family bonds tend to consist mostly of siblings and elderly parents (Tuffrey-Wijne 2010). It is often much more difficult for people with intellectual disabilities to create new bonds, including new family bonds, as they get older. It is also worth noting that many people with intellectual disabilities consider their professional support staff as their friends.

Some people with intellectual disabilities have lived with their parents all their lives and have developed interdependent relationships. Others may have been separated from their families at an early age and spent a lifetime in institutional care. Sometimes, relatives who have had little contact during the person's lifetime would like to be more involved at the end of life, which can at times cause tensions with those who have supported the person on a daily basis. It is important to consider the wishes and perspectives of the people with intellectual disabilities themselves. Family bonds may be crucially important to them, even if there has been a lack of contact (Hubert and Hollins 2006).

The risk that people with intellectual disabilities lose contact with the people that are important to them is heightened during a (final) illness, when they may not be able to organize visits or phone calls independently. Those who need to move into a new care setting are particularly vulnerable to losing contact with friends and familiar care staff.

3.8 Collaboration

Collaboration between services is key to successful provision of palliative care for people with intellectual disabilities. The importance of collaboration has been consistently highlighted in the literature as essential in ensuring that people with intellectual disabilities are well supported at the end of life (Read 2006; Cross et al. 2012; Friedman et al. 2012). Collaborative working should also include family carers and people with intellectual disabilities themselves; in fact, people with intellectual disabilities should be at the center of partnerships at all times.

Collaboration between palliative care services and intellectual disability services is particularly important. Developing a relationship with other services, built on mutual trust and respect for each other's knowledge base and skills, can enable a more robust assessment of the needs of people with intellectual disabilities. This can ensure better outcomes for this population, such as continuity of care and dying peacefully in their place of care with people familiar to them (McLaughlin et al. 2014). Building collaborative links may involve a concerted effort, in particular if professionals are not aware of each other's existence or range of services and expertise. It is important, therefore, that palliative care services and intellectual disability services actively reach out to each other. Often, a particularly complex situation with a person with intellectual disabilities in need of palliative care leads to services getting to know each other and work together. However, it is much better not to wait for a crisis, but to get to know other services within a catchment area in advance. The effectiveness of a proactive approach to collaborative working has been highlighted by the Palliative Care for People with Learning Disabilities Network (PCPLD Network 2016), which encourages an exchange of best practice. One example of a good practice initiative is a group of nurses and social workers from the community intellectual disability teams, who meet monthly with local palliative care specialists, to discuss service users who are known to be at the end of life or suspected to die within a year. The group follows nationally established frameworks and pathways and has developed these to suit the needs of people with intellectual disabilities. Each service user within their catchment area is now offered and of life planning, with a clearly recognizable folder for their health action planning and communication tool (PCPLD Network 2013).

3.9 Support for Families and Carers

3.9.1 Families

Families and carers are usually deeply affected when someone with intellectual disabilities reaches the end of life. This person has often been at the center of their family's or carer's life, sometimes for decades. Their death is a significant and difficult loss. For families of those who have needed active support throughout their lives, the death also signifies a loss of their role and identity as a care giver (Todd 2007; Young et al. 2014). All family carers need considerable and sensitive support, a recognition of their expertise in relation to

the cared-for person, and a regular assessment of their needs (Payne and Morbey 2013). For carers of people with intellectual disabilities, whose situation is so much more complex, this is especially important.

The grief of families and carers is sometimes "disenfranchised" (where the relationship is not recognized, the loss is not recognized or the mourner is not recognized) (Doka 2002). Carers (and especially parents) of people with intellectual disabilities can experience their deaths as a painful physical loss of part of themselves. However, families may be given the message that the death of their relative is "for the best" or even a blessing (Young et al. 2014).

3.9.2 Paid Support Staff

The extent to which professional care givers are affected by the death of a person with intellectual disabilities is often under-estimated. Staff can form strong attachments with the people they support, and sometimes see themselves as surrogate family members, building relationships that last many years (Tuffrey-Wijne 2010). The death of a client of resident with intellectual disabilities can have a complex physical and emotional dimension for staff that is seldom recognized (Todd 2013). Many such staff have little experience of death and dying, and are likely to find the situation difficult on both a professional and a personal level. It is important that the grief of all those who loved and supported the person with intellectual disabilities is recognized and validated, including not only family carers but also paid support staff. Staff working with people with intellectual disabilities who are dying will benefit from training on self-care.

3.9.3 People with Intellectual Disabilities

The caring role of people with intellectual disabilities can go unrecognized. Sometimes, the carers of people with intellectual disabilities who need palliative care have intellectual disabilities themselves: they may be partners, friends, housemates, or adult children, for example. They will need a significant amount of support to cope with changing needs and impending losses.

It is also worth noting that people with intellectual disabilities who live at home with elderly parents often become carers within highly interdependent relationships, but they are often invisible to services because of a lack of recognition of mutual caring (Department of Health 2009). In a study of people with intellectual disabilities who were affected by a relative with cancer (usually a parent or partner), most had taken on a caring role (Tuffrey-Wijne et al. 2012). Palliative care services should be alert, therefore, to the possibility that adults with intellectual disabilities who live with a patient (including patients without intellectual disabilities) may need support as carers.

3.10 Preparing for Death

If people with intellectual disabilities are protected from knowledge about death, including their own impending death (See Sect. 3.2), it will be very difficult for them to prepare themselves for the future or be involved in care planning, if they so wish. Giving people opportunities to participate in decision making around their care and treatment, or discuss funeral wishes and make a will, it is necessary to have a culture of openness and inclusion. Conversations about death should happen throughout the life cycle, in order to build a foundation to help prepare people for their own final illness.

Discussions about the person's preferences could take place as early as is appropriate, even before the need for palliative care arises. Once the need for palliative care has been identified, a care plan should be put into place, taking into consideration any anticipated future needs for treatment and care.

3.10.1 Advance Care Planning

Within the field of palliative care, there is growing emphasis on Advance Care Planning (ACP). This has been described as a process where a patient's current condition and prognosis is reviewed, and likely dilemmas and options discussed with the patient and their family. It is a structured way of eliciting their wishes and thoughts for the future

(goldstandardframework.org.uk). Important elements of ACP include:

- *Deciding what you want* – what care elements are important now and in the future? What is the preferred place of care?
- *Deciding what you don't want* – this can include legally binding statements, such as Do Not Attempt Cardiopulmonary Resuscitation orders
- *Who will speak for you* – e.g., appointing a proxy spokesperson or legal representative (the terminology and powers of others to decide for you will vary in different countries)

With the person's permission, all those involved in their care should be made aware of the patient's wishes and advance decisions.

There are several easy-read advance care planning documents available online. Within some of these documents, there tends to be a focus on funeral planning rather than care planning. These resources have not yet been properly evaluated. In order to use advance care planning documents, professionals and carers must have an understanding of the process of advance care planning, including an appreciation of the fact that it is indeed a *process* – it is not a one-off event, but involves discussions over time and should be revisited regularly. How advance care planning with people with intellectual disabilities is best instigated and supported needs further investigation.

3.11 Bereavement Support

The importance of supporting families, carers, and staff through a person's final illness and after their death has already been highlighted (See Sect. 3.9). This section deals specifically with the need for people with intellectual disabilities to receive bereavement support. People with intellectual disabilities often experience more losses than the general population. Most children within the general population will not have experienced the death of a friend; but it is not unusual for children who attend special schools to experience the deaths of their peers, not just once but repeatedly.

The impact of losing a significant person is always enormous, but can be particularly devastating for people with intellectual disabilities who may have been dependent on the deceased person in many ways. If the death of a relative precipitates a move into a care setting, there are multiple losses associated with the bereavement, including the loss of home and all that was familiar.

There is growing recognition of the bereavement support needs of people with intellectual disabilities. This is a relatively recent development; until the 1990s, it was assumed that people with intellectual disabilities did not experience grief (Oswin 1991). Even today, people with intellectual disabilities do not always get recognition for their loss and are not always given opportunities to talk about it or express their feelings (Tuffrey-Wijne et al. 2012). The grief responses of people with intellectual disabilities can be delayed, prolonged, or expressed in atypical ways, so it may not be recognized as a grief reaction (Hollins and Esterhuyzen 1997).

3.11.1 Risk of Complicated Grief

Not all people with intellectual disabilities need specific or specialist bereavement support, but the possibility of difficult grief processes must be borne in mind. A number of risk factors make people with intellectual disabilities more vulnerable than the general population to complicated grief reactions, including (McHale and Carey 2002; Blackman 2008; Blackman 2003):

- Social isolation
- High dependency on a small group (or even a single) significant other(s), with limited opportunities for developing new roles and relationships
- Exclusion from death rituals (such as attending funerals or visiting the grave)
- Difficulties with attachment in early life
- Low self-esteem
- Limited power or control over one's situation
- Associated, often hidden and multiple losses that accompany the death of a parent or close relative (e.g., loss of home)

In assessing the need for bereavement support, is can be useful to focus on how the loss has affected the following three areas of someone's life (Blackman 2008):

- The person's ability to communicate with others (e.g., a parent who dies may have been the only person who could interpret their adult son or daughter's communication)
- The impact on the person's familial network
- The person ability to recognize and express their emotions

3.11.2 Providing Bereavement Support

The following hints and tips can be helpful in providing support for people with intellectual disabilities who have been bereaved or for whom bereavement is anticipated (Blackman 2003; Read 2005; Read 2007).

- Prepare the person for the loss if at all possible. People with intellectual disabilities are often protected from knowing that someone close of them is going to die (perhaps because those around them want to spare them distress), but if they are unprepared, the death will be experienced as an unexpected, sudden death. Sudden death is usually more difficult to cope with and increases the risk of complicated grief (Murray Parkes 1998).
- Ensure that the person participates in death rituals, such as funerals. It can also be very helpful to hold additional rituals, such as memorial events, planting a tree in someone's memory, etc. People with intellectual disabilities are often excluded from active involvement in rituals, including the planning of funerals and memorial events. They are also less likely to have opportunities to share their grief with others, for example, through seeing others cry about the loss or through receiving cards of condolence.
- Provide information about bereavement in a format that the person can understand. This may need to be repeated often. Be open and honest. Often, the truth is easier to cope with than uncertainties.
- Tangible ways of remembering are often helpful. Consider the use of life story books, memory books, or memory boxes. These can also help the person talk about the loss with others; for example, taking photographs at a funeral and showing these to others afterward can help to process what has happened.
- Bereavement counsellors may also need to use a variety of approaches to help someone with an intellectual disability experiencing grief, such as art work, creating family trees, use of pictures, photographs, videos, poetry, and reminiscence work.

Supporting people with profound intellectual disabilities in grief can be particularly complex. They will need to be provided with supportive relationships and sensory experiences in order to increase their sense of safety, enhance a sense of security, and facilitate expression of their grief. The resource created by PAMIS is particularly useful for this group (Young et al. 2014).

For some people with complicated grief responses, specialist bereavement support is indicated. In one randomized controlled trial, bereavement counsellors who worked with the general population received training on intellectual disabilities and then worked with bereaved people in one-to-one sessions; staff working within intellectual disability services received training on providing bereavement support, and worked with bereaved people within their own settings. The study found that the generic bereavement counsellors were able to improve outcomes for people with intellectual disabilities, while many of the staff within intellectual disability services dropped out of the program (Dowling et al. 2006). It seems that engaging with issues of death, dying, and loss is very difficult for staff working with people with intellectual disabilities on a daily basis; a finding that has been confirmed in later studies (Ryan et al. 2011; Tuffrey-Wijne and Rose 2017).

There are very few specialist bereavement services available for people with intellectual disabilities, but it is worth looking for generic bereavement services willing to take on clients with intellectual disabilities. They may need to know how to use different approaches, such as art work, creating family trees, using pictures, photographs, videos, poetry, and reminiscence work.

3.12 Education and Training

3.12.1 Training for Staff Providing Generic Palliative Care Services

Staff working in palliative care services have consistently reported that they lack of confidence, knowledge, and skills in supporting people with intellectual disabilities. They find assessment and communication issues particularly difficult (Tuffrey-Wijne et al. 2008; McLaughlin et al. 2014). Palliative care professionals may see relatively few people with intellectual disabilities, so their knowledge and skills are not being developed. The following areas are not exhaustive, but are important training priorities:

- What are intellectual disabilities and how does it affect people's lives?
- How are people with intellectual disabilities supported within the local area? Where do they live, who provides them with daily support, what specialist intellectual disability services are available? How skilled or experienced are these services or carers in providing end-of-life support, and what help do they need?
- Communication needs; interpreting communication; alternative communication methods; breaking bad news
- Assessment of symptoms and other problems

3.12.2 Training for Staff in Intellectual Disability Services

Staff working in intellectual disability services may not have any experience of death and dying, and may be frightened by it (Todd 2005; Tuffrey-Wijne 2010). Many will be unfamiliar with the needs of people at the end of life. It is easy to assume that people with intellectual disabilities who live within staffed homes or institutions are well supported, but such assumptions may be erroneous. In the UK, for example, support staff for people with intellectual disabilities tend to have very little training; most have limited knowledge of looking after people with failing health. In addition, they may experience anticipatory grief reactions themselves (See Sect. 3.9), making the delivery of support at the end-of-life challenging on many levels – practical as well as emotional. Training and support may be best delivered by outside experts (such as community palliative care nurses or district nurses) on an as-needed basis, showing staff who to support specific individuals. Generally, the following areas are important in training staff in intellectual disability services:

- Thinking about death and dying in general; your own attitudes, issues, reactions, fears, etc. In order for staff to be able to provide good support for others, it is usually helpful for them to think about and articulate these issues.
- What support services are available locally for people who need palliative care? Who is in the multidisciplinary team? (This could include: primary care services including general practitioners and district nurses; specialist services, including hospices and community palliative care services)
- The process of dying: what to expect, how you can help, when to ask for support
- How to communicate about death and dying with people with intellectual disabilities
- Loss and bereavement, and how people with intellectual disabilities can be supported

Cross-fertilization of knowledge and skills between palliative care staff and intellectual disability staff is particularly effective and useful. This could be through formal mutual training sessions and through informal exchange of expertise around a particular individual with intellectual disabilities. It can also be also highly effective to include carers and people with intellectual disabilities themselves, as experts-by-experience. Hearing their stories and perspectives can have a powerful impact on staff.

Training for People with Intellectual Disabilities

People with intellectual disabilities themselves often lack essential and basic knowledge around illness, death, and dying, and will benefit from education in this area. It is possible, and important, to create opportunities for them to learn about

death and dying throughout their lives. Families and carers may need help and support in encouraging such discussions. Open discussions at home are particularly important; for example, the death of a celebrity or a soap opera character may prompt conversations about illness, dying, and funerals. There could also be planned sessions at day centers or special educational facilities.

3.13 Developing and Managing Services

In order to ensure that people with intellectual disabilities are adequately supported at the end of life, in the place that is most appropriate to their needs (and that is, ideally, their preferred place of care), it is essential to know where and how they die. Services need to be able to anticipate the likely need. Many people with intellectual disabilities may wish to choose to remain in their existing home environment. If this is a residential care setting, provision will have to be made to make that possible. This is likely to need advance planning, as it will require adequate resources in terms of staff and physical environment. Such services need to anticipate, therefore, the likelihood that their clients reach the end of life with an associated need for increased support. This will reduce the need for hospital admissions or a last minute search for a nursing home able to cater for the person's changed needs.

Palliative care services will need to consider whether they are sufficiently prepared to have patients with intellectual disabilities on their caseload. This is likely to require extra resources. They may need extra staff time, additional resources to help them communicate and additional time to manage their often complex needs. There may be a wide range of carers and professionals involved. Policy makers should commit adequate resources to this.

The following are particularly important in ensuring high-quality care for people with intellectual disabilities at end of life:

- Develop and encourage continuity of care across settings
- Ensure that good basic palliative care skills and knowledge are held within staff teams working in intellectual disability services
- Facilitate collaborative partnerships among palliative care programs, community hospices, and a wide range of other healthcare delivery settings.

4 Conclusion and Summary

Ensuring that people with intellectual disabilities are well supported at the end of life is highly challenging and needs focused attention. One key challenge is the "invisibility" of this population within health and social care services. The vast majority of people with intellectual disabilities are on the mild end of the spectrum, and this group may be particularly difficult to identify. Their needs are largely hidden, but their problems may be significant, and require skilled support. Even if the problems are identified and known, many staff, services, and systems are unprepared for meeting the needs of this population. Across Europe, good practice often depends on the dedication of individual practitioners, rather than effective services and systems (Tuffrey-Wijne and McLaughlin 2015).

4.1 Recommendations

The EAPC White Paper has set out key areas for practice, which have been discussed in this chapter. It also makes the following recommendations.

- **Palliative care services should actively reach out** to *find* the population of people with intellectual disabilities within their catchment areas.
- **Ongoing exchange** of experiences, expertise, and best practice should be encouraged on a range of levels:
  - Locally, between palliative care and intellectual disability services
  - Nationally, between individuals and organizations involved in supporting people with intellectual disabilities at the end of life
  - Internationally within Europe

- **International exchange of expertise,** for example through:
  - An ongoing, regularly updated online multilanguage resource, signposting relevant literature, resources, contacts, etc.
  - A dedicated person or team who can act as a "point of contact" for palliative care provision to people with intellectual disabilities in Europe. Their role could include: collating relevant information and resources (see above online resource); facilitating contact between different services in different countries; organizing exchange visits; signposting training opportunities.

4.2 Future Research

The following areas have been identified as priorities for future research by an international group of academics and practitioners (Tuffrey-Wijne et al. 2016a):

- Investigating issues around end-of-life decision making
- Mapping the scale and scope of the issue (in order to be able to plan adequate care provision)
- Investigating the quality of palliative care for people with intellectual disabilities, including the challenges in achieving best practice
- Developing outcome measures and instruments for palliative care of people with intellectual disabilities.

4.3 Benefits for Everyone

Is it worthwhile spending time and resources on supporting people with intellectual disabilities at the end of life, even for services who may see relatively few such patients? Practitioners, service managers, policy makers, and funders may well raise this question. Clearly, there is an argument for ensuring that the most vulnerable people in society are provided with the same quality of palliative care as the rest of the population. But the benefits of focusing on the needs of people with intellectual disabilities, and ensuring that staff and services are ready to meet those needs, go well beyond this. The skills needed to care for people with intellectual disabilities are transferrable and will benefit all patients. Services that can care for people with very severe communication problems, complex social situations, multiple comorbidities, unconventional ways of expressing symptoms, and perhaps high levels of anxiety, can probably care for all patients, whatever their complexities. Such services need flexibility. Their service delivery needs to be highly adaptable to individual need.

The quality of a palliative care services could be measured by the way in which they are able to support people with intellectual disabilities. It is worth the effort to "get it right."

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Pou Aroha: An Indigenous Perspective of Māori Palliative Care, Aotearoa New Zealand

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_121

Abstract

An indigenous perspective of palliative care is not commonly known. The aim of this chapter is to describe key caregiving strengths of New Zealand Māori whānau (family) to illustrate how they draw on their cultural customs at end of life. Cultural customs are informed by knowledge passed down from tūpuna (ancestors) and the relationship with the whenua (land). End of life cultural care customs ensure the highest quality of care is provided to the ill and dying person and their bereaved whānau. Whānau are critical "pou aroha" (care stalwarts); they carry out the bulk of end of life care. Whānau ensure the best physical, emotional/mental, and spiritual care is received before the person dies, no matter what healthcare setting they are in. A holistic healthcare approach is required at this time as this supports whānau cultural aspirations to prepare the person's spirit to pass through the ārai (veil) as they transition from the physical realm to the metaphysical realm at time of death. The chapter highlights the need for care that is genuinely holistic and relational as this is most likely to meet the needs of indigenous peoples. The facilitators and barriers associated with providing care are discussed within the context of a set of complex end of life circumstances. Barriers include health inequities, racism, poor access to palliative care and statutory (government) support, inadequate information, and poor communication. Whānau carers often experience high levels of stress and have too few informal family carers to share the care responsibility and the high financial costs associated with end of life care (Gott et al., Palliat Med 29:518–528, 2015a). However, the values of aroha (compassion, empathy, concern), whanaungatanga (relationships and connections), manaakitanga (caring for the mana (status, prestige, authority)) of the dying, kotahitanga (collective decision-making processes), and wairuatanga (spirituality) are introduced as guiding forces that protect and strengthen whānau carers.

1 Introduction

Increasing the health and palliative care sectors' understanding of indigenous peoples' end of life care needs and preferences is essential for designing palliative care services that are aligned with the aspirations of indigenous peoples. The aim of this chapter is to provide a description of indigenous end of life care by exploring Māori whānau (family, including extended family) experiences of caregiving. We introduce some strengths that support whānau to do this critical work, and we identify some of the challenges families encounter. Research evidence is drawn on to highlight the needs of Māori whānau (referred to as "whānau" henceforth). We highlight that whānau carers are *pou aroha* (care stalwarts) for family members who have a life-limiting illness.

Changes in the population of New Zealand will have significant future health policy, funding, and planning implications (Associate Minister of Health 2016) as well as implications for whānau in relation to the future palliative care needs of Māori. For example, the total number of deaths each year is projected to increase in New Zealand by 47.5% between 2016 and 2038. While the proportion of Māori deaths relative to the total deaths in New Zealand is expected to remain reasonably constant (10.9% by 2038) (McLeod 2016), the Māori population is projected to grow at a higher rate than non-Māori (Statistics New Zealand 2015) and is expected to exceed one million by 2038 (Statistics New Zealand 2017). An important feature of this period for both future

health and palliative care services and whānau is not only the expected increase in the number of Māori deaths but also the significant shift in the age structure of Māori deaths where it is expected that there will be a large increase in the number of Māori deaths in all age bands above 75 years (McLeod 2016). The anticipated rise in the number of Māori deaths and the increasing age of Māori deaths over the next 20–30 years means that it is crucial for health and palliative care services to increase their cultural responsiveness to better support Māori whānau to care for their own at end of life.

Research evidence identifies that Māori whānau, like other families, carry out the majority of end of life care, not health and palliative care services (Gott et al. 2015a, 2018; Moeke-Maxwell et al. 2014). To die symptom- and pain-free is a strategic goal of the New Zealand Palliative Care Strategy (Ministry of Health 2001). However, in New Zealand, the biomedical approach often remains dominant, and the psychosocial (relational, cultural, psychological, and spiritual) aspects of care, if offered, appear to be included as an addendum or optional to the medical model of care provided. By and large, the indigenous desire for complimentary comfort treatments such as rongoā Māori (Māori herbal medicines and other complimentary therapies such as mirimiri/massage) is often unsupported within the mainstream health system. Rongoā Māori remains unregulated, and therefore these types of indigenous palliative care approaches are unavailable, resulting in the continued use of Western medical interventions and medications.

2 The New Zealand Palliative Care Context

Under the strategic provision of New Zealand's palliative care funding initiatives, the New Zealand Palliative Care Strategy (Ministry of Health 2001) requires that "[all] people who are dying and their family/whānau who could benefit from palliative care have timely access to quality palliative care services that are culturally appropriate and are provided in a co-ordinated way" (p. 7). Palliative care in this context includes care that is carried out by primary and secondary health services as well as specialist palliative care services (hospices). It comprises all health providers and health professionals including pharmacists, ambulance services, volunteer workforces (Palliative Care Subcommittee 2007), emergency departments (Laurenson et al. 2013), and statutory support from the social service sector (such as Work and Income, New Zealand) and Māori health providers. Collectively, these services provide support within the community (at home care), hospitals, hospices, and aged residential care facilities. Despite the implementation of cultural frameworks that govern the generalist palliative care sector (e.g., administered within public hospitals and services), the demands of busy medical services can mean that holistic cultural care may be lacking.

3 Palliative Care and Māori

Palliative care is a new concept for Māori. Within a relatively short period of New Zealand colonial history, indigenous New Zealanders have undergone significant cultural changes that have impacted their traditional caregiving and customs. Many challenges continue to confront Māori, such as institutionalized and personally mediated racism (Jones 2000) within the health system. According to Jones (2000), institutionalized racism is defined as "...differential access to the goods, services, and opportunities of society by race...[that] is normative, sometimes legalized, and often manifests as inherited disadvantage...[and] is often evident as inaction in the face of need..." (p. 1212). Jones (2000) defines personally mediated racism as "...prejudice and discrimination, where prejudice means differential assumptions about the abilities, motives, and intentions of others according to their race, and discrimination means differential actions towards others according to their race..." (pp. 1212–1213). Pascoe and Smart Richman (2009), in a meta-analysis of discrimination and health, link repeated exposure to experiences of perceived discrimination, such as racism, to an

increased risk of mental and physical ill health. Māori are also confronted by other complications of colonization that have resulted in disproportionately poorer health outcomes than their non-Māori counterparts. According to Reid (2011), "...the state of Māori health is exemplified by systemic inequities..." (p. 40) evidenced by higher morbidity and mortality rates across most measures; lower utilization of health services relative to need; unequal distribution of socioeconomic, environmental, and political determinants of health; as well as issues pertaining to the delivery of quality health services that are accessible, affordable, effective, and non-discriminatory (Reid and Robson 2007).

The individual end of life circumstances and preferences of whānau are diverse (Moeke-Maxwell et al. 2014; Reid 2005). For Māori it is essential that care administered at end of life is inclusive of their whānau and is culturally informed, relevant, and well-supported by health professionals. As indigenous people, Māori are at risk of not receiving the full range of benefits from palliative care due to late diagnosis resulting in less opportunity to access and benefit from treatment (Ministry of Health 2001). As descendants of ancestors whose language was subjugated to the dominance of the English language, and whose lands were confiscated or stolen during the colonial epoch, Māori have experienced significant changes to their economic livelihoods and communal lifestyles directly influencing upon their health determinants. Māori are also further marginalized by a wider health system that, despite becoming more holistic in its palliative care approach, still privileges a biomedical model of healthcare. The delivery of palliative care is marginalized as a result of the focus of the wider system. The current health systems' strategic goals are obliged to ensure Māori needs are met within the provisions set by the Treaty of Waitangi (1840) whereby the Crown has an obligation to care for Māori taonga (treasured objects) of which health is a vital taonga. But in reality, despite the improvements made to the health system in recent years, very little is known about what Māori need to support them to provide the type of end of life care congruous with their customary values, beliefs, processes, and cultural practices.

New Zealand hospices provide specialist palliative care services in New Zealand (Palliative Care Subcommittee 2007). Specialist palliative care services may also offer psychosocial services such as bereavement support for the ill person and their whānau. While specialist palliative care services have made efforts to practice compassionate holistic care, the degree that individual hospices effectively respond to the cultural aspirations or needs of Māori who are dying, and their whānau carers, may be variable. Often this will depend on access to and relationships with local Māori healthcare workers or kaumātua (elders) to guide the service.

Hospice professionals work in expert interdisciplinary teams. Hospice staff receive specific training and are accredited in palliative care and/or medicine. The use of the Whare Tapa Whā health model (Durie 1994) guides hospice practice. The increased presence of Māori staff within hospices and the introduction of specific cultural training to ensure staff are upskilled to be inclusive of Māori peoples has gone a long way to ensure a more inclusive approach to tangata whenua (people of the land) (Hospice New Zealand 2012). Importantly, the introductory spiritual care training program developed by Hospice New Zealand (2012) has started to increase an awareness and understanding of the cultural differences between Māori and non-Māori among staff (Mcleod et al. 2015). It has also made a start toward strengthening the capacity of health professionals to discuss spirituality with colleagues. Further, it has begun to increase confidence in recognizing spiritual distress and working more empathically with patients and their whānau (Mcleod et al. 2015). However there is still much to learn about Māori identity, culture, cultural diversity, and needs at end of life.

While specialist palliative care has made effort to practice compassionate holistic care, this does not necessarily reflect the unique cultural aspirations or needs of Māori at end of life or their whānau carers. Holistic care offered within primary and secondary healthcare may include initiatives to create welcoming cultural

environments; observing hosting obligations and appropriate ways of greeting and working respectfully with Māori and offering environments that are spatially set up to accommodate whānau are often greatly appreciated.

Today, Māori, like everyone else, are reliant on medical services to ensure they live for as long as possible and remain symptom- and pain-free until death. Whānau generally assume end of life care either from the time of diagnosis or when the whānau member who has a life-limiting illness can no longer manage their own care. When informal carers become involved, the decision is usually determined by the wishes of the ill person. In this context, whānau includes close biological relatives, non-biological family, extended kin, and close friends. The combination of both indigenous and Western palliative care approaches is anticipated to bring the best outcomes for Māori whānau.

4 Historic Māori End of Life Care Traditions

Traditional customs associated with caring for the ill and dying are described to provide a foundation to understand the values Māori place on end of life caregiving. The aim of this section is to provide a general account enabling an understanding of Māori cultural values that inform their end of life requirements. Much of the references drawn upon reflect historical ethnographic accounts recorded by non-Māori academics. The authors provide the information to give an overview of the literature while recognizing that tribal differences prevailed. Optimal palliative care approaches and models of care are described as these influence the best outcomes for Māori before, during, and following death. Recommendations to improve end of life care for Māori are also identified.

Contemporary models of Māori end of life care generally highlight that Māori want to die at home surrounded by family who love and care for them (Ministry of Health 2001; Ngata 2005). An indigenous Māori model of care places the ill or dying person firmly at the heart of their whānau and their hapū (community) (Brown 1851; Dieffenbach 1843; Hiroa 1950). Historically, care was often carried out by older women or tohunga (spiritual experts) although there were tribal differences between iwi (tribes). Sickness was attributed to the transgression of tapu (breach of spiritual lore) (Brown 1851; Dieffenbach 1843; Polack 1840). Because treating illness and death was considered a spiritual phenomenon, male and female specialists were on hand to administer spiritual care (karakia; prayers, incantations, chants) to remove tapu and restore health. The practice of immersing the sick in wai tapu (purified water) at dawn was one method used to cleanse and heal the sick; the sick were often placed in temporary shelters to ensure the tapu would not contaminate the broader whānau (Phillipps 1954). Rongoā (natural medicine) was also used to provide comfort at end of life (Hiroa 1950; Jones 2012; Tregear 1890).

Traditional end of life care was also based on hierarchical status and was generally informed by whakapapa (Brown 1851; Dieffenbach 1843; Polack 1840). Best (1934) asserts that when death was inevitable, the dying did not fear death and on their deathbed were made to feel calm and clear-minded; this enabled them to express their last wishes, or in the case of an infectious illness, they may have been taken to a cave to avoid the spread of sickness (Hiroa 1950). A temporary shelter was usually erected some distance to the main living site outside the village. Māori preferred to die in the open air so they could greet the world one last time "mihi ki te ao marama" (Best 1934). Sometimes the person would die peacefully, unattended. Another important death wish was to return the dying to their ancestral land, and often they were carried long distances to achieve this.

Historically, major illnesses Māori encountered were attributed to the action of malignant spirits, usually the result of breaking the laws of tapu (sacred/restricted); the treatment of illness came under the jurisdiction of tohunga (spiritual experts). Lange (2011) explains that when caring for the sick and dying, the emphasis of the tohunga's actions was to rid of the malignant spirit or to remove the transgression responsible for it,

rather than on patient care. Of central concern was the well-being of the entire settlement and people.

By the early 1900s, the traditional lifestyles of Māori tribal peoples had changed significantly in response to the prevalence of sickness and the efforts of Māori leaders to encourage people to seek medicine to treat illnesses such as tuberculosis (Ngata 1939). Tohunga and rongoā specialists were perhaps less visible following the Tohunga Suppression Act in 1907; however, they continued to provide spiritual healthcare to support their communities. This Act helped to place the medicalization of dying in the hands of Western medical discourse (Walker 1990). During the early 1900s, based on the observations of Beaglehole and Beaglehole (1945), the practice of "death watching" was undertaken by women of the pa (ancestral communal homes). By the 1940s and 1950s, influenced by Christianity and conforming to a Western work ethic, Māori men worked outside the home; death care primarily became the domain of women who had specific cultural knowledge and skills in this end of life area.

As stated above, the provision of care for Māori who were dying in the 1900s has been described by non-Māori scholars as "death watching" (Beaglehole and Beaglehole 1945). For Māori this involves the practice of helping to prepare the spirit for death and is congruous with other indigenous peoples' end of life care aims (Duggleby et al. 2015). This activity may include sitting with the ill, observing them, and tending to their physical, emotional, and spiritual needs. This custom tended to have greater significance depending on the rank of the dying person. The status of the ill person coincided with the number of visitors they would receive in their final days of life. Farewell speeches poroporoaki or ohaki were commonplace and considered an important part of the dying ritual (Reed 1963). The importance of Oo Matenga (death journey food) aimed to fortify the person for the death journey (Oppenheim 1973).

The increasing need for land by new European settlers led to conflicts between British government forces and tribes. Despite the signing of the peace treaty between the British Crown and Māori chieftain/chieftainess (Treaty of Waitangi 1840), the ensuing swell of British immigrants and the legal and illegal procurement of Māori lands resulted in a bloody land war (Walker 1990). At the turn of the twentieth century, Māori iwi and hapū were at risk of becoming extinct from colonial diseases such as the flu epidemic and tuberculosis (Walker 1990). This led Māori health professionals to politically advocate for Māori to adopt more Western lifestyles to ensure the survival of the Māori. Initiatives such as the Tohunga Suppression Act (1907) were believed to help Māori to survive decimation due to illness; tohunga (spiritual experts and healers) provided healing based on traditional philosophies and practices. However a small group of prominent Māori at that time believed that Māori Western medical interventions were needed to cure these new diseases (Durie 1994). This helped to further displace traditional customs and collective tribal lifestyles that were already being eroded through the discursive forces of neocolonialism. Despite these restrictions, tohunga and lay healers continued to work for their communities (Durie 1994).

5 An Indigenous Model of Illness and Death

Indigenous peoples share in common core beliefs about illness, dying, and death that are contrasted to a Western model (Hampton et al. 2010). A critical and overarching theme is the relationship indigenous people have with the land and the importance of the land to the ill and dying person. A second belief concerns the philosophy that life and death is part of the continuum of life and is an accepted and normal part of the life cycle (Dembinsky 2014). A meta-synthesis review of indigenous palliative care literature by Duggleby et al. (2015) discovered that the key commonality among indigenous peoples was the belief in the spirit and the transition of the spirit to the afterlife. For indigenous peoples then, the purpose of palliative care is to provide physical, emotional, and spiritual comfort to support the ill and dying person and their family; when combined, the

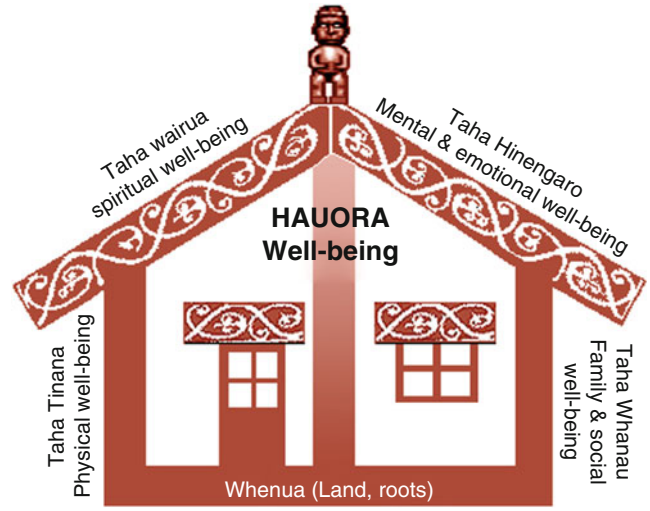

Fig. 1 Whare Tapa Whā (Durie 1994)

activation of these health domains helps to prepare the dying person's spirit to transition through the ārai (the veil between the physical and metaphysical realms) at time of death.

Māori are not dissimilar to other indigenous peoples when it comes to end of life care. Māori whānau prefer to care for their own. Caring for a loved one who is dying is a profound expression of aroha (love, empathy, compassion, concern), where the emotional, physical, familial, and, most importantly, spiritual needs of the ill or dying person are foremost (Moeke-Maxwell et al. 2013). In terms of any care provided by health and palliative care professionals, Māori prefer a holistic approach where the whole person is placed at the center of care. In this context, the desire for holistic care fits well in principle, with a palliative care approach.

Philosophically a palliative model of care is relationally driven and is focused on an inclusive holistic approach informing a "good death" (Clark 2002). This holistic model of a good death is based on a Western concept of palliative care but may not sit congruously with indigenous peoples' culturally diverse end of life care preferences. For example, New Zealand Māori favor a holistic model of care that takes into account their cultural values, spiritual beliefs, and customs (Ngata 2005). However, in reality the current palliative care approach is influenced by the cultural values of the dominant white cultural majority. Four healthcare domains are critically important to a holistic Māori healthcare model; these are the tinana (physical), hinengaro (mental and emotional), whānau (social and relational), and wairua (spiritual) domains; these are best represented in the Māori health model, Te Whare Tapa Whā (Four-Sided House) (Durie 1994), featured in the illustration below (Fig. 1):

5.1 Care Māori whānau Provide at End of Life

At times Māori whānau can be very resourceful; however, the capacity of individual whānau can vary in their ability to access information about palliative care support (Kidd et al. 2014; Moeke-Maxwell et al. 2014). When someone in the whānau has knowledge of the health system or has the ability to source information, there is a greater opportunity for whānau to navigate the health sector and statutory support services to seek the support and resources they require to help them carry out their caregiving activities. In the following example Moeke-Maxwell et al. (2014) provide an example of this.

Tia spoke about the end of life care she and her siblings carried out to care for their mother at home. Tia's brother's provided financial support while she and her sisters set up a care management plan; Tia stated:

> Ariana [sister] was in charge of making sure that her medication was [taken care of] . . .She was in charge of taking Mum to the doctor to her appointments and what have you. Moana's [midwife] role was everything; it was making sure that the house was well looked after for our mother's comfort . . . I was sort of like a floater, I would sort of float, but if it was anything to do with her medication. . . anything to do with that it was primarily Ariana. (Tia) (p. 144)

Whānau provide the bulk of caregiving (Gott et al. 2015b, 2018). They provide a broad range of caregiving tasks including the provision of personal and spiritual cares as well as attending appointments with health providers and hosting visitors (Angelo and Wilson 2014). Whānau are diverse and have various capacities and resources to provide care to a dying loved one (Reid 2005). Large whānau can span several generations and include 200 relatives or more, particularly if they are involved with their iwi (tribes). Whānau may be well connected to te ao Māori (the Māori world) and cultural resources (land, marae, language, and traditional customs); they may be well organized and able to share the care duties across the broader whānau and navigate health services effectively (Moeke-Maxwell et al. 2014). However, sometimes whānau are a lot smaller, and at times there may be only a sole caregiver with limited or no whānau support (Johnston Taylor et al. 2014; Moeke-Maxwell et al. 2014). Or, on occasion, an individual Māori person with palliative care needs may wish to be independent, and therefore they do not require their whānau to provide their end of life care (Moeke-Maxwell and Nikora 2015).

Whānau draw on their cultural knowledge, values, and practices to inform end of life caregiving practices. This point is reflected on by Gott et al. (2015b):

> Māori participants' caregiving commitment was often informed by cultural values steeped in āroha (compassion) and manaakitanga (preservation of mana and dignity), which were prioritised over care costs. Many participants' invoked notions of reciprocity in their discussions:
>
> The way I see it is a parent raises a child, their whole role is to look after the child until they become an adult and then I see it, once you're an adult we should repay that back. You know, because your parent's health and everything starts to fail as they get older. So my obligation is to them. (STA, Māori daughter) (p. 521)

Johnston Taylor et al. (2014) identified a range of traditional Māori end of life cultural care customs carried out by whānau that benefited the ill and dying person and their whānau:

- The use of te reo Māori (Māori language)
- The incorporation of rongoā (traditional healing) including mirimiri (massage)
- The observance of tapu (protocols and practices that govern things restricted, profane)
- The observance of noa (protocols and practices that return a state of tapu back to its ordinary state, safe)
- The inclusion of karakia (incantations, prayers, chants)
- Inclusion of waiata (songs, singing)
- The presence of Māori kaumātua (older Māori) who oversee and provide cultural guidance and support
- The use of kai (food)
- Taking care of personal taonga (treasured objects)
- Observance of hygiene principles; for example, cleanliness with linen
- Correct disposal of body tissue

Moeke-Maxwell et al. (2014) identified that the use of traditional customs sustained and strengthened families who were tasked with providing care, often over weeks or months. By drawing on their vital cultural language, knowledge, values, and customs, whānau were fortified to manage with the demands placed on them, such as coping with poverty, too few carers, and limited knowledge of the health and palliative care systems as well as being confronted with structural and systemic inequities.

5.2 Dying and Caring for the Body Following Death

Death and post-death care (funeral customs) are part of an indigenous caregiving continuum. Caring for the dying and caring for the body

following death are important cultural markers that reflect differences between cultural groups (Dembinsky 2014). In common with other indigenous peoples, Māori like to attend to and companion the ill and dying day and night; many gather at the bedside to say their farewells and to encourage the person to leave their body (Duggleby et al. 2015; McGrath and Holewa 2006; Ngata 2005). Whānau are responsible for providing aroha, manaakitanga (practical support based on reciprocity), and relational and spiritual care, before, during, and following death. Despite the pressures imposed by colonial domination on iwi (tribes), hapū (sub-tribes), and whānau, Māori have retained their tangihanga (customary funeral rituals). According to Nikora and Te Awekotuku (2013), tangihanga (ritualized mourning) practices have evolved, with contemporary practices adapting to both new environments and technologies while resonating with customary ways. Traditional caregiving practices of whānau have also changed in response to the assimilating forces that have shaped contemporary Māori lifestyles.

The important cultural criterion is that the care environment, no matter what setting, is flexible enough to become a culturally responsive home deathscape (Moeke-Maxwell and Nikora 2015). A home death may not be a preferred place of death if urgent medical care is required or if the home is not big enough to host visitors before or after death or if whānau are under resourced to provide this critical care (Gott et al. 2014; Moeke-Maxwell and Nikora 2015). Sometimes dying in a hospice, hospital, or residential care facility is preferable to the ill person and their whānau due to personal reasons (living at distance to family) or for complex medical issues (Moeke-Maxwell and Nikora 2015).

The Western health system can impede the death rituals of indigenous people and care needs to be taken to enable cultural processes to be carried out (Hampton et al. 2010). Māori whānau appreciate having the use of whānau rooms at hospitals and hospices where the whānau can stay to support their loved person to die. Whānau are crucial in helping to prepare the wairua to transition to the spiritual realm. However, many whānau are still reluctant to use hospitals or hospices because they view these places as spaces to die in as opposed to places to help people live longer or to have a better quality of life (Dembinsky 2014; Johnston Taylor et al. 2014).

The spiritual health domain is extremely important to indigenous peoples at end of life. Health providers can benefit from engaging in cultural competency training to strengthen their knowledge of traditional end of life customs (McGrath and Holewa 2006). Increasing awareness of traditional healing is also essential to forge a bicultural health framework to meet the multicultural needs of all New Zealanders. Underpinning traditional end of life care is a strong emphasis on wairuatanga (indigenous spiritual belief system) (Ngata 2005). Hampton et al. (2010) research emphasized that improving indigenous care will require health professionals to work together with traditional healers, patients, and family carers.

6 Barriers Māori Encounter at End of Life Care

Palliative care must take into consideration the culture and cultural needs of the person with a life-limiting illness and their whānau who care for them by preventing and relieving suffering (World Health Organisation 2002); this is more likely to be achieved when the culture and cultural needs of Māori are recognized and supported. Culture is recognized as an important determinant of health because it can positively or negatively influence health (National Advisory Committee on Health and Disability 1998). Culture influences attitudes, views, beliefs, and behaviors including those associated to health. Despite the fluidity of culture and cultural identity, Dein (2006) argues that the concept of "culture" is helpful in understanding the needs of different groups of people:

> . . . It [culture] is an important variable in the perception, experience and expression of suffering. There are very real differences between cultural groups. . . People actively draw on elements of their culture to manage life stresses. Culture influences, rather than determines, the way people live.

> It provides ideas about the appropriate behaviour in a given situation, their response to illness and to medical ideas about treatment. (p. 20)

As colonized people, Māori share a number of things in common with other indigenous people at end of life (McGrath and Holewa 2006; Moeke-Maxwell et al. 2014; O'Brien 2012).

- Poverty.
- High financial burden of care.
- Lack of adequate whānau support people due to smaller whānau; whānau living away from home.
- Carer burden and stress.
- Poor communication from health and palliative care service providers (assistance to discuss and explore preferences for place of care and death).
- Lack of support from health and palliative care services.
- Lack of community services (particularly relevant for rural and remote places).
- Whānau cultural preferences differ to palliative care provided by Western healthcare providers.
- Lack of support for caregivers (financial, respite, information).
- Lack of bereavement support (counseling).

Māori whānau may prefer to provide care for their relations who are terminally ill or have high needs at home or in a hospital or hospice setting. But there are many barriers in support provided by the state and in the services provided within hospitals or hospices. Improvements to palliative care services are urgently required, and these need to be flexible in terms of how and where the services are provided. We have to ensure that whānau are supported in carrying out their care obligations. Treating whānau on a "whānau-by-whānau" basis and ensuring services are flexible enough to respond to the diverse circumstances and needs of whānau are essential to providing good end of life care. Reid (2005) states:

> Māori whānau often want to provide care for their relations who are terminally ill or have high needs—either at home, or in a hospital or hospice. But there are many barriers still in the way of this, in the kind of state support provided, and in the services in hospitals or hospices. We have to improve the palliative care services themselves, and the flexibility of how and where the services are provided. And we have to ensure that whānau are supported in their care for family members. That's not only providing real choice—it's also meeting needs and rights. (p. 45)

It is generally accepted by the palliative care sector that Māori want to die at "home" (Ministry of Health 2001; Ngata 2005). A home death is generally considered an important cultural preference for Māori. However, not all Māori want to die at home indicating there is diversity of end of life preferences (Moeke-Maxwell et al. 2014). In the following quote, a bereaved woman reflects on her perception that her husband's preference was to avoid dying at home:

> I didn't have the facilities here [at home] either, and I know that's what [he], I know he would have been thinking that . . . "I don't want to die at home." . . . Not that he said it, not that he said it. But I know, knowing [him], he wouldn't have wanted to die at home. (Moeke-Maxwell et al. 2014, p. 147)

Health providers may have a different concept of home than Māori. Māori have multiple homes; these can include a kainga (house whānau dwell in), ancestral landscapes, and tribal homes (marae) as well as the homes of other whānau (Gott et al. 2014; Moeke-Maxwell and Nikora 2015). Returning home to die or visiting an ancestral home or special place such as a graveyard before death helps to settle the wairua for the journey home to the spiritual realm (Moeke-Maxwell et al. 2014). Similarly Yamatji people felt that to die "in country" was essential for completing the cycle of life and death. Here the Yamatji would be reunited with ancestors which brought deep peace (Dembinsky 2014).

6.1 Access to Services and End of Life Support

Living rurally can present a challenge for whānau as palliative care support is limited, particularly in remote areas. Difficulties have been identified with accessing hospitals, specialists, and specialist

palliative care services (Penney et al. 2009). However, living in an urban environment can also prove challenging, particularly for whānau who have moved away from their ancestral homes. They may find it difficult if there are not enough whānau available to support their care requirements. Sometimes friends and neighbors may fill the gap, or a local health service or hospice may be accessed (Moeke-Maxwell and Nikora 2015).

6.2 Personal Factors Affecting Palliative Care Among Older Māori

There are unique challenges for Māori kaumātua (older Māori), particularly for those of advanced age (over 80). Moeke-Maxwell et al. (2014) highlighted the diverse needs of Māori kaumātua. For example, many older Māori continue to be connected to their tribal roots, and they remain active within their whānau, communities, ancestral homes, and tribal groups (Dyall et al. 2011). Similarly, Moeke-Maxwell et al. (2014) identified that some Māori were socially well connected with their communities, and they relied on their whānau to support them at end of life; however, a small number of kaumātua resisted whānau support and were determined to care for themselves. Self-determination, particularly for older Māori, challenged their cultural connections and relationships with whānau (Oetzel et al. 2015b), highlighting differences between Māori as well as different end of life priorities between people of advanced age. Furthermore, whānau associate kaumātua with leadership qualities and cultural knowledge, and as such they are imbued with mana (authority, prestige, and spiritual status). Kaumātua may even find it difficult to receive caregiving support from whānau when they require end of life care as the relational balance of power is jeopardized (Oetzel et al. 2015b). Another reason older Māori may resist their whānau being involved in caregiving is to protect them against the burden of caregiving particularly when there are other concerns (financial, housing, other care obligations, work). For example, Gott et al. (2017) found in a New Zealand longitudinal study, Te Puawaitanga o Ngā Tapuwae Kia Ora Tonu – Life and Living in Advanced Age – that older Māori wished "... to not be a burden to family..." (p. 3). This may reflect the ill person trying to protect their whānau from enduring additional stress. This point is highlighted in a qualitative study of Māori end of life experiences and needs (Moeke-Maxwell and Nikora 2018). The findings revealed that kaumātua recognized their whānau were already burdened with responsibilities (work, caring for others, unwell themselves) and financial hardship. Kaumātua believed that the family's stressful circumstances would be further exacerbated by caring for their end of life needs. Therefore, despite whānau desperately wanting to help the older person, three kaumātua resisted their informal support until death was near (Moeke-Maxwell and Nikora 2018).

6.3 Financial Costs of End of Life Care

The financial costs associated with caring for someone at end of life are intensified at a time when whānau are already under pressure. A pilot bicultural study by Gott et al. (2015a) on the financial costs of care at end of life revealed that the 11 whānau who took part experienced financial hardships associated with meeting the demands of end of life caregiving. Direct costs to whānau, such as medical expenses, pharmaceutical costs, transport, hospital' parking fees, complementary therapies, and linen, were exacerbated by specific cultural care imperatives. These are costs related to cultural obligations associated with care practices such as hosting visitors, travel, and special foods. The costs associated with tangihanga are also high:

> For Māori, the cultural obligation and preference to return to ancestral homes before death and/or post-death (tangihanga) incurred additional transport costs and other expenses associated with meeting these cultural end-of-life needs. In several cases, customary funeral traditions were interrupted due to a lack of resources. Some participants also reported that caring had negatively affected their own health and well-being. (Gott et al. 2015a, p. 521)

Manaakitanga is a social and cultural responsibility (Moeke-Maxwell et al. 2013) that whānau, as hosts, express by taking care of visitors. The study (Gott et al. 2015a) found that feeding manuhiri (visitors) of a dying whānau member at a private home or in a hospital setting can become a very costly expense associated with end of life care. Further, the study highlighted that cultural obligations such as manaakitanga take place before, during, and following death. Other financial costs of care in Gott et al.'s (2015a) study included travel expenses associated with a dying loved one to visit their ancestral lands, homes, or a sacred place before death (e.g., ancestral gravesites) and purchasing kai rangatira (special foods consumed by someone prior to death). Kai rangatira may include delicacies that a kaumātua enjoyed in their youth such as seafood (e.g., crayfish, oysters, kina) and can come at considerable cost to whānau if they are unable to gather these foods themselves. As a result, some caregivers experienced significant debt associated to the financial costs of caregiving at end of life (Gott et al. 2015a). To provide end of life care requires at least one person to support the ill person on their journey. This can have a huge financial and personal impact on the carers, especially when they have to give up work to provide care:

> For example, a Māori participant terminated paid employment to provide full-time care for her older mother, knowing that it would incur financial hardship to nurse her at home: So I gave up my [job]; I resigned from my job which, yeah, which I knew would put me in a position where I wouldn't be able to cope financially. (CTH, Māori daughter) (Gott et al. 2015a, p. 523)

Moeke-Maxwell et al. (2014) similarly identified in a study of Māori end of life experiences that seeking support is not always easy for Māori. For example, accessing respite in a hospice setting may be challenging for whānau, particularly as whānau often have great attachments to their own homes. Financial hardships can make the decision to use hospice services almost essential, especially when the pressure to meet cultural obligations (e.g., such as hosting visitors) is an important, yet often expensive, cultural custom:

> It was brave [to go to hospice]. Boy I cried. It made me think as if I didn't want him [husband], I didn't love him, but I told him . . . I said, "Gee I'm tired." He said, "Tired of what?" I said, "I'm tired, there's too much going on. Your family's coming 'round, I've got to feed them, plus feed our kids and then—we've got nothing to feed them on." (Moeke-Maxwell et al. 2014, p. 146)

Furthermore, costs associated with cultural end of life care can be prohibitive. For example, the preference to use complementary therapies can be expensive for whānau. For example, a participant in Gott et al. (2015a) stated, "That was really costly, alternative medication, it was a Chinese herbalist, I think it cost us about $340 or $350 per week for 4 weeks" (MR, Māori daughter caring for father) (p. 522).

6.4 Māori Health Literacy

Māori carers have a greater opportunity to access palliative care and statutory services support (such as Work and Income, New Zealand) when they have the knowledge or skill to access information (Moeke-Maxwell et al. 2014). Confidence is increased when whānau carers know what is available and how to access it (Kidd et al. 2014). Through necessity whānau often have to rely on their own resources and informal community networks to access palliative care and statutory support information (Kidd et al. 2014). Whānau struggle to access information often due to a lack of the competency of health and palliative care providers to confidently lead and carry out a process of informational exchange between whānau and health professionals.

Hospices can provide invaluable support as they can often be a one-stop-shop of information and referrals. Increased understanding of services can lead to better opportunities to discuss with health professionals critical issues concerning diagnosis, prognosis, treatment, and end of life decision-making and to convey what the needs of the ill person are. Conversations that are helpful require a two-way dialogical process. To be effective, health professionals need to understand the Māori patient and their whānau's needs as much

as the patient and their whānau need to understand the health and palliative care systems. For example, positive experiences among Māori whānau are often associated with accessing and receiving hospice support. A kaupapa Māori qualitative study by Johnston Taylor et al. (2014) examined Māori perspectives of hospice care in a large urban city in New Zealand. In line with the benefits enjoyed by Māori New Zealanders, the study highlighted that hospice benefited Māori carers by providing respite care, caregiving equipment, resources, and information and by offering a compassionate service including bereavement and spiritual care. Other benefits hospice provides to Māori have been identified by Slater et al. (2015) and include good communication that is inclusive and supportive of whānau, responsive in-patient units that can cater for whānau, after-hour services and continuity of care, and support with post-death arrangements.

7 Improvements Needed in Palliative Care Services

There are some specific areas in the current palliative care services provided to Māori that need addressing to redress health inequities at end of life. Reducing the gaps is critical given that Māori are often resource-poor and are likely not to be well-informed about the provisions provided by the health and palliative care sectors and statutory support services (Johnston Taylor et al. 2014; Penney et al. 2009).

A Māori preference for a holistic and relational model of healthcare that takes into consideration the mind, body, and spirit has largely been obscured within the mainstream healthcare system. Historically, the healthcare system's medical paradigm has privileged the medical domain almost to the exclusion of the psychosocial and cultural domain. The current health system arguably has some way to go to ensure its services are holistic and that healthcare professionals are equipped to meet the cultural end of life needs of Māori. The indigenous values that are critically important to Māori at end of life are often obscured beneath a preoccupation with the aWestern societal medicalization of dying (Duggleby et al. 2015; Ngata 2005).

A key principle of good palliative care is that people have access to information (Johnston Taylor et al. 2014; Kidd et al. 2014; Ministry of Health 2001; Penney et al. 2009). However, cultural differences between health providers and those receiving services create an additional barrier for Māori accessing and using palliative care services (Frey et al. 2013). In a study by Frey et al. (2013), the researchers discovered that New Zealanders were often unaware of specialist palliative care and that Māori participants had misconceptions about palliative care. This can lead to misunderstanding, further obstructing access to quality care (Frey et al. 2013). Study participants also found it difficult to access information, and prior experiences or knowledge of discrimination encountered within the sector also acted as a barrier.

7.1 Quicker Referrals to Palliative Care Services

Quicker referrals to palliative care services will result in whānau being able to access support and resources much earlier. Research evidence in one rural study highlighted concern over late presentations, late referrals, and late diagnoses delaying the palliative care pathway (Penney et al. 2009). Similarly, a study undertaken by Koti (2013) found that despite numerous visits to a primary healthcare provider over several years for the same health issue, a general practitioner failed to refer the patient to a specialist within a reasonable time-frame. A core component of good palliative care is the delivery of support within a timely manner (Ministry of Health 2001).

7.2 Communication and Information

Of vital importance is the information whānau need to prepare them make informed decisions about the end of life trajectory (Kidd et al. 2014; Penney et al. 2009) and what whānau need to

support them to provide care. Closely associated with this is the level of communication needed to convey information to whānau. To date, communication from health providers has at times been of a variable and even disrespectful quality (Koti 2013). Commonly reported issues reflect the use of jargon, lack of information being shared, and the form in which the information is given (Penney et al. 2009). Whānau respond to effective communication employing multiple methods (verbal, pictorial, written) across the care continuum, at the time of diagnosis, during treatment, prior to death, and following death (Moeke-Maxwell et al. 2014; Oetzel et al. 2015a; Penney et al. 2009).

7.3 Racism and Palliative Care

From an indigenous Māori perspective, palliative care should aim to support families to whakamana (uplift the status, authority, and prestige) of an ill or dying family member. Racism acts as a barrier to Māori accessing and receiving end of life care (Harris et al. 2006; Moeke-Maxwell et al. 2014; Penney et al. 2009). Frey et al. (2013) identified that Māori can also be influenced by experiences of discrimination within the health system shared by other Māori.

Racism is broad-based and can include inequitable access to services or discriminatory treatment based on ethnicity that can lead to stereotypes, negative assumptions, and treatment toward Māori. For example, a young kaumātua in the study conducted by Moeke-Maxwell et al. (2014) experienced personal discrimination from hospital staff who stereotyped the unwell man as a drug user. The withholding of his pain medication caused him to suffer unnecessary physical, emotional, and spiritual pain.

8 Conclusion

Māori are culturally and ethnically diverse. Given this heterogeneity, there are often diverse care preferences within and between whānau at end of life (Moeke-Maxwell et al. 2014; Reid 2005). Despite colonialism and the disruptions Māori have faced, many whānau have held on tightly to their mātauranga Māori (knowledge), tikanga (customs), and kawa (protocols) as these fortify and guide Māori caregiving practices (Mead 2003). These customs must actively be retained within the health and palliative care sectors (Durie 1998). The prioritization of the care of the ill and dying remains a critical and core cultural custom of Māori whānau, and it is one that is driven by indigenous cultural and spiritual values, including the cultural imperative to prepare the spirit to transition (Duggleby et al. 2015). A critical role of whānau is to ensure the ill and dying person has their physical, medical, mental and emotional, relational, social, and spiritual needs met.

The New Zealand government has an obligation under the Treaty of Waitangi (1840) to ensure health equity for Māori. This is urgently needed to reduce disparities and the high need for palliative care among Māori. Attention must be focused on ensuring Māori are supported to seek help early to reduce the high numbers of late admissions and the shortened opportunity to access palliative care support. Whānau also desperately need support from health and palliative care services and statutory services (government) to resource them to carry out their caregiving activities (Gott et al. 2015a). These services have a responsibility to fully align their palliative care approach within a framework that is congruous with Māori culture and customs to ensure the best end of life health outcomes for Māori. However, there are critical issues that need improving to reduce the burden on Māori whānau. Whānau often encounter obstacles on the end of life journey (Gott et al. 2015a; Moeke-Maxwell and Nikora 2015; Johnston Taylor et al. 2014; Moeke-Maxwell et al. 2014; Koti 2013; Penny et al. 2009; Harris et al. 2006) including difficulty accessing and receiving the benefits of palliative care (e.g., rural New Zealanders), and there are reduced opportunities via late admissions to palliative care. Furthermore, as a result of neocolonial forces, many whānau have social and economic hardships making the task of caregiving difficult due to the high financial costs associated with end of life care (Gott et al. 2015a; Moeke-Maxwell 2014). Giving

up paid work to provide caregiving adds extra financial pressure on whānau carers.

Specifically focused Māori palliative care cultural competency training will help to ensure that health professionals have an understanding of New Zealand history, Māori language, local tribal knowledge and traditional end of life care customs (rongoā Māori – Māori medicines), spiritual practices, and customary rituals. Training in these areas will support health and palliative care services and statutory services to make cultural improvements and to continue to develop services that are aligned with Māori cultural aspirations. Additionally, health provider cultural literacy and communication must also be improved to ensure that communication is simple and straightforward to assist whānau to navigate the health system and access services and statutory support as required (Kidd et al. 2014). Furthermore, once help is accessed, there must be clear, direct, and respectful communication from health professionals toward whānau (Kelly et al. 2009).

The four Te Whare Tapa Whā (Durie 1994) healthcare domains work in synergy with each other and are not separate health fields. The Te Whare Tapa Whā holistic health model "whare" (meeting house) is symbolically viewed by tangata whenua (people of the land) as a place of well-being, safety, and protection. The whare symbolizes the body of a woman; it is protective as it is filled with the spiritual energy forces of the spiritual realms, atua (gods), deities, and ancestors. As such, the Te Whare Tapa Whā health model predates a holistic Western palliative care approach. There is not *one* specific healthcare domain that requires strengthening to support Māori whānau carers to meet the increasing caregiving demands anticipated over the next 30 years. *Every* healthcare domain needs to be strengthened and united to ensure the cultural customs of Māori whānau are supported. This is required to uphold the mana of the dying Māori individual and their whānau carers at end of life. These initiatives will go some way to ensuring there is the desired balance between the physical, emotional, relational, social, and spiritual healthcare domains. A strong community public health approach could help support whānau carers to undertake this critical and sacred end of life work by increasing the opportunity for local psychosocial support (counseling, bereavement, financial assistance, care navigation).

Living with a life-limiting illness and the process of dying are critically important times in the human life span for Māori; it is the sacred time when the wairua is prepared for its journey across the ārai during its transition to the spiritual realm. Whānau, health and palliative care providers, and statutory support services all play an interconnected and critical role on this journey. Their combined efforts will ensure whānau are able to fulfill their cultural obligations as *pou aroha*. The popular Māori adage is relevant here, "if we get this right for Māori, we will get it right for everyone."

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End-of-Life Healthcare Experiences of Indigenous People and Ethnic Minorities: The Example of Canada

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Contents

Abstract

This chapter will explore understandings of culture, ethnicity, indigeneity, intergenerational trauma, and othering and how they relate to health outcomes, experiences with illness and death, accessing healthcare and palliative care, and patient/practitioner interactions predominantly in Canada. Discussions will define indigenous and ethnic minorities and examine the commonalities in health disparities experienced by both groups. Although commonalities will be discussed, they will be paired with the continual need to avoid "pan-Indigenous" or

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_65

"pan-cultural" understandings that oversimplify the reality of diverse populations. Culture, spirituality, the desire to provide palliative care within the home and community, and subsequent barriers to doing so will be introduced. Though rumblings of culturally safe models of care continue to grow throughout the country, they are often overpowered by stories of mistreatment, discrimination, and colonial behaviors in the healthcare system. In an effort to overcome these barriers and provide the best possible end-of-life care to individuals, a brief overview of cultural safety and culturally safe models of palliative care will be introduced. Finally, recommendations and best practices are presented along with a case study highlighting the importance of patient/practitioner communication when offering culturally safe palliative care.

1 Introduction

The introduction of cultural safety and cultural awareness models into healthcare practice over the past few decades has brought about a much-needed conversation on the roles of culture and othering that inform patient/practitioner interactions in palliative care and healthcare in general. Culture plays an important role in palliative care, as one's understanding of, and approach to, end of life is largely determined by their cultural upbringing. By incorporating the principles of cultural safety into healthcare provision, the patient and their family may guide the process, enabling healthcare practitioners to provide care that aligns with the beliefs of the individual patient. The progress toward implementing these models, including recommendations made by guiding bodies for healthcare practitioners, has seen the widespread enactment of, and support for, training programs for practitioners to ensure relevant and appropriate care for diverse groups of patients, including Indigenous populations and other ethnic or cultural minorities. Existing cultural safety training in Canada approaches training with a focus on the historical experiences of Indigenous peoples in Canada, specifically discussing the colonial efforts to "kill the Indian to save the child" mentality of residential schools, criminalization of Indigenous spiritual practices, and attempted eradication of languages and cultural practices. While this is an excellent way to educate non-Indigenous Canadians on our colonial history, its focus on Indigenous experiences does not address the experiences of immigrants or non-Indigenous ethnic minorities. As is often the case in intercultural relationship building, there is a tendency to skew toward painting marginalized groups with broad brushstrokes, assuming that a homogenous solution may be applied to all members. Indigenous people in Canada hold a vast array of beliefs, traditions, practices, and experiences, yet most of the training programs and recommendations for implementing culturally safe practices assume a shared history and experiences. Add to this the attempt to prescribe the same cultural safety model to other minority and immigrant groups, and it begs the question: is cultural safety doing more harm than good, as it tries to improve patient outcomes and experiences? How is this model enacted with palliative care patients and their families? Are the changes actually accommodating cultural needs, or is lip service being paid to the unique experiences and needs of individuals?

This chapter will explore understandings of culture, ethnicity, indigeneity, intergenerational trauma, and othering and how they relate to health outcomes, experiences with illness and death, accessing healthcare and palliative care, and patient/practitioner interactions. Discussions will pull information from specific Indigenous communities and will also highlight high-level commonalities that are relevant when examining current and potential models of end-of-life care for Indigenous communities. Although commonalities will be discussed, they will be paired with the continual need to avoid "pan-Indigenous" or "pan-cultural" understandings that oversimplify the reality of diverse populations. Indigenous groups and individuals have a vast array of cultures, traditions, beliefs, practices, and experiences. Like all palliative care provision, each individual, family, and community will have unique understanding of death and what they desire for end-of-life care.

2 Defining Indigenous

Indigenous populations live across the globe and are defined by their long-standing connections to the land. Throughout the course of history, Indigenous populations have adapted and migrated, but a vast majority have been displaced or significantly impacted by Euro-western colonization of their lands. This chapter will focus largely on Canada but will also include reference to the British colonized areas of the United States, New Zealand, and Australia, as a result of commonalities in colonial histories, as well as some similarities in their healthcare systems and the way care is provided. This is not to say that there is not vast importance in palliative care models of other Indigenous countries across the globe, but in an area where research is often limited, this serves as a starting point and a foundation to begin identifying specific effective recommendations for communities and geographic locations.

Indigenous peoples are a dynamic and diverse group with their own unique cultural traditions and practices, languages, histories, and ways of knowing. For many Indigenous people in Canada, their sense of identity is connected to definitions created through Canada's colonial history and the creation of legislation such as the *Canadian Constitution Acts of 1867* and *1982*, *the Indian Act*, and subsequent amendments to these documents (Palmater 2011). The Canadian Constitution recognizes three groups of Indigenous people in Canada: Indians (commonly referred to as First Nations), Métis, and Inuit. Currently, many Indigenous people and communities throughout Canada have been granted "Indian status" under *the Indian Act*, while others have not. This is significant as status determines whether or not individuals, even those within the same family and community, can access land rights, band membership, and treaty benefits. Furthermore, creating divisive categories of who is considered Indigenous and who is not demonstrates the Canadian government's continued control over Indigenous peoples, their rights, and their identities (Palmater 2011).

Data from the National Household Survey (NHS) of 2011 reports that 4.3% of the total Canadian population self-identified as Indigenous. Of these citizens, 60.8% are identified as First Nations (this could include status or non-status First Nations), 32.3% identified as Métis, while another 4.2% identified as Inuit (Statistics Canada 2013). The total number of Indigenous peoples in Canada has increased from 3.8% of the population enumerated in the 2006 Census, 3.3% in the 2001 Census, and 2.8% in the 1996 Census (Statistics Canada 2013). Furthermore, Canada's Indigenous population increased by 20% between 2006 and 2011, compared with just over 5% for the non-Indigenous population. The largest numbers of Indigenous people live in Ontario and the western provinces (Manitoba, Saskatchewan, Alberta, and British Columbia) (Statistics Canada 2013).

Indigenous identity has been utilized for centuries to assist colonial efforts, which first aimed to take imperial control of land, and later strove to limit treaty and legally prescribed Indigenous rights. Limiting the power of Indigenous peoples was essential to colonization, and defining and controlling who they were was a strategy consistently employed by colonizers. Although the umbrella term of "Indigenous" refers to connections to a portion of land for a long period of time, centuries of assimilation policies and intentional suppression of Indigenous identities have generated circumstances where indigeneity has become riddled within complex legal and political discourse. And, ultimately, the political and social impacts on identity move into the everyday lives of Indigenous populations and are tied directly to health and wellness. Identity is central to holistic well-being for individuals and communities. Indigenous populations and other minorities face realities where they are "othered" and are socially categorized outside the mainstream.

Despite the complex legal and political discourse surrounding indigeneity, many Indigenous people feel they are able to define their own identity and determine what it means to be Indigenous in Canada. According to Palmater (2011), there is no need to maintain the archetypal "Indian," and Indigenous peoples are free to grow and expand their identities while still having a connection to shared history, ancestors, and

traditional territories. As such, palliative care models for Indigenous populations require flexible definitions of indigeneity and should work from an inclusive model that allows for self-identification. Indigenous populations were, and continue to be, disempowered through the denial of their ability to self-identity. They also faced blatant oppression as a result of their identities, as well as subliminal oppression through the exclusion of identities in mainstream discourse. To counter this oppression, models that empower self-identification are of the utmost importance, and the development of any care model should ensure that the power associated with identity is placed with the patient, their family, and their community.

Indigeneity, as discussed, refers to people who have a connection with land. It is distinct from ethnicity and culture but yet remains intertwined with both of these concepts. Ethnicity and culture are two different notions, and it is important to create this distinction when discussing culturally responsive healthcare models. Ethnicity is categorized as the distinctive shared origins or social backgrounds and traditions of a group of people that are maintained between generations. It should not be confused with race, migration, or nationality. Ethnicity is fluid and creates a sense of identity that may include a common language and religion (Busolo and Woodgate 2015). Culture, on the other hand, refers to beliefs, values, and customs expressed in daily living including diet, clothing, or rituals. It also influences language and social or political systems. In this way, culture may be fluid because of developments in people's lives (Busolo and Woodgate 2015).

Identity and culture evolve and are renegotiated and recreated over time. Aggressive colonial practices have created identities for Indigenous people, which has resulted in Indigenous identities and cultures being framed as homogenous, static, and valued through another society's agenda. This has led to a lack of agency and created health inequities that still exist today (King et al. 2009). For example, trauma histories are highly prevalent among Canadian Indigenous populations and occur from collective and individual experiences with discrimination and social exclusion, poverty, emotional abuse, physical violence, sexual assault, torture, and war (Guilfoyle et al. 2008). For Indigenous Canadians, these traumatic experiences are not merely historical and relegated to the experiences of past generations. Rather, these traumatic experiences are intergenerational, meaning the psychological, spiritual, emotional, and physical pain and suffering continues today and is experienced by each new generation of Indigenous youth (Browne 2006; Guilfoyle et al. 2008). As a result of this deep historical trauma, health disparities cannot merely be mitigated by matching socioeconomic status or altering individual lifestyle factors. Intergenerational trauma is a collective experience that has created and continues to create structural inequalities and violence in the healthcare context.

3 Indigenous and Ethnic Minority Disparities in Healthcare

In addition to the increasing population of Indigenous peoples around the globe, globalization is driving immigration, with millions of people uprooting from their birthplaces to seek greener pastures and brighter futures. In 2011, Canada had a foreign-born population of nearly seven million people, representing 20.6% of the total population. In the past 5 years, the majority of newcomers have come from Asia and the Middle East (Statistics Canada 2013). Furthermore, 19.1% of Canadians identified themselves as a member of a visible minority group, and only 30.9% were born in Canada, while 65.1% were born outside the country and came to live in Canada as immigrants. Visible minorities also experience health disparities that may be the result of the direct effects of discrimination or unequal treatment by healthcare providers, or indirectly, through the effects of race-related socioeconomic inequalities (Khan et al. 2015). However, there is a lack of data and research on the role of race or visible minority status on health in Canada compared to Indigenous peoples and the impacts of applying universal cultural safety models to visible minorities, despite similar healthcare

disparities or experiences (Khan et al. 2015). The continuous impact of colonization leaves Indigenous and non-Indigenous people in a deep-rooted systemic issue around healthcare. Healthcare professionals are encouraged to be mindful not to "homogenize" an individual's end-of-life care plan based on cultural heritage alone, as many individual differences need to be taken into consideration (Bellamy and Gott 2013).

Both Indigenous and immigrant Canadians experience health inequalities compared to their non-Indigenous, Canadian-born counterparts (Anderson et al. 2015; Kirmayer and Brass 2016). Through the destructive process of "othering," racial, cultural, and ethnic stereotypes are enacted in healthcare creating a social distance that marginalizes and disempowers Indigenous people and immigrants. Othering marks certain individuals and devalues their identity as it is continually created and recreated in the eyes of those who are unmarked or valued in society, producing positions of domination and subordination (Barter-Godfrey and Taket 2009; Johnson et al. 2009). In the healthcare context, othering has led to large health disparities for Indigenous peoples and newcomers. Several Canadian studies have found that both Indigenous and foreign-born Canadians face barriers to accessing healthcare services (Guilfoyle et al. 2008).

The impacts of these disparities between Indigenous people and ethnic minorities share a common connection. Much like how Indigenous people in Canada can trace a decline in their health to European contact, new immigrants also face a decline in health upon entering the country. Research suggests that those new to Canada actually enter the country with high levels of health but experience a deterioration in their health status after settling in the country (De Maio and Kemp 2008). The reasons for this change in health from the so-called healthy immigrant are often the results of discrimination and inequitable experiences in healthcare but are also due to difficulties transitioning to a new country (De Maio and Kemp 2008). Therefore, the healthcare rhetoric of "treating everyone the same" runs counter to the experiences of marginalized groups, claiming they are "being treated differently" by healthcare providers because of their identity (Tang and Browne 2008).

Despite the commonalities, there are some differences to consider when examining health disparities among Indigenous and immigrant Canadians. Studies highlight one area where there is a critical divergence in the healthcare status and experiences between the two populations. The health inequities between foreign-born Canadians and those born here converge after controlling for sociodemographic and socioeconomic status and lifestyle factors (Kobayashi et al. 2008). When these factors are controlled for Indigenous people, disparities still remain (Browne et al. 2012). This can partially be attributed to the intersection of race with other social categories including class, substance use, and history that creates inequitable access to health and healthcare for Indigenous people (Tang and Browne 2008). Specifically, it is the historical intergenerational trauma that continues to entrench these health disparities into contemporary contexts (Browne et al. 2012; Guilfoyle et al. 2008).

4 Culture, Spirituality, and Dignity in Dying

The experiences of each person, family, community, and culture throughout, and at the end of one's life, are unique. Everyone will experience death differently, and people will require different supports at the end of life. There are similar characteristics and experiences among Indigenous groups; there is also significant variation between regions and communities. When discussing or providing palliative care for Indigenous people and ethnic minorities, it is essential to avoid the assumption that everyone will have the same understandings and experiences. Care models should avoid generalist approaches that assess diverse individuals and groups strictly based on their cultural identity. Space must be generated that allows for cultural and communal similarities and subsequent connections but, at the same time, allows for diversity and individual care needs. Creating this balance is necessary to providing anti-oppressive healthcare.

This chapter will further address this concept, and its practical applications, through discussions of cultural safety. To further examine the intricacies of implementing cultural safety, the following sections will highlight some high-level concepts of how culture and indigeneity influence dying and the end of life and, subsequently, palliative care.

Culture influences the way we see and experience the world; therefore, one's culture influences understandings of death and dying. The experiences of all people, including Indigenous peoples, at the end of life are connected to their cultural understandings of life, death, and health. The meaning of health, life, and death is influenced by familial, social, and cultural experiences, and therefore it is not only individual but also social and cultural. One cannot detach meanings of death, dying, grief, and care from family, community, and culture.

For many Indigenous populations, health is holistic and involves a cyclical journey that incorporates death as a meaningful and important part of this journey (Clarke and Holtslander 2010). Despite cultural differences between many groups, preparing the personal spirit for end-of-life journeys is a shared worldview that is important for connection, healing, and protection during this time (Duggleby et al. 2015). Elders and traditional teachers from communities in Saskatchewan, Canada, emphasized that death was a necessary part of completing the circle. It was an essential part of the life cycle and was not necessarily seen as an end – it was seen as essential to living (Hampton et al. 2010). This sentiment was echoed, and highlighted, by community-based researchers in Northern Alaska as well (DeCourtney et al. 2010b). These traditional views impact not only the emotional and mental state of the individual near the end of their life but also those of family members and community members.

The value of balance, and the understanding that life and death are all part of the same process, is foundational to how someone approaches death. In some instances, traditional elders speak of a "good death." The very fact that the concept of moving on to the "spirit world" and having a "good death" demonstrates how understandings of end-of-life processes are rooted in culture and how one sees the world. In some instances, dying well is connected to living well (Baydala et al. 2006). If death is part of completing the circle of life, then living in balance, and living a good life, is the foundation of a good death. In some cultural discourses, including biomedical ones, life and death are seen as opposites, and the belief that a good life means a good death would be counterintuitive. Different worldviews and different cultural teachings, including those from Indigenous communities, emphasize the spectrum that exists for how people experience death. When asked for their traditional views on death and dying, the elders from Saskatchewan, referenced earlier, were quick to point out that they could only relay what they knew, their own experiences, and the teachings they had been handed down from their ancestors. This reiterates that cultures and communities may share common teachings and traditions but that one cannot generalize assumptions of beliefs or experiences onto entire groups.

Spirituality may also play a significant role for many Indigenous populations at the end of life. For some, death is the process of traveling to the spirit world (Duggleby et al. 2015). Some Mi'kmaq communities explain death as a journey to the spirit world that is taken alongside your ancestors and kin who have already passed (Johnston et al. 2012). In line with this belief is a story from Alaska that outlines a young Indigenous girl's experience caring for her grandmother on the day she died. She remembers helping her grandmother get dressed for tea. The visitors that came for tea were her grandmother's previously deceased husband and son. Once the tea was drunk, she assisted her grandmother to her bed where she then died (DeCourtney et al. 2010a). This story is just one anecdotal example, but it highlights how spirituality and ancestral traditions will greatly impact experiences around end-of-life care.

5 Care in the Community and Dying at Home

Family and community often play an important role at the time of death, and culture also impacts the role they play at the end of life. An important

consideration is that the definition of family is influenced by culture. For many Indigenous communities, the extended family and community played a large role in palliative care (McGrath 2010). For some Indigenous communities, the gathering of the community in a person's final days is very important (Hampton et al. 2010). As palliative care facilities are not always located within their communities, the thought of physically moving a patient would be conflicting with their desires to die at home or die in an environment that allows for the gathering of community members. Preparing the spirit for the journey ahead is very important for many Indigenous people. Duggleby et al. (2015) discusses the positive impact that hospital staff could have if they truly understood where (Indigenous) patients came from. Family and community members may also provide a key role in providing care for someone at the end of life. A study conducted in Ontario outlined aboriginal women as the primary caregivers of aboriginal elderly in geographically isolated areas. The value of passing on tradition and caring for the elderly started when women were young. Caring was perceived as a traditional role for women as they are strong and fundamental to holding their communities together (Crosato et al. 2007). These beliefs surrounding care were mirrored in both Alaska and Australia. In Alaska, traditional beliefs outlined that taking care of the elderly was both an obligation and a source of pride and joy (DeCourtney et al. 2010b). Research in the Northern Territory of Australia found strong value associated with caring for your own family members, and within some communities, it is strongly believed that families should look after the elderly. In this region, kinship rules outline who the most appropriate person would be to look after someone at the end of their life (McGrath 2008). The role of family members and community members in care provision influences experiences of care both in the community and in healthcare settings.

Many people wish to spend the time at the end of their life in their homes and in their communities, but most patients in palliative care in Canada die in hospital (Canadian Hospice Palliative Care Association 2007). This trend is consistent across most populations; however, there are some additional considerations that are particularly relevant for both ethnic minorities, as well as Indigenous populations. It has been recommended that enabling family members to provide "hands-on" care to their older relatives in an institutional setting creates a collaborative environment for the patient (Bellamy and Gott 2013). There are obvious comforts to familiar surroundings, as well as familiar people at the end of life. However other influences could be included: preferences for speaking and hearing traditional language, passing on traditional knowledge to community members, strong connections to the land they lived once, and accessing culturally relevant care, including traditional medicine.

6 Barriers to Providing End-of-Life Care at Home

There are several barriers that emerge when patients and families choose to provide palliative care at home. Some of these factors are similar to all individuals and families regardless of culture or ethnicity. These include the unpredictable time length of care, isolation and caregiver fatigue, financial strain, and the potential comorbidity with other illnesses that may require interventions and care. However, the largest barrier to dying at home for all Canadians is the inadequacy of home care and other forms of support for families caring for a dying person. Individuals and families that wish to have a home death need to be aware that the demands may be greater than their abilities and resources and they might be unable to satisfy a loved one's wish to die at home (Arnup 2013).

The physical environment of some institutional care settings can be a barrier to culturally appropriate palliative and end-of-life care. In one particular study, this was seen as an unwelcoming environment for some cultural groups, having historically served the needs of those from primarily white, Christian middle-class backgrounds (Bellamy and Gott 2013). For Indigenous Canadians, the choice to die at home becomes even more challenging and can be attributed to the complex historical, social, and political dynamics

that have hindered Indigenous people's agency and control. For many Indigenous Canadians and other ethnic minorities, this means relocating to hospitals and care facilities far from home and away from their families (Bellamy and Gott 2013). Furthermore, family members may lack the financial resources needed to relocate with their loved one (Castleden et al. 2009). A lack of quality housing necessary to provide home care services and sustain the dying at home process is also a barrier for many Indigenous Canadians. Intergenerational trauma, systemic racism, and low socioeconomic status may mean that many families do not meet the necessary criteria for keeping a loved one in the home (Arnup 2013).

7 Cultural Safety in Healthcare

Cultural safety was developed during the 1980s in New Zealand as a concept in nursing, specifically as a result of observed inequities in healthcare services being offered to Māori, the Indigenous peoples of New Zealand. At that time the nursing profession, and most of the healthcare field, was focused on "transcultural" care or, as was the case in Canada, the notion of offering services in a multicultural context. Transcultural healthcare or offering healthcare in multicultural context considers all cultures as having an equal claim on government services and societal attention and downplays differences and historical context (Brascoupe and Waters 2009; Kirmayer 2012). This model of healthcare invalidates the unique experiences of Indigenous people because it assumes that health inequalities can, and should, be overcome by merely acknowledging cultural differences. It does not, however, acknowledge the power dynamics present. Healthcare staff should be cognizant of widespread variations of culture to be able to facilitate end-of-life care; it is a major challenge to care delivery when a heterogeneous approach is taken (Bellamy and Gott 2013). In Canada, cultural safety has been included in many health discourses, proving its applicability to a multicultural policy context. However, while cultural safety has been applied across ethnic and culturally diverse populations, the main focus in Canada has been on cultural safety in relation to Indigenous peoples (Brascoupe and Waters 2009).

In contrast, cultural safety requires the explicit and detailed recognition of the cultural identity of healthcare practitioners and patients. Cultural safety acknowledges the power imbalance present in healthcare and demands the transfer of this power to Indigenous people so that they might determine the quality and type of care services available. It recognizes that the current circumstances of Indigenous people are the result of contact and colonial history and that aggressive assimilation policies, the legacy of residential schools, and cultural genocide have resulted in power structures that continue to limit Indigenous peoples' agency in their own healthcare. Canadian healthcare practitioners have implemented it in conjunction with community-based healthcare and offering traditional healing methodologies in communities to increase positive health outcomes and mitigate risk (Brascoupe and Waters 2009; Kirmayer 2012).

A respectful, responsible, reciprocal, and relevant safe healthcare model must focus on a strategic and practical plan to change how healthcare is delivered to Indigenous people. The focus on the word safety is purposeful, and unlike previously utilized models of healthcare such as transcultural, cross-cultural, cultural sensitivity, or cultural competency, it involves the notion of safety as a critical part of delivering culturally based care and the harm that may occur in its absence (Brascoupe and Waters 2009; Kirmayer 2012). For example, cultural competency and cultural sensitivity ensure that service providers acknowledge cultural differences but still retain all of the power. Cultural safety realigns the power structure so that trust and positive relationships play a central role in the quality of care administered. It aims for equality and shared responsibility and allows patients to determine their needs rather than enforce the previously acknowledged western medical professional-client relationships with unilateral, practitioner-based decision-making (Brascoupe and Waters 2009; Kirmayer 2012).

In order to create culturally safe healthcare models, healthcare professionals must identify their own values, beliefs, and assumptions and then engage in a reflective practice that encourages honesty, active listening, and the sharing of power and knowledge. Education in healthcare must focus on training about Indigenous peoples and the social determinants of health in order to implement best practices for ensuring culturally safe healthcare practice. These best practices include understanding colonization and post-colonial forces and their impacts; principles of reciprocity, respect, inclusivity, community, and self-determination; culturally safe communication and language; and acknowledging Indigenous knowledge and practices in terms of health/healing/wellness (Brascoupe and Waters 2009; McGrath 2010).

8 Creating a Culturally Safe Palliative Care Model

Ethnocultural meaning of illness, suffering, and dying define the relationship foundations that patients and healthcare providers draw upon during interactions. Recent research demonstrates that ethnocultural factors influence the provision and receipt of palliative care more than age, education, gender, or socioeconomic status. Therefore, when they are overlooked or not acknowledged, inferior or unsafe care occurs (Busolo and Woodgate 2015). Given the importance of culture on an individual's well-being, healthcare professionals have recognized the need for a culturally safe palliative care model when working with Indigenous patients and their families. Though still in its infancy, a fluid, living model has emerged that can be adapted to meet the unique needs of the individual as well as the community (McGrath 2010). It rejects the notion of pan-Indigeneity, acknowledging that not all people will require the same end-of-life care and support in the same ways simply because they are Indigenous and that individuals are complex with varying healthcare needs (Kelly and Minty 2007).

This model is based on the principles of equity, autonomy, trust, nonjudgment, continuity of care, an emphasis on living rather than dying, and cultural respect. A more Indigenous holistic model differs from western medical palliative care models in that it places the individual and their family or kinship network at the center of the model rather than just the individual patient (McGrath 2010). In this way, it recognizes the importance of family and community in the healthcare and lives of individuals. Specifically, culturally safe palliative care models center on notions of choice, empowerment, and community participation. There is a deep respect for family and community relationships and effective communication. Palliative care models that are culturally safe must ensure respect for Indigenous languages, build community practices, attempt to offer on-site services, educate healthcare providers, understand and support cultural issues, develop culturally appropriate facilities, offer transportation services, deal with relocation issues, provide respite, and respect the importance of Indigenous grief practices (Kelly and Minty 2007; McGrath 2010).

One example of creating a culturally safe model that pertains to palliative care is the *Aboriginal Home Care Project*. The Regina Qu'Appelle Health Region (RQHR) operating in Saskatchewan identified a gap in home care service delivery and First Nations and Métis people living in the region. People were not accessing home care supports prompting RQHR to partner with the Eagle Moon Health Office, a local, Indigenous-based health services agency, initiating an *Aboriginal Home Care Project*. Following a community-based, culturally safe model of practice, the partnership assembled a working group with representation from First Nations, Métis, government, and home care to meet with community members and identify key issues. The barriers identified by this working group included a lack of case management and restrictive policies preventing home care access for Indigenous patients. This discovery allowed RQHR to adapt home care services to make them more culturally safe by offering additional services not utilized or valued in western practices (i.e., elder consultations, traditional healing, ceremony, etc.) and changing how practitioners work and communication with patients.

Specifically, RQHR Home Care created new staff positions and incorporated cultural practices into management, as all Indigenous patients using home care services now have more comprehensive case management and are linked to an Indigenous liaison worker (Health Council of Canada 2012).

9 Regulatory Bodies and Recommendations: Creating Best Practices in Culturally Safe Palliative Care

Kelly et al. (2009) sought the advice of palliative care patients and their families, and they found the recommendations ranged from intensive training of all staff that would interact with patients and their families to larger rooms for extended family and friends to visit with patients and to simply providing tea and cookies to visitors. Above all other recommendations, however, was communicating directly and clearly. Incorporating the former recommendations and excluding the latter would be an example of a homogenous approach to cultural safety: prescribing the same treatment to all perceived members of an ethnic group minimizes the importance of their individual experiences, traditions, and beliefs. There have been important elements of the intentions behind cultural safety that have been lost in the translation to enacting it in a broad system. Focusing training and policy on clear and direct communication (if this itself is culturally appropriate) puts the power in the hands of patients and their support networks to feel safe in communicating their wishes and needs.

Case Study: Communication as a Central Goal of Care

A 75-year-old woman from a rural First Nation community was transferred to a tertiary care center for heart valve replacement. She had experienced significant functional decline due to shortness of breath on exertion and associated weakness since she was unable to remain active because of her shortness of breath. By the time of admission to the rural hospital, she was bedbound, but her heart condition was stabilized enough for transfer to a tertiary care center so she could be assessed for a possible heart valve replacement. Her condition continued to deteriorate during the course of the work-up, and the heart valve replacement surgery was considered to be too high risk. In the intensive care setting, she required intravenous medications to support her blood pressure, but she became delirious and her level of consciousness continued to deteriorate. At this time, her treatment orders included full cardiopulmonary resuscitation in the event that her heart or breathing stopped. This included chest compressions, electric shocks to restart the heart, and ventilator support through a breathing tube. She would be unlikely to survive this intervention, and the chances of her surviving to return to her community were extremely poor. The patient was unable to participate in any discussions regarding goals of care, and there were no advance directives to limit the level of treatment being provided.

As the geriatrician consulted, I initiated discussions with her family (her husband who had traveled with her and her adult children who lived locally) to establish goals of care and the approach to care that would best support their goals. Her husband and adult children understood that she had been flown to the tertiary care hospital to have her heart problem "fixed"; in essence, the possibility of a miracle had been offered, and now the medical team realized that a palliative approach to end-of-life care was needed. In this situation, the patient's husband becomes the substitute decision-maker, but he spoke The (native) Language and had a limited understanding of the English language. Although the children spoke some of The Language and could interpret for their father, they felt that incorporating some of the "old" words of The Language would be important for the discussion of goals of care and levels of treatment. Thus, an interpreter was arranged. Through this discussion, the patient's husband and children came to understand that cardiopulmonary resuscitation would most likely be futile and would prevent her from dying in peace. They also understood that some of her current medications kept her blood pressure within a range that would keep her alive for a

while, but they make no difference to her mental status or to her inevitable death. The level of treatment changed to no cardiopulmonary resuscitation but to continue full medical treatment including the medications to stabilize her blood pressure. While they recognized that their mother was nearing the end of her end-of-life care, they wanted to have time for the rest of the family to gather at her bedside and hoped that by continuing the blood pressure medication, there would be time for this to happen. This gathering was not a simple matter of having family quickly drive to the hospital – it involved applications for and approval of travel grants and other arrangements that would allow for the rest of the family to be with her. The family was also referred to the Medicine Lodge for any ceremony that they wanted, including preparations for a cedar bath for their mother. As each of the member of the family arrived, clinical staff were available to review the patient's condition and answer any questions.

Once the family had gathered without restrictions on the number of visitors that could be in the room, the intravenous treatments were discontinued and the patient crossed to the spirit world a few hours later. The family remained with her through this journey and was supported in the room with her for many hours after her passing. Arrangements were then made to have her body transported back to her home community for the wake that followed.

Reflecting on the lessons learned from discussions with Indigenous people regarding palliative care in their communities, I can understand that the healthcare system often serves Indigenous people poorly – particularly at the end of life. This can be related to many factors, such as a lack of cross-cultural awareness, poor cross-cultural communication, and a lack of flexibility within the healthcare system. Issues of racism, discrimination, and bias manifest as culturally unsafe practices and result in delays in Indigenous people seeking healthcare and in the failure of the health system to recognize and effectively and respectfully integrate the essential role of traditional healing and need for spirituality during their journey to the spirit world (Duggleby et al. 2015).

In this case, it was important to communicate with the patient's husband (through an interpreter) in a way that all of the family members and the providers could understand – especially her substitute decision-maker – her husband, who in this case understood very little English. Goals of care decisions are as important to the family as they are to the patient and help them with the processes of grieving and healing from the loss of a loved one. Having clarified that the goal of care was to support a good death, the next task was to determine how the patient could be medically supported until the rest of her children arrived and her whole family could gather at her bedside. It was important to ask about cultural and religious traditions that were not only important for the patient but also her family. Cultural traditions to provide care and comfort to all through the transition and honoring the need of her family to be with her in the moments and hours after her passing were supported.

Respectful, compassionate, and culturally appropriate care may be more time-consuming. Healthcare systems may be reluctant to take the extra time required or to be flexible on rules that more typically govern practices, such as limiting the number of visitors or moving the body quickly after death. Yet, our commitment to "Patients First" and to compassionate care that appropriately meets the needs of individual patients demands that we take the time and commit to our own learning with respect to the provision of culturally sensitive care.

10 Conclusion

While many attempts have been made to remedy the existing issues of discrimination, racism, bias, and the ignorance of the complexities of intercultural healthcare provision, the absence of a guiding policy or overarching framework tells us much about the current healthcare system in Canada. Though rumblings of culturally safe models of care, especially near the end of life, continue to grow throughout the country, they are often overpowered by stories of mistreatment, discrimination, and colonial behaviors in the

healthcare system, whether in emergent care or through long-term hospice supports. Attempting to solve these issues through cultural competency, transcultural awareness, and other pan-Indigenous and pan-immigrant models falls flat in the face of the diversity of which Canada tries so hard to be inclusive. The disparity between ethnic groups and Indigenous peoples, and non-Indigenous Canadians, is the symptom of a deeper malady, one which stems from a common approach to healthcare that punishes those who do not conform to the majority. Palliative care endeavors to provide truly person-centered care but may still fall short in many instances. The message, then, is loud and clear: there is still more work to be done globally for our Indigenous communities and ethnic minorities that represent each distinct group in a culturally safe way.

Appendix

For further information regarding conversation on palliative care with Indigenous people, please see the *Completing the Circle* video series at https://www.youtube.com/user/EndofLifeCareProject.

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Part VII

Palliative Care Emergencies

Hypercalcemia of Malignancy

72

Kathryn A. Tham and Davinia S. E. Seah

Contents

Abstract

This chapter discusses hypercalcemia of malignancy which is the commonest biochemical complication of cancer and recognized as a medical emergency. Hypercalcemia presents with a wide range of clinical symptoms which in some cases can be severe and life-threatening. It is essential for clinicians to consider hypercalcemia as a differential diagnosis in patients with nonspecific symptoms, as hypercalcemia is potentially reversible. The following sections will review normal calcium homeostasis and discuss the mechanisms of how cancer disrupts this tightly regulated

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_70

system. It is recognized that hypercalcemia is normally associated with advanced disease and, unless antineoplastic treatments are available, is a poor prognostic sign. It is therefore important to consider the individual clinical situation before deciding on an appropriate management plan. Hypercalcemia results in hypovolemia, and the initial management should consist of rehydration. Following this, specific calcium-lowering treatment should be considered. Following rehydration, bisphosphonates have been the treatment of choice for the last 20 years and are effective in the initial treatment for the majority of cases. Unfortunately, it is common for hypercalcemia to relapse, and the best approach to treatment of recurrent and refractory hypercalcemia is not clear. Denosumab is an emerging option, and the initial evidence appears favorable. Further research regarding the use of denosumab for hypercalcemia of malignancy is warranted.

1 Introduction

Malignant hypercalcemia is a common metabolic complication of cancer seen in oncology and palliative care. It is important for clinicians to remain vigilant as its presentation can often be insidious and mimic general disease progression. It may cause significant symptoms that can often be reversed, resulting in major improvements in quality of life. The occurrence of malignant hypercalcemia is a poor prognostic marker with or without treatment. Despite a number of anti-hypercalcemic agents available, bisphosphonates are currently considered the mainstay of treatment.

2 Epidemiology

Hypercalcemia is a common presentation seen both in primary care and in the emergency department. Ninety percent of cases are due to either primary hyperparathyroidism or malignancy (Lafferty 1991). Hypercalcemia due to malignancy typically evolves rapidly and often leads to significant symptoms and therefore acute clinical presentation. Patients admitted to the hospital with hypercalcemia have an almost 50% chance of having a malignancy, compared with those that present to primary care where hyperparathyroidism is the most likely cause (Lindner et al. 2013).

Malignant hypercalcemia is reported to develop in up to 40% of all cancer patients, although incidence varies quite widely depending on the literature (Burt and Brennan 1980; Vassilopoulou-Sellin et al. 1993; Alsirafy et al. 2009). This may be in part due to the variation in defining hypercalcemia. It is also dependent upon which patient group is included, as it is more common in advanced disease and in certain malignancies. The most common solid malignancies associated with malignant hypercalcemia are breast, renal, lung, and squamous cell cancers where the incidence may be close to 50% (Alsirafy et al. 2009). Multiple myeloma, leukemia, and non-Hodgkin's lymphoma are the most common hematological malignancies associated with malignant hypercalcemia (Burt and Brennan 1980; Vassilopoulou-Sellin et al. 1993).

The presence of malignant hypercalcemia is recognized as a marker of advanced disease and is a poor prognostic sign (Stewart 2005; Rosner and Dalkin 2012). Up to 50% of patients with treated hypercalcemia will have died within 1 month and 75% within 3 months (Ralston et al. 1990; Stewart 2005). Treating hypercalcemia alone has a limited impact on the overall prognosis as it does not modify the underlying advanced malignancy. Antineoplastic treatments together with anti-hypercalcemia management offer the best chance of a longer survival time (Ralston et al. 1990; Kristensen et al. 1998).

3 Pathophysiology

3.1 Normal Homeostasis of Calcium

Calcium is an essential element that is important in maintaining normal cellular function and signalling and maintaining physiological processes,

e.g., neuromuscular signalling, hormonal secretion, and blood coagulation (Kasper et al. 2015). As a result, calcium homeostasis to maintain the extracellular calcium ions (ca^{2+}) is tightly regulated. Broadly, calcium levels are controlled by four organs: small intestine, bones, kidneys, and the parathyroid glands. About 10–20% of dietary calcium is absorbed by the small intestine, and the rest is excreted in feces.

Over 90% of the calcium in the body is stored as hydroxyapatite in the skeleton, acting as a reservoir. The remaining 10% is present in the plasma via two forms: the physiologically active calcium ions (ca^{2+}) and calcium bound to carriers, particularly albumin.

Several hormonal systems are involved in controlling the level of calcium ions in the plasma. The main systems affect the bone remodeling process to increase or decrease the release of calcium from skeletal stores, as well as affect the kidneys to increase or decrease renal calcium excretion. Fig. 1 shows the basic mechanism.

The most significant system is a negative feedback mechanism regulated by two main hormones, parathyroid hormone (PTH) and the active vitamin D metabolite 1,25-dihydroxyvitamin D [Calcitriol] (Kasper et al. 2015).

Calcium sensors on the parathyroid glands activate the release of parathyroid hormone (PTH) when the levels of extracellular calcium ion are low. PTH acts on the kidneys and bones to increase the extracellular calcium levels. PTH affects the kidneys in two ways to increase calcium levels: the reduction of calcium excretion and the production of Calcitriol. The renal production of Calcitriol assists the PTH in mobilizing calcium release from bones and also stimulates the small intestine to increase calcium absorption.

The release of PTH triggers calcium release from the bones by altering bone remodeling, a process that is complex and involves bone-forming cells (osteoblasts) and bone-resorbing cells (osteoclasts). It is the balance between osteoblasts and osteoclasts that controls the rate of bone turnover and calcium release. An important element of this process involves the receptor activator of nuclear factor kappa-B (RANK). This receptor is carried on the osteoclast precursor cells and when stimulated by a ligand (RANKL), which is expressed on the osteoblast, results in the formation of mature osteoclasts leading to increased bone resorption and calcium release (Kasper et al. 2015).

The final important hormone of note is calcitonin, which is produced by thyroid C cells in response to increased calcium levels. The effect of calcitonin reduces bone turnover and calcium reabsorption in the kidneys, which in turn reduce serum calcium.

Understanding this complex relationship between calcium levels, PTH, active vitamin D, and bone cells have allowed effective treatments to be developed that modify this system.

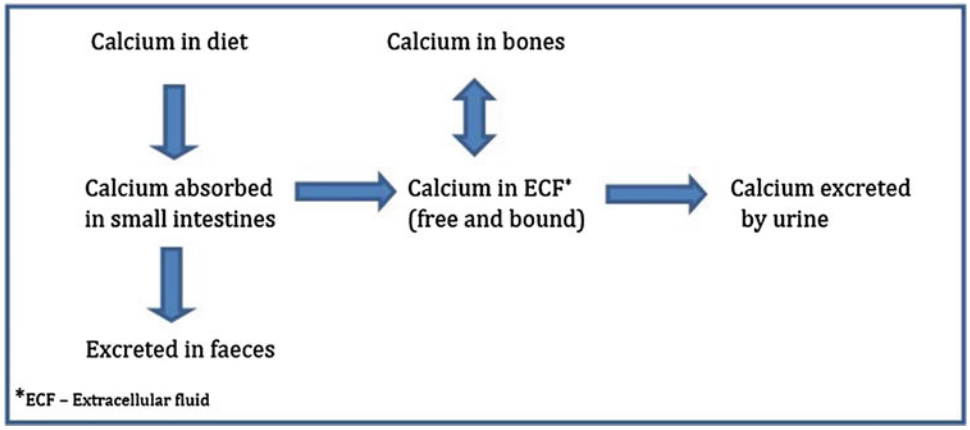

Fig. 1 Physiological schema of calcium

3.2 Mechanism of Malignant Hypercalcemia

The role of bone remodeling and PTH in calcium homeostasis is important in the understanding of the pathophysiology of hypercalcemia in malignancy. Normal calcium homeostasis is disrupted in advanced cancer through two main mechanisms described below.

3.2.1 Humoral Hypercalcemia of Malignancy

The humoral mechanism is responsible for approximately 80% of hypercalcemia related to malignancy, via an increased release of parathyroid hormone-related protein (PTHrP) from the tumor. PTHrP is structurally similar to PTH and initiates calcium release from the bones through increased osteoclastic activity, as well as reduced excretion from the kidneys, causing increased extracellular calcium levels. Unlike PTH, it does not influence the production of Calcitriol and hence has minimal influence on small bowel absorption of calcium (Horwitz et al. 2005). PTHrP acts on osteoblasts, which in turn increase the production of RANKL, and activates osteoclasts and bone resorption. The humoral mechanism does not depend upon the presence or absence of bone metastases and is most commonly seen in breast cancer, squamous cell cancers (e.g., head and neck, esophagus, cervix, or lung), and endometrial and renal cell cancers (Stewart 2005).

3.2.2 Local Osteolytic Hypercalcemia

Patients who have high volume metastatic, osteolytic bone involvement may develop hypercalcemia, via the production of local cytokines from increased osteoclastic activity (Francini et al. 1993). Osteoblastic metastatic disease, such as those typically seen in prostate cancer, is not associated with increased risk of hypercalcemia of malignancy. PTHrP is also a likely mediator of this mechanism, acting on the microenvironment within the bone; hence systemic PTHrP levels may not be raised (Rosner and Dalkin 2012). Metastatic breast and lung cancers, as well as myeloma, commonly involve an osteolytic mechanism which is causing hypercalcemia.

Other rare causes of malignant hypercalcemia include those mediated by increased active vitamin D production, seen most commonly in lymphoma (Seymour and Gagel 1993). In addition, parathyroid carcinoma can cause ectopic PTH production leading to hypercalcemia (VanHouten et al. 2006). A combination of mechanisms may occur simultaneously. In one study of 443 patients with cancer and hypercalcemia, 53% of patients had osteolytic hypercalcemia, 35% had humoral hypercalcemia, and 12% had both osteolytic and humoral factors (Soyfoo et al. 2013).

4 Clinical Presentation

Clinical presentation and development of symptoms in hypercalcemia are related to the rate of increase in serum calcium, rather than simply the absolute value. Hypercalcemia may be asymptomatic in severe levels if it has evolved slowly (Stewart 2005). This is particularly true in younger patients that have no pre-existing comorbidities. Hypercalcemia may therefore be only diagnosed due to an incidental finding on a blood test. It can however also present with very severe symptoms requiring urgent treatment.

The well-known mnemonic often associated with hypercalcemia of "painful **bones**, renal **stones**, abdominal **groans**, and psychic **moans**" is typically associated with the presentation of primary hyperparathyroidism. Hypercalcemia due to primary hyperparathyroidism often develops over a longer period, allowing for a patient to remain relatively well, but resulting in the development of complications such as renal stones and peptic ulceration.

In hypercalcemia of malignancy, the rapid rise in calcium level results in a patient becoming more constitutionally unwell. A combination of neurological and gastrointestinal symptoms is most common, especially confusion, somnolence, nausea, and constipation. Patients are often significantly dehydrated due to many factors: reduced oral intake, vomiting, and polyuria. In the most

Table 1 Symptoms and signs of hypercalcemia

	Mild	Severe
Neurological	Fatigue Mental dullness Muscle weakness Headache	Confusion Delirium Reduced conscious state Seizures
Gastrointestinal	Anorexia Constipation	Nausea Vomiting Abdominal pain
Renal	Thirst Polyuria (often not present)	
Cardiac	Shortened QT interval on ECG	Arrhythmias Bradycardia Hypertension Bundle branch/ AV blocks Cardiac arrest (in most severe)

severe cases, cardiac complications and seizures may occur. Table 1 details the mild and severe symptoms and signs of hypercalcemia.

5 Diagnosis and Investigation

As the symptoms can be varied and nonspecific, often the most important element of diagnosis is in ensuring that it is part of the differential diagnosis. A patient's corrected calcium levels should be checked if there is a clinical suspicion that it may be raised. Serum calcium is present in two forms: calcium that is bound to protein, predominantly albumin, and ionized calcium. The physiologically active form is the ionized calcium, and this is maintained despite fluctuations in albumin levels. Laboratories routinely test total serum calcium levels. In healthy individuals, 45% of total calcium is in the active ionized form and 55% bound to carriers. Reference ranges for normal total calcium levels are made assuming an albumin level of 40 g/L (4 g/dL). In patients where albumin levels are low, this ratio is disrupted, and therefore a total serum calcium level will not reflect the active ionized calcium level. Some laboratories can directly measure ionized calcium; however in most cases, it is calculated from the total serum calcium level using the following formula to give a corrected calcium level:

Table 2 Severity of hypercalcemia based on serum ionised levels

Mild	<3 mmol/L or <12 mg/dL
Moderate	3.0–3.5 mmol/L or 12–14 mg/dL
Severe	>3.5 mmol/L or >14 mg/dL

$$\text{Corrected calcium [mmol/L]} = \text{Measured total calcium [mmol/L]} + 0.02(40 - \text{albumin [g/L]})$$

As patients with advanced malignancy commonly have low albumin levels, it is important to ensure that the *corrected calcium level* is known before a diagnosis of malignant hypercalcemia is made or excluded.

There can be variation in the diagnostic level of hypercalcemia, depending on local guidelines, but it is often classified as mild, moderate, or severe based on the serum ionized calcium level below (Stewart 2005). See Table 2.

In patients who have advanced cancer, it may not be necessary or appropriate to investigate the mechanism of hypercalcemia once it has been diagnosed, particularly as the treatment in most situations is the same regardless of cause. There are occasional situations where there is uncertainty or there is a suspicion of simultaneous mechanisms occurring. Primary hyperparathyroidism is a relatively common diagnosis across the general population with around 20 cases per 100,000 (Ayuk et al. n.d.). Therefore, primary hyperparathyroidism may occur concurrently with hypercalcemia of malignancy, and there is evidence that it may be more common in certain tumor types than the general population (Fierabracci et al. 2001). Primary hyperparathyroidism can be successfully treated with surgical resection of the parathyroid glands. Therefore, in a patient who has a low disease burden and a favorable prognosis, it may be of benefit to confirm the underlying cause of the hypercalcemia. Fig. 2 represents an approach to the diagnosis. In summary, serum PTH level will be raised in primary

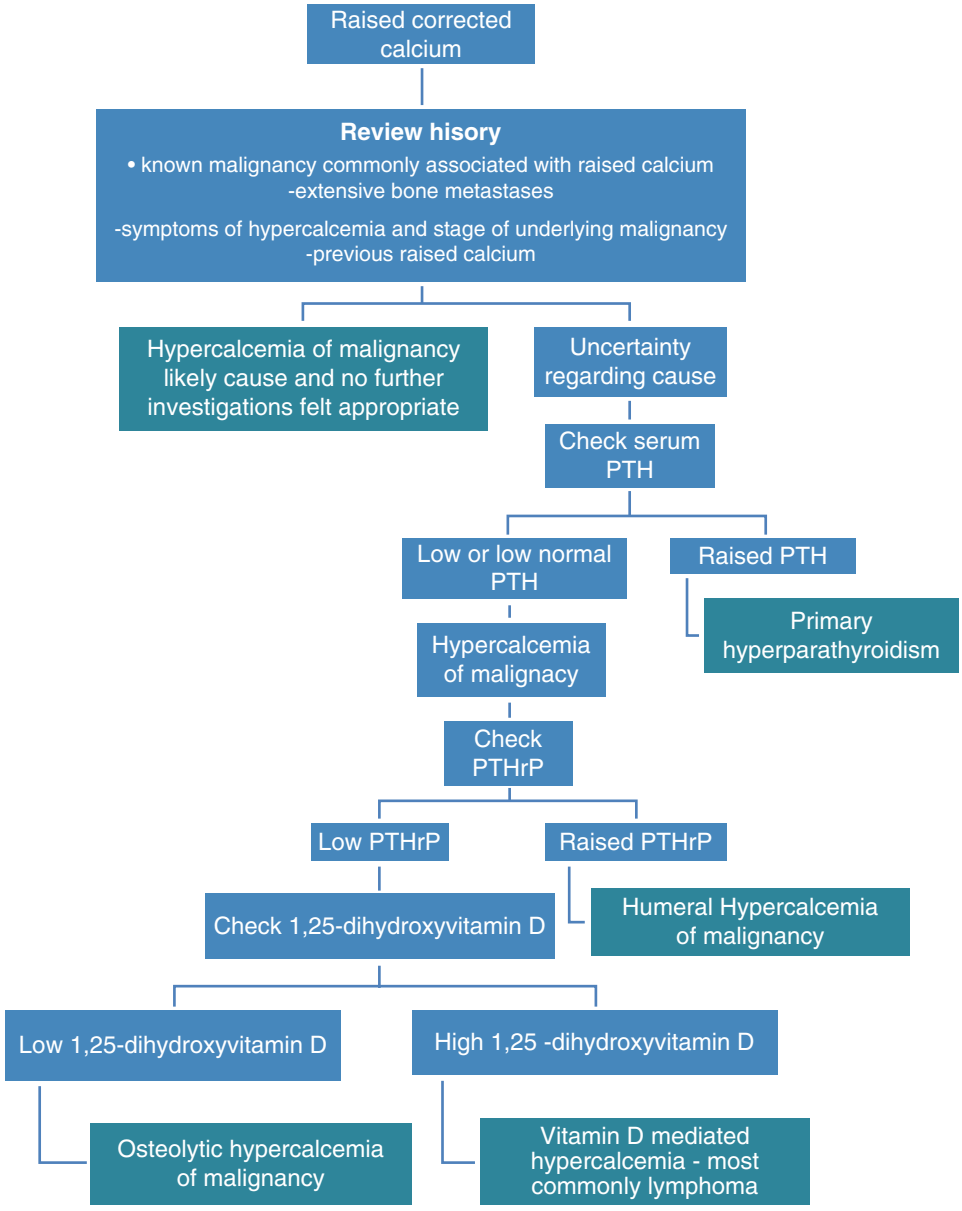

Fig. 2 Diagnostic approach to investigating hypercalcaemia

hyperparathyroidism and suppressed in hypercalcemia of malignancy. It is also possible to check PTHrP levels which can help confirm the underlying mechanism involved in those who have hypercalcemia of malignancy.

While PTH or PTHrP is not routinely requested for a patient with advanced cancer, one study suggests that the level of PTHrP may inform prognostication and predict likely response to the common treatment of bisphosphonates (Wimalawansa 1994b). In this study it was suggested that higher PTHrP levels would result in a poorer response to bisphosphonates treatment possibly due to the nonskeletal effects of PTHrP, such as the renal response, which bisphosphonates will not modify.

6 Treatment

6.1 General Approach

Multiple factors should be considered before deciding on a treatment plan. These include goals of care, severity of hypercalcemia, symptomatology, previous episodes of hypercalcemia (including response to treatment), and finally patient wishes.

Firstly, it is important to establish whether treatment is appropriate. If a patient is moribund due to their advanced malignancy, then treatment is likely to be futile. The difficulty can be distinguishing between disease progression and reversible symptoms secondary to hypercalcemia. Treatment may also not be appropriate in patients who have recently been treated for hypercalcemia and have either rapidly relapsed or been refractory to treatment. In these uncertain situations, a frank discussion about the limitations about efficacious treatments with a patient and their family is required.

When the treatment of the hypercalcemia is considered appropriate, the severity of the hypercalcemia and the symptom burden should be considered next. In asymptomatic patients with mildly raised hypercalcemia, conservative measures can be taken. These measures may include ensuring sufficient parenteral hydration, as well as stopping any contributory medications, e.g., calcium, vitamin D supplements, and thiazide diuretics.

In symptomatic patients with calcium levels greater than 3.0 mmol/L (12 mg/dL), further management is indicated. This initially involves parenteral rehydration, followed by specific antihypercalcemic treatments. The most commonly used agents are the bisphosphates and more recently denosumab. Calcitonin is frequently given, although it has limited benefits due to its short-acting effects. There are a number of other medications that are mentioned in the literature, including loop diuretics, gallium nitrate, and octreotide (Stewart 2005; Mirrakhimov 2015; Rosner and Dalkin 2012).

If a more active management approach is warranted, then antineoplastic treatments should also be considered to maintain normocalcemia after hypercalcemia is treated. Antineoplastic treatments such as chemotherapy provide optimal long-term treatment of hypercalcemia and offer the best prognosis (Ralston et al. 1990; Kristensen et al. 1998).

Regardless of the decisions pertaining to the goals of care, the occurrence of hypercalcemia of malignancy is a marker of poor prognosis and a harbinger of death within a few months in the majority of patients. Clear and sensitive information regarding the patient's advanced illness should be communicated to the patient and their family. It is important to explain to them that the correcting of the calcium levels is a temporizing measure, with the management and control of their underlying malignancy offering the best chance in prolonging survival. Patients and their family are also often fearful of the symptoms caused by hypercalcemia. Irrespective of the decision to treat the hypercalcemia, reassurance should be provided to the patient and the family that the treating team will endeavor to ensure the patient's comfort by managing the patient's symptoms utilizing other medications.

6.2 Intravenous Hydration and Role of Loop Diuretics

Hypercalcemia causes significant hypovolemia through a combination of mechanisms. Firstly, raised calcium results in an acquired nephrogenic diabetes insipidus cause polyuria. Secondly, gastrointestinal symptoms may result in nausea, reduced fluid intake, and vomiting. Finally, the hypovolemia itself results in a reduced glomerular filtration rate and therefore reduces the kidney's ability to excrete calcium. In all cases of symptomatic hypercalcemia, intravenous fluid hydration should be given to correct the volume deficit and to treat the hypercalcemia. The volume and rate of fluid replacement administered should be considered according to the clinical picture, severity of hypercalcemia, renal dysfunction, and cardiac insufficiency. In severe hypercalcemia, the fluid deficit can be profound, and aggressive fluid replacement is required. Current evidence recommends the use of

intravenous normal saline at a rate of 200–300 mls/h (Mirrakhimov 2015). The total volume required may be as much as 4–6 l; however caution must be given to avoid fluid overload, particularly in the elderly. Historically, loop diuretics have been used to treat hypercalcemia to promote renal calcium loss. With the availability of more effective treatments, loop diuretics are now only indicated in situations of fluid overload following rehydration (Stewart 2005; Mirrakhimov 2015).

All current evidence recommends the intravenous route for rehydration. In the palliative care population, intravenous access can often be challenging, and the administration of fluids via the subcutaneous route is commonly utilized. The evidence regarding the benefits of administration of subcutaneous fluids is limited, and there is no research available at present assessing the use of subcutaneous fluids in the treatment of hypercalcemia. As most calcium-lowering treatments are given intravenously, using the same route for rehydration would be a sensible option, particularly as aggressive fluid replacement is often required. In situations where intravenous access is challenging, 2 l of normal saline can be administered subcutaneously in 24 h (Barton et al. 2004).

6.3 Specific Calcium-Lowering Treatments

6.3.1 Bisphosphonates

Bisphosphonates have been the mainstay in the treatment of malignant hypercalcemia for over 20 years (Saunders et al. 2004). As pyrophosphate analogs, bisphosphonates inhibit intracellular osteoclast activity, as well as bind to hydroxyapatite and stabilize the bone matrix (Rogers et al. 2000). Following administration, about 50% of the drug is selectively retained in the skeleton, and the remainder is eliminated in the urine without being metabolized. Skeletal uptake and retention are dependent on bisphosphonate potency for bone matrix, as well as patient factors including renal function, rate of bone turnover, and binding site availability. This adhesion to the bone matrix results in a prolonged half-life and mechanism of action. It is this enduring effect that has made bisphosphonates so important in the management of hypercalcemia of malignancy.

There are two groups of bisphosphonates: first-generation, non-nitrogen-containing bisphosphonates which include etidronate and clodronate; and the second-generation, nitrogen-containing bisphosphonates which include pamidronate, ibandronate, and, most recently, zoledronate. The second-generation bisphosphonates are considered more potent. There are both oral and parenteral bisphosphonates available. In the treatment of hypercalcemia, they are always given parenterally to ensure absorption and to avoid gastrointestinal side effects often seen with oral preparations. While most parenteral bisphosphonates can only be given intravenously, clodronate can be given intravenously or subcutaneously (Roemer-Bécuwe et al. 2003). The subcutaneous route may be useful in cases where intravenous access is difficult or when the patient is seen in the community setting.

Although extremely well-tolerated, bisphosphonates do have potential adverse effects. The most significant adverse effect is the risk of renal injury with possible nephrotic syndrome. To prevent renal toxicity, intravenous rehydration prior to the administration of bisphosphonates is always recommended. Where renal impairment also exists, a dose reduction may be considered to reduce the risk of further renal damage. A rare, but significant, adverse effect of bisphosphonates is osteonecrosis of the jaw. This is typically associated with prolonged and repeated use of bisphosphates (greater than 4 months). In the acute management of hypercalcemia of malignancy, the risk of osteonecrosis of the jaw is low (Saad et al. 2012). It may be worthwhile assessing the dentition of the patient prior to administration; however there is no evidence to support this approach when bisphosphonates are being used in the treatment of hypercalcemia. Other reported adverse effects include drug-related induced fevers, hypophosphatemia, and hypocalcaemia (Major et al. 2001). The drug-related induced fever is part of an acute phase reaction that causes transient flu-like symptoms. The true incidence of hypocalcaemia associated with bisphosphonate use in

the treatment of hypercalcemia is unknown due to underreporting of cases. However, in clinical trials comparing zoledronate versus denosumab in the prevention of skeletal-related events in cancer patients, hypocalcaemia occurred in about 3.4–5.8% of patients treated with zoledronate (Body et al. 2015; Dranitsaris and Hatzimichael 2012). Although the frequency of bisphosphonate administration in the prevention of skeletal-related events is different compared to the treatment of hypercalcemia, clinicians should be vigilant of the possible complications of bisphosphonate-related symptomatic hypocalcaemia if using a bisphosphonate.

When selecting a bisphosphonate, the systematic review by Saunders et al. provides some limited guidance. The review showed that all bisphosphonates are effective when compared with placebo, with normal calcium being achieved in at least 70% of cases, regardless of which drug was used (Saunders et al. 2004). Table 3 details typical dose and administration regimes.

Pamidronate and zoledronate are the most commonly used bisphosphonates in the treatment of hypercalcemia. Although both drugs are effective in achieving normocalcemia, zoledronate tends to be favored for its ease in administration (15 min for zoledronate versus 2 h for pamidronate), potency, and efficacy (Major et al. 2001). In a pooled analysis of two randomized controlled trials involving 275 patients with hypercalcemia of malignancy, 87–88% of patients achieved normocalcemia after a single dose of zoledronate (4 mg or 8 mg) compared to 70% of patients who were treated with pamidronate. The mean duration of normocalcemia in patients who had received zoledronate was 32–43 days, compared to 18 days in patients who had received pamidronate (Major et al. 2001).

Although pamidronate and zoledronate have been shown to have a similar side effect profile, the 8 mg dose of zoledronate has shown an increased risk of causing renal injury compared to the 4 mg zoledronate dose and pamidronate (Major et al. 2001; Saunders et al. 2004). It is generally not recommended for patients with severe renal impairment (creatinine clearance <30 mL/min) to receive bisphosphonates. However, in some clinical situations where patients have limited effective options, the use of bisphosphonates may be indicated. Limited data suggests that ibandronate may be the safest option

Table 3 Bisphosphonates dosing and regimes

Bisphosphonate	Initial dose	Route/diluent/rate	Renal adjustment	
			CC[a]	Dose
Second generation				
Pamidronate	60–90 mg	IV, 375–500 m1 0.9% saline or 5% dextrose, over 90 min	30–90	No dose adjustment infusion rate of 4 h
			<30	Not recommended
Zoledronate	4 mg (consider 8 mg in refractory hypercalcemia)	IV, 100 m1 0.9% saline or 5% dextrose, over 15 min	>60	4 mg
			50–60	3.5 mg
			40–49	3.3 mg
			30–39	3 mg
			<30	Not recommended
Ibandronate	4 mg	IV, 500 m1 0.9% saline or 5% dextrose, over 2 h	No dose adjustment needed (Limited data suggest that this may be well tolerated in patients with renal impairment)	
First generation				
Clodronate	1500 mg	IV or SC, 50–250 m1 0.9% saline or 5% dextrose, over 2–3 h	Minimal data available	
Etidronate	7.5 mg/kg/day	IV, 250 ml of saline infused, over 2 h for 3 consecutive days	Minimal data available	

[a]*CC* Creatinine clearance mL/min

(Jackson 2005). Dose reduction, slowing the rate of the infusion, and the addition of increased hydration therapy can also be considered; however there is minimal literature to support this (Conte and Guarneri 2004; Kyle et al. 2007). Denosumab may potentially be an option in this scenario, and this will be discussed later.

Manufacturers suggest that the dose of pamidronate administered should depend on the severity of hypercalcemia. However, a systematic review from 2004 suggests that higher doses of bisphosphonates correlate with increased efficacy and therefore recommend use of the highest dose irrespective of the calcium level (Saunders et al. 2004). Given this review, pamidronate 90 mg or zoledronate 4 mg are appropriate first-line options in the treatment of malignant hypercalcemia.

Ibandronate and etidronate are less commonly used bisphosphonates. Ibandronate is a second-generation bisphosphonate and has been shown to be as effective as pamidronate. It appears to have a lower risk of renal injury; however there is limited data (Jackson 2005). Etidronate is a first-generation bisphosphonate and one of the first bisphosphonates to show efficacy in the treatment of hypercalcemia of malignancy. As it is administered via a 2-h intravenous infusion on 3 consecutive days, it has been superseded by newer more potent drugs that can be administered over a shorter time frame.

Regardless of which bisphosphonate is used, the reduction in calcium levels takes approximately 2–4 days to occur with the maximum effect between 4 and 7 days (Major et al. 2001). It is recommended that the serum-corrected calcium is rechecked 5–7 days following treatment with a bisphosphonate (Fleisch 1998). In most cases, intravenous rehydration given prior to bisphosphonate reduces the calcium level sufficiently while waiting for the bisphosphonates to act. In patients who have severe symptoms, needing immediate calcium reduction, calcitonin may be used. (See section below for further details.)

Up to 30% of cases of hypercalcemia are refractory to treatments with a bisphosphonate (Major et al. 2001; Saunders et al. 2004). There is limited evidence about which drug should be used in these cases. In the pooled analysis of the two randomized controlled trials by Major et al., patients who were refractory to zoledronate (4 or 8 mg) or pamidronate were retreated with 8 mg of zoledronate. Up to 55% of patients with refractory hypercalcemia responded to retreatment with zoledronate (Major et al. 2001). It is important to note that with time, hypercalcemia will usually become more difficult to treat and eventually may become resistant to bisphosphonate treatment. It is uncertain exactly why this occurs, but it is thought most likely related to the advancing underlying disease. In situations of refractory hypercalcemia, there is emerging evidence that the use of denosumab may be effective and is discussed further below. In patients with refractory hypercalcemia, zoledronate 8 mg may be trialled following initial treatment (Major et al. 2001).

Despite relapse being common in those who achieve normal calcium levels, there are no clear guidelines regarding how often serum calcium levels should be checked. However, given that the median time for relapse is between 2 and 4 weeks (Major et al. 2001; Wimalawansa 1994a), calcium levels could be checked 2–4 weeks posttreatment. A more conservative option would be to retest only if symptoms reoccur.

Finally, there is limited evidence to support the regular administration of bisphosphonates rather than waiting for relapse. One small study with 34 patients, investigating optimal frequency of pamidronate in the treatment of hypercalcemia, showed that a regular infusion every 2 weeks decreased the incidence of symptomatic hypercalcemia and prolonged survival compared to the regular infusion every 3 weeks (Wimalawansa 1994a). Until further evidence becomes available, the decisions regarding follow-up and the best drug to use in retreatment should be determined on an individual basis.

6.3.2 Denosumab

Denosumab is the latest treatment option in the management of hypercalcemia of malignancy. It is a human monoclonal antibody that specifically binds human RANKL. Denosumab inhibits osteoclast activity resulting in reduced bone

resorption. Originally developed as an alternative option in the prevention and treatment of osteoporosis, it was subsequently used in the management and prevention of skeletal complications in cancer.

Currently, there are no randomized controlled trials comparing denosumab and bisphosphonates as first-line therapy for the management of hypercalcemia of malignancy. There is one single-arm study carried out by Hu et al. involving 33 patients who had bisphosphonate refractory hypercalcemia. The patients in this study had to have a corrected serum calcium level of >3.1 mmol/L (12.5 mg/dL) despite intravenous bisphosphonate treatment within 7–30 days. In this study, 64% of patients had serum calcium levels below 3.0 mmol/L (11.5 mg/dL) by day 10 after receiving denosumab. An improvement in symptoms was observed in over 50% of patients. The treatment effects were durable with an estimated median duration for compete response being 34 days (Hu et al. 2014). In this study the dose used was 120 mg given subcutaneously, every 4 weeks, with additional loading doses of 120 mg on days 8 and 15 of the first month. A repeat dose of denosumab was given successfully to patients who had relapsed. About 80% of the patients responded to the repeat dose. Therefore, a repeat dose of denosumab treatment on day 8 and 15 after initial treatment could be considered if calcium levels have not previously responded.

A retrospective case series of seven patients treated with single doses of denosumab for the management of hypercalcemia was described. In this small study, six of the seven patients had received bisphosphonates prior to treatment with denosumab. The mean corrected calcium levels were 3.06 mmol/L (12.24 mg/dL) on the day of the denosumab administration, and the last mean corrected calcium while in the hospital was 2.48 mmol/L (9.92 mg/dL) (Dietzek et al. 2015).

With the exception of the study by Hu et al. and Dietzek et al., the vast majority of the research performed utilizing denosumab is in the context of the management or prevention of skeletal-related events, and these results have been extrapolated to the management of hypercalcemia. Although the administration and dose of the drug are similar in both clinical scenarios, and the patient population appears similar, one must exercise caution in presuming that the use of denosumab in both clinical situations are identical. Patients with hypercalcemia typically have advanced disease, a different calcium metabolism profile and a poor prognosis, and may be different from patients who only have metastases to bones.

However, because of the scarcity of studies with the primary purpose of determining the role of denosumab in the management of hypercalcemia, understanding the effects of denosumab in the management and prevention of skeletal-related events will inform clinicians about the issues to be aware of when using denosumab for management of hypercalcemia.

In studies comparing denosumab and zoledronate in the prevention of skeletal complications in advanced cancer, the denosumab arm had fewer episodes of hypercalcemia compared to the zoledronate arm. Furthermore, the time to hypercalcemia was also delayed with the use of denosumab compared to zoledronate (Martin et al. 2012; Stopeck et al. 2010; Diel et al. 2015; Henry et al. 2011).

In regard to its safety and adverse effects, denosumab was well-tolerated in the management of osteoporosis and the skeletal complications of cancer. The most serious risk is that of osteonecrosis of the jaw; however this is rare, and rates appear similar to that of bisphosphonates (Stopeck et al. 2010; Fizazi et al. 2011; Henry et al. 2011; Martin et al. 2012; Dranitsaris and Hatzimichael 2012). The most clinically relevant risk is hypocalcaemia, extrapolated from studies where denosumab has been used in management of malignant bone disease and not in hypercalcemia. Up to 12.8% of patients treated with denosumab for skeletal complications develop significant hypocalcaemia, compared with 1–5% of those treated with zoledronate (Henry et al. 2011; Fizazi et al. 2011; Body et al. 2015; Dranitsaris and Hatzimichael 2012). In one study in patients with skeletal-related events, the median time to first occurrence of hypocalcaemia was 3.8 months with denosumab and 6.5 months with zoledronate (Body et al. 2015). It is worth noting that the highest incidence of

hypocalcaemia was in the treatment of metastatic prostate cancer. As discussed, prostate cancer is associated with osteoblastic bone metastases, which in themselves may contribute to development of hypocalcaemia (Henry et al. 2011; Fizazi et al. 2011). In the context of the management of hypercalcemia, it is unclear what the clinical impact of denosumab-induced hypocalcaemia has. In a case series where denosumab was used for the management of hypercalcemia, one of seven patients developed symptomatic hypocalcaemia (Dietzek et al. 2015).

In a study by Body et al. (2015), the pooled results of three randomized controlled trial comparing the efficacy and safety of denosumab versus zoledronate in the prevention of skeletal-related events in metastatic bone disease showed that patients who took calcium and/or vitamin D supplements had a lower incidence of hypocalcaemia. This may suggest that adequate supplementation of both vitamin D and calcium reduced the risk of hypocalcaemia in patients treated with either denosumab or zoledronate. Patients with skeletal-related events have a different calcium profile compared with patients with hypercalcemia. There is no evidence for the routine monitoring of vitamin D levels and its replacement in the patients with hypercalcemia treated with denosumab. Indeed, the replacement of vitamin D has the potential to exacerbate hypercalcemia by mobilizing calcium release from bones and also stimulating the small intestine to increase calcium absorption.

In addition, the study found that patients who were at risk of developing hypocalcaemia include patients with prostate cancer or small cell lung cancer, reduced creatinine clearance (30 to <60 mL/min), and higher baseline values of urinary *N*-telopeptide of type 1 collagen and bone-specific alkaline phosphatase (Body et al. 2015). Given these findings, it would be prudent to monitor the calcium levels in patients who have these risk factors who are treated with denosumab regardless of reason.

Despite the limited information about the use of denosumab, there are some definite advantages identified. Denosumab is less likely to cause the acute phase reactions that are commonly seen with bisphosphonates (Henry et al. 2011; Fizazi et al. 2011; Stopeck et al. 2010; Dranitsaris and Hatzimichael 2012). It is also safer in renal impairment and not associated with renal injury (Henry et al. 2011; Stopeck et al. 2010; Martin et al. 2012; Dranitsaris and Hatzimichael 2012). In addition, it is administered via the subcutaneous route which may facilitate the use of denosumab in the community. Despite denosumab being more expensive compared to zoledronate, the ability to administer it at home subcutaneously may save on hospitalization costs.

6.3.3 Calcitonin

Calcitonin is a hormone produced by the parafollicular C cells of the thyroid gland. It inhibits the resorption of the bone by reducing both the number and activity of osteoclasts. Calcitonin also acts on the kidneys to reduce calcium reabsorption and inhibits intestinal calcium absorption. Administration of calcitonin occurs subcutaneously or intramuscularly every 12 h, with an initial dose of 4 international units/kg that can be increased up to 8 international units/kg every 6 h. As calcitonin works rapidly within 4–6 h (Vaughn and Vaitkevicius 1974), it may be used in combination with another anti-hypercalcemic agent such as bisphosphonates or glucocorticoids (Binstock and Mundy 1980; Sekine and Takami 1998).

Tachyphylaxis, the rapid reduction in the efficacy of a drug with repeated doses, seems to occur, therefore limiting long-term use after approximately 48–72 h (Vaughn and Vaitkevicius 1974). The reasons for tachyphylaxis are unclear and controversial but thought to be due to the formation of antibodies against heterologous calcitonins like salmon calcitonin (Grauer et al. 1995). The co-administration of glucocorticosteroids may prevent tachyphylaxis (Binstock and Mundy 1980). The main side effects of calcitonin include flushing, nausea, and vomiting.

6.3.4 Corticosteroids

Corticosteroids are most likely to benefit patients who have hypercalcemia as a result of increased Calcitriol production, as seen in some patients with lymphoma or chronic granulomatous disease. Steroids inhibit 1-alpha-

hydroxylase conversion of 25-hydroxyvitamin D into Calcitriol, where reduced Calcitriol levels cause a decrease in intestinal absorption of calcium. In patients with hypercalcemia due to granulomatous diseases, prednisolone 20–40 orally daily would be a reasonable starting dose. The calcium levels should decrease within 3–5 days (Sharma 1996).

6.3.5 Gallium Nitrate

Gallium nitrate was initially developed because of its anticancer effect but was observed to cause a transient hypocalcaemia. Gallium nitrate works by inhibiting the release of calcium from the bone, but the mechanisms by which gallium nitrate exerts its effects are unclear (Warrell et al. 1984). It appears to have multiple effects such as the inhibition of osteoclast-mediated bone resorption, stimulation of bone formation, and alteration of the mineral composition and properties of bone.

The usual dose of gallium nitrate is a 5-day continuous intravenous infusion of 200 mg/m^2 per day. It is the long duration of treatment that limits its clinical use. There have been three randomized controlled trials comparing gallium nitrate and pamidronate, etidronate, and calcitonin. Gallium nitrate was effective in achieving normocalcemia and appeared to have a longer duration of normocalcemia compared to the bisphosphonates (Cvitkovic et al. 2006; Warrell et al. 1991). In a phase two randomized, double-blind trial of gallium nitrate versus pamidronate, 69% of the patients treated with gallium nitrate achieved normocalcemia compared with 56% of patients who were treated with pamidronate. The duration of normocalcemia was 14 days in patients who responded to gallium nitrate compared to 10 days in patients who responded to pamidronate (Cvitkovic et al. 2006). Gallium nitrate is generally well-tolerated, with the main side effects being asymptomatic hypophosphatemia (Warrell et al. 1991).

6.3.6 Mithramycin

Mithramycin is an antineoplastic antibiotic used as a chemotherapy agent. It is works by reducing both bone resorption and renal tubular calcium reabsorption (Ralston et al. 1985). It is usually administered as a single intravenous injection of 25 mcg/kg in 500 ml dextrose and can be repeated after 2 days. The serum calcium levels fall within 24–48 h of administration with a maximal effect at 2–4 days and a duration of action of 9–10 days (Godfrey 1971). The side effects of mithramycin include nausea, vomiting, fatigue, thrombocytopenia, and worsening liver function (Ralston et al. 1985). As the bisphosphonates are more efficacious and safer, mithramycin is rarely used in practice today.

6.3.7 Ocreotide

The evidence supporting the use of octreotide for the management of hypercalcemia is weak. Most of the evidence in the literature is based on single case reports (Mantzoros et al. 1997; Shiba et al. 1996).

6.3.8 Dialysis

Dialysis is effective in reducing serum calcium levels by hemodialysis with little or no calcium in the dialysate fluid. It is usually only used if no other options are available and has to be considered in the context of the clinical goals of treatment. Dialysis is likely to be considered when a patient has renal impairment or cardiac failure and where aggressive fluid hydration may be challenging.

7 Conclusion and Summary

Hypercalcemia of malignancy is a common condition and must be considered in a patient who presents with nonspecific symptoms and functional deterioration. The symptoms of hypercalcemia may be reversible with a number of treatments. Initial treatment should include intravenous hydration, followed by bisphosphonates. If urgent reduction of calcium levels is required and the patient is distressed by the symptoms, commencing calcitonin could be considered. Bisphosphonates such as zoledronate 4 mg or pamidronate 90 mg are currently the main medications of choice in the management of hypercalcemia of malignancy. The evidence for the use of denosumab is limited but can be considered if the hypercalcemia is refractory to bisphosphonates or if the patient has renal impairment.

Hypercalcemia signifies a poor prognosis and antineoplastic treatments to manage the underlying cancer which has the best chance of improving survival where appropriate.

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Thromboembolism and Bleeding

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_71

Abstract

While thromboembolism and bleeding appear, at first glance, to be hematological processes at opposite ends of the clinical spectrum, they share many commonalities of relevance to palliative care teams. Both are increased in the malignant state, particularly with metastatic disease, and consequently confer a significant symptom burden, resulting in high level of distress for patients and carers. Furthermore, they are often the cause, or contributory cause, of death and frequently complicate care at the end of life.

The evidence base for the management of cancer-associated thrombosis (CAT) has increased significantly over the past 15 years, yet few studies have included or considered patients with advanced cancer or those nearing the end of life. With respect to the management of bleeding at the end of life, particularly terminal hemorrhage, management is informed by little more than case reports and expert opinion.

This chapter will comprise of two sections. First, it will provide an overview of the management of bleeding in the palliative setting with particular focus on terminal hemorrhage. The second section will focus on the treatment and prevention of venous thromboembolism in the advanced cancer setting, including the management of patients with recurrent thrombosis, thrombocytopenia, and bleeding. It will also review the new oral anticoagulants and consider their place in CAT management.

1 Introduction

Among the many physiological processes affected by the presence of malignancy, a derangement in the hemostatic system is characteristic and predisposes patients to both thrombosis and hemorrhage. Not only do these complications of hemostasis impact on the cancer journey; they also may even herald an as yet undiagnosed malignancy. Bleeding is a common presentation of many new cancers including bowel, bladder, renal, and lung, with tests for fecal occult blood or urinalysis for hematuria being commonplace in detecting early malignancy. Likewise, the presence of venous thromboembolism (VTE) without any obvious precipitating risk factors may indicate the presence of cancer. Data suggests 4–10% of patients will be diagnosed with cancer within a year of developing a VTE (Carrier et al. 2015).

For the palliative care team, bleeding and thrombosis will complicate the journey of many patients with advanced cancer, be it during palliative chemotherapy or at the end of life. The management will be determined by several factors including the severity of the event, the clinical environment, the presence of reversible factors, the overall prognosis of the patient, and the agreed ceilings of care. For some patients, complications of hemostasis may be anticipated. In such situations, wherever possible, teams should discuss the likelihood of bleeding or VTE with patients in order to ensure the treatment plan is congruent with their wishes.

2 Thrombosis and Hemorrhage Two Sides of the Same Coin

While this chapter will cover the management of thrombosis and bleeding separately, it is important to recognize that these two conditions are inextricably linked in both healthy people and those with cancer. Furthermore, these processes do not always occur in isolation; many cancer patients will have a level of disseminated intravascular

Table 1 Cancer associated mechanisms of increased risk of thrombosis and bleeding (TNF-α = tumor necrosis factor alpha, IL-1 = interleukin-1)

Risk factors	Increased risk of thrombosis	Increased risk of bleeding
Alteration of hemostatic system	Local release of procoagulants by tumor Tissue factor Local release of inflammatory cytokines TNF-α, IL-1 Increase platelet activity Disseminated intravascular coagulation	Reduction of vitamin K dependent clotting factors Thrombocytopenia due to marrow failure Disseminated intravascular coagulation
Anticancer treatments	Chemotherapy and targeted anticancer treatments Surgery Radiotherapy Central venous access	Chemotherapy Surgery
Local tumor effects	Reduction in venous return Pelvic tumors Lymphadenopathy	Local bleeding from vascular tumor Erosion of tumor into local blood vessel
Concurrent medications	Estrogen containing contraceptive pill Hormone therapies	Antiplatelet agents Non-steroidal anti-inflammatory drugs
Concurrent illness	Any inflammatory condition including Infection Congestive heart failure	Liver disease Hypersplenism

coagulation (DIC), a coagulopathy which causes widespread thromboembolic phenomena and, as platelets and clotting factors are consumed, bleeding at multiple sites. In addition, several mechanisms by which cancer cells are known to disseminate and metastasize are integral within the hemostatic system, particularly through clotting-dependent and clotting-independent activities of tissue factor, thrombin, and fibrin.

Abnormal coagulation tests will be common in cancer patients, regardless of the presence of thrombosis and/or bleeding. The results of laboratory tests demonstrate that a process of fibrin formation and fibrinolysis parallels the development of malignancy, increasingly in those with metastases, thereby worsening as the cancer progresses. Subtle hemostatic alterations may be identified, including high levels of plasma by-products of clotting reactions (i.e., prothrombin fragment 1 + 2 [F1 + 2], fibrinopeptide A [FPA], thrombin–antithrombin complex [TAT], and D-dimer) or an acquired protein C resistance, as well as high levels of circulating microparticles (MP) shed by cancer cells and platelets (Rickles and Falanga 2009). In addition to cancer-associated alterations to the hemostatic system, there are many other factors that may increase the risk of thrombosis and bleeding, and these are summarized in Table 1.

3 Section 1: Management of Hemorrhage

3.1 Risk Factors

Bleeding or hemorrhage occurs in 6–14% of advanced cancer patients and is the immediate cause of death in approximately 6% of these (Pereira and Phan 2004). Its presentation will depend on the site and severity of the bleed, although overt bleeds are a cause of significant distress for patients, carers, and even their healthcare professionals. The incidence varies according to the type of cancer, its stage, its anatomical site, hemostatic derangement, concurrent drug use, and the current (or previous) use of cancer-modifying treatments. Such factors will also influence whether the bleeding is clinically apparent or internal. Knowledge of the factors that influence the likelihood of bleeding will allow the team to identify those at greatest risk of bleeding and make anticipatory plans accordingly.

3.2 Alterations in Hemostatic System

3.2.1 Disseminated Intravascular Coagulation

As mentioned previously, many cancer patients will have DIC although it is important to recognize that this term covers a broad spectrum of clinical and hematological parameters ranging from asymptomatic to catastrophic hemorrhage. In the otherwise healthy person, hemostasis is a dynamic process involving the formation of a stable fibrin clot through coagulation followed by breakdown and reabsorption through fibrinolysis. In DIC, these processes are dysregulated, resulting in widespread thromboembolism in the small blood vessels. The ongoing coagulation consumes clotting factors and platelets, thereby leading to abnormal clotting and bleeding. In clinical practice, bleeding is a later manifestation of DIC, which is usually identified first in the laboratory. Several diagnostic criteria have been suggested which are usually based around scoring points, depending upon the presence of certain hematological blood parameters including the platelet count, presence of fibrin degradation products, prothrombin time, and fibrinogen level (Gando 2012). These are summarized in Table 2.

Table 2 Scoring tool for diagnosis of disseminated intravascular coagulation (DIC). (Score of 5 or more is suggestive of diagnosis of DIC)

Factor	Potential points
Presence of underlying disorder known to be associated with DIC	Yes = 2 No = 0
Platelet count	$>100 \times 10^9$/L = 0 $<100 \times 10^9$/L = 1 $<50 \times 10^9$/L = 2
Fibrin degradation products e.g., D-dimer	No ↑= 0 Moderate ↑= 2 Strong ↑= 3
Prolonged prothrombin time	< 3 s = 0 > 3 s = 1 > 6 s = 2
Fibrinogen level	> 1.0g/L = 0 < 1.0g/L = 1

3.2.2 Thrombocytopenia

Thrombocytopenia and platelet dysfunction is commonly seen in hematological malignancies such as leukemia and lymphoma. While less common in solid tumors, it may also occur if metastases are present in the spleen or the marrow of hematopoietically active bones.

3.2.3 Vitamin K-Dependent Clotting Factors

The liver is responsible for the synthesis of the vitamin K-dependent clotting factors II, VII, IX, and X. Liver dysfunction or biliary obstruction secondary to metastatic disease can lead to deficiencies in these clotting factors, with an increased bleeding tendency.

3.3 Anticancer Treatments

The myelosuppressive effects of certain chemotherapy agents will result in a nadir, 8–14 days after chemotherapy is given, leading to a temporary thrombocytopenia. The degree of thrombocytopenia will depend upon the agent used, doses administered, and if used in combination. While the list is not exhaustive, thrombocytopenia is typically seen with the use of gemcitabine, carboplatin, dacarbazine, docetaxel, and platinum-based compounds. Myelosuppression is also seen in patients who have received radiotherapy to the larger marrow-producing bones such as the pelvis.

3.4 Local Tumor Effects

Bleeding from highly vascular tumors may be the initial presenting symptom for several cancers including lung, bowel, nasopharyngeal, bladder, and cervical. Other patients will not show visible signs of blood loss but will bleed internally. Many patients will continue to show signs of hemorrhage throughout their illness. The risk of bleeding increases with disease progression, be it through the increase in the size of the primary or the development of metastases.

Table 3 Drugs that interfere with platelet function

Adenosine diphosphate (ADP) receptor inhibitor	Inhibition of prostaglandin pathways	Inhibition of platelet phosphodiesterase
Clopidogrel Prasugrel Ticagrelor Ticopidine	Aspirin Non-steroidal anti-inflammatory drugs	Dipyridamole Aminophylline Theophylline Vincristine Vinblastine Colchicine Caffeine

Table 4 Anticoagulants used in medical practice

Coumarins (vitamin K antagonists)
Warfarin
Heparin and derivative substances
Unfractionated heparin
Low molecular weight heparin
Bemiparin
Dalteparin
Enoxaparin
Nandroparin
Tinzaparin
Ultra low molecular weight heparin
Semuloparin
Synthetic pentasaccharide inhibitors of factor Xa
Fondaparinux
Idraparinux
Direct factor Xa inhibitors
Apixaban
Edoxaban
Rivaroxaban
Direct thrombin inhibitors
Dabigatran

Some tumors may be anatomically or radiologically located in close proximity to a major blood vessel, where direct infiltration can lead to a sudden catastrophic bleed. This is a particular risk in locally recurring head and neck cancers, particularly following localized radiotherapy. Warning signs of visible pulsations in malignant wounds, herald bleeds, or a sudden increase in pain should prompt a swift assessment of the patient.

3.5 Concurrent Medications

There are many drugs that interfere with platelet function, and these are summarized in Table 3. The use of anticoagulants will also increase bleeding risk and is summarized in Table 4.

3.6 Concurrent Illness

Local infection within tumor cavities can also increase the risk of bleeding. If infection is suspected, antibiotic therapy should be considered in order to reduce this risk and also help alleviate other symptoms of infection such as pain.

4 General Principles for Bleeding Management

4.1 Ceilings of Care

The scope of patient conditions falling under the care of palliative care teams has extended far beyond those requiring end of life care. Even within the hospice setting, it is not unusual to admit patients for whom escalation of care would be appropriate, in the event of a deterioration in their condition. Facilities for interventions such as surgery, radiotherapy, or interventional radiology may not be readily available in small or stand-alone centers. Likewise, escalation of care or transfer to another site may not be appropriate for patients at the end of life if there is no certainty of significant survival benefit or improvement in quality of life. For patients with a history of bleeding, or who have been identified at risk, a decision regarding what should be done in the event of a further bleed should be made as early as possible, so that clinical teams can act appropriately in the patient's best interests. Where appropriate, steps should be taken to minimize the likelihood of bleeding, including consideration of preemptive interventions to prevent crises arising.

4.2 Principles of Management

The management of a bleeding episode should be individualized and based on the following factors:

- The underlying cause(s)
- The likelihood of reversing or controlling the underlying cause
- The burden/benefit ratio of the interventions
- The patient's wishes within the context of disease burden, life expectancy, and goals of care

For patients in whom, aggressive management of bleeding is warranted, an acute bleeding episode may require general resuscitative measures, such as volume and fluid replacement, and specific measures to stop the bleeding. For those whose care is solely palliative/symptom control, management may include measures to stop the bleeding but not involve full resuscitative measures. In the case of irreversible catastrophic bleeds and anticipated terminal hemorrhage, comfort measures only may be most appropriate, and these will be covered separately within the chapter.

As a general principle, management should focus on identifying the underlying cause(s) and, where possible, controlling the bleeding. This should include:

- Resuscitation as appropriate
- Examination/investigations to:
  - Identify site of bleeding
  - Severity of bleed
- Stopping the bleeding:
  - Local measures/hemostatic agents
  - Correct reversible abnormalities:
    Correct coagulopathies
    Stop medicines which may worsen bleeding
  - Systemic interventions:
    Blood products
    Antifibrinolytics
    Vasoconstrictors
  - Interventions as appropriate:
    Interventional radiology
    Radiotherapy
    Endoscopy

A review of concurrent medications and other illnesses may identify the etiology or contributing factors, such as the concurrent use of nonsteroidal anti-inflammatory drugs, antiplatelets, and anticoagulants. Many inpatients will be on primary thromboprophylaxis. However, the risks of prophylactic anticoagulation may outweigh the potential benefits in patients with very advanced disease; one study suggested 10% of palliative care patients experience clinically relevant bleeding with primary thromboprophylaxis (Tardy et al. 2017).

Investigations should be considered, dependent upon how aggressive the management is intended. For most patients, full blood counts and clotting profiles may reveal systemic problems, while in some cases endoscopy or angiography may be appropriate in order to identify bleeding sites.

4.3 Local Measures/Hemostatic Agents

Where a bleeding point can be visualized, application of a dressing, with or without pressure, may be sufficient to achieve hemostasis. However, if simple dressings do not control bleeding, many different hemostatic agents have been reported to assist hemostasis or promote vasoconstriction. The myriad of predominantly topical agents that have been used to manage bleeding are outlined in Table 5. The evidence base is predominantly limited to case reports or series, and the type of agent used will vary according to the bleeding area, severity of the bleeding, and tumor type. For example, hemostasis can be facilitated by coating dressings with acetone in vaginal packing but cocaine in nasal packing. Wherever possible, the frequency of dressing changes should be reduced and non-adherent dressings used. In severe epistaxis, catheters with inflatable balloons may be used to control the bleeding. However, balloon tamponade should be considered a temporary measure since prolonged pressure may cause local ischemia. Many agents are derived from known coagulation factors, while some will form a scaffold upon which platelets or fibrin may allow a clot to form. Other agents, such as silver nitrate, are used topically to cauterize bleeding vessels, while topical epinephrine may be used on dressings as a vasoconstriction agent for localized capillary-based bleeding such as cutaneous melanoma.

Table 5 Hemostatic agents

Agent	Composition/derivation	Application	Uses
Thromboplastin	Powder Bovine derived	Topical	Wound healing
Oxidized cellulose	Cellulose derivative	Topical	Promotes local clotting Wound dressing
Collagen	Structural protein Bovine derived mesh dressing	Topical	Wound dressing
Epinephrine	Naturally occurring hormone Solution	Topical	Cutaneous
Silver nitrate	Inorganic silver salt	Topical	Nasal
Formalin	2% or 4% solution	Topical	Rectal Bladder
Prostaglandins E2 and F2	Naturally occurring hormone	Intravenous	Hemorrhagic cystitis
Alum	1% solution Aluminum derived	Continuous irrigation	Bladder
Sucralfate	Tablet Powder Solution/ gel	Oral Topical	Upper GI bleeds Cutaneous oozing
Gelatin Gelatin	Sponge like dressing or powder	Topical	Nasal Rectal Vaginal

4.4 Systemic Interventions: Blood Products

4.4.1 Packed Red Cells

Packed red cells are the most commonly administered blood product in the hospice setting, usually for fatigue and dyspnea. However, blood transfusions are potentially hazardous as well as beneficial, so should only be undertaken when the perceived clinical benefits to the patient outweigh the likely risks. The evidence base supporting the use of blood transfusions for the improvement of symptomatic anemia is limited to "before and after studies," with variable methods of evaluation. Transfusion is associated with a 31–70% subjective improvement in fatigue and dyspnea, although its effects tend to wane after 14 days (Preston et al. 2012). Furthermore, there is a risk of harm from blood transfusion in frail patients nearing the end of life, due to fluid overload or higher plasma viscosity.

4.5 Platelets

Thrombocytopenia is commonly encountered in advanced cancer and associated with an increased risk of bleeding. The frequency and severity of bleeding episodes increase as the platelet count drops below 20×10^9/L with severe bleeding associated with counts below 10×10^9/L. Platelet transfusion in the setting of advanced cancer should be on a case-by-case basis with the aim of controlling symptoms. Since platelets have a half-life of 4 days, their utility in severely thrombocytopenic end-stage cancer patients is limited. Criteria for platelet transfusions in end-stage hematological cancers have been proposed and include continuous bleeding of the mouth or gums, epistaxis, extensive and painful hematomas, severe headaches, or disturbed vision of recent onset, as well as continuous bleeding through the gastrointestinal, gynecological, or urinary systems (Schiffer et al. 2001). As a "rule of thumb," prophylactic platelet transfusion is only reserved for counts below 10×10^9/L or 20×10^9/L in the presence of sepsis. However, assuming normal splenic pooling, a single unit of platelets will increase the platelet count by $6–10 \times 10^9$/L in an average adult, and four to six units are usually required to control bleeding.

From a practical perspective, the decision to commence platelet support should also involve consideration criteria for stopping platelet

transfusions. These decisions pose ethical challenges, since ongoing transfusions may become futile. However, the patient or their family may perceive cessation of transfusions as withdrawal of life-sustaining therapy.

4.6 Fresh Frozen Plasma

Fresh frozen plasma, the liquid component of whole blood, can be used to correct deficiencies of coagulation factors such as factor V and VIII and other proteins. Its clinical uses are limited, and guidelines only recommend their use in the management of bleeding in patients on warfarin, with DIC, and as a plasma exchange medium for thrombotic thrombocytopenic purpura (O'Shaughnessy et al. 2004). In patients with advanced cancer, its use is limited to patients with a prognosis of several weeks or more.

4.7 Systemic Interventions: Drugs

4.7.1 Vitamin K

Vitamin K deficiency occurs in over 20% of advanced cancer patients, with 6.5% having evidence of clotting dysfunction (Harrington et al. 2008). This may include prolonged prothrombin time (PT) or international normalized ratio (INR) and partial thromboplastin time (PTT) with normal thrombin time, fibrinogen, and serum fibrin-fibrinogen degradation products. While there is little to be gained in the use of prophylactic vitamin K based solely on abnormal clotting studies, replacement therapy may help further bleeding in patients with previous bleeding episodes. The recommended dose varies between 2.5 and 10 mg depending on the severity of clotting dysfunction and should ideally be given orally or by the subcutaneous route. Intravenous vitamin K is associated with anaphylactoid reactions in 2% of patients and should be used with caution and administered slowly, at a rate no faster than 1 mg per min.

4.8 Antifibrinolytics

Plasmin is a serum protease that degrades fibrin in a process called fibrinolysis. It is formed when the liver-derived zymogen plasminogen is converted by tissue plasminogen activator (TPA) to plasmin. Tranexamic acid is a synthetic antifibrinolytic agent that blocks the plasminogen binding sites, thereby inhibiting the conversion of plasminogen into plasmin by TPA. This results in a decreased lysis of fibrin and a consequent reduction in clot breakdown and resorption (Hunt 2015). Tranexamic acid has been reported to reduce bleeding from several metastatic cancers including lung, esophageal, gynecological, colorectal, and prostate. The evidence base in this population is limited to case reports and case series, but tranexamic acid has recently been evaluated in two large RCTs (CRASH-2 and WOMAN) comprising 20,000 participants in each study (Roberts et al. 2013). These studies were undertaken in different populations (trauma and postpartum hemorrhage), and both saw significant reductions in bleeding and mortality. Importantly, they also demonstrated no increase in thrombotic events (venous or arterial). These data strongly suggest that concerns about tranexamic acid having a procoagulant effect are unfounded.

Tranexamic acid is usually given orally 1 g three times a day or intravenously as 10 mg/kg three to four times a day, infused over about 1 h. There are also case reports of it being administered topically, rectally, or by intrapleural instillation.

4.9 Interventional Radiology

Developments in interventional radiology have led to transcutaneous arterial embolization (TAE) becoming a readily available option in the palliative treatment to control hemorrhage, pain, reduce tumor bulk, and lower hormone production in hormone-secreting tumors (Broadley et al. 1995). Its role in the control of bleeding has been reported in cancers of the head and neck

(Dequanter et al. 2013), pelvis (Nabi et al. 2003), lung (Kawaguchi et al. 2001), liver, and upper gastrointestinal tract (Eriksson et al. 2008). The procedure is usually performed under local anesthetic via a femoral or axillary approach. The blood vessel supplying the affected site is first identified by arteriography and then occluded by particles (e.g., polyvinyl alcohol), mechanical devices (e.g., coils), or liquids (e.g., glue, alcohol). Embolization is not suitable for all cases; it is restricted to areas where blood vessels are accessible by catheter and where embolization will not result in ischemia of key organs. Furthermore, embolization is not without its risks; there are complications associated with the puncture site bruising/hematoma, bleeding, or vessel occlusion. To minimize bleeding complications, coagulopathies should be reversed wherever possible. Any embolization procedure may be associated with the post-embolization syndrome, which comprises varying degrees of pain at the site of embolization, nausea/vomiting, and flu-like symptoms. These are related to tissue ischemia/necrosis and may last for several days following embolization. Readily available analgesia or a patient-controlled analgesia (PCA) pump should be considered. Careful liaison with a suitably experienced interventional radiologist is essential and best considered sooner rather than later.

4.10 Radiotherapy

The use of external beam and internal radiotherapy in management of bleeding in cancer patients can be highly effective. External beam radiotherapy (EBRT) may control hemoptysis caused by lung cancer in up to 80% of patients (A Medical Research Council (MRC) 1992; Langendijk et al. 2000). The optimal dose and fractionation is best guided according to patient performance status and prognosis. Studies suggest that higher dose/fractionation palliative EBRT regimens (e.g., 30 Gy/10 fractions equivalent or greater) are associated with modest improvements in survival and total symptom score, particularly in patients with good performance status. However, these improvements are associated with an increase in esophageal toxicity. Shorter EBRT dose/fractionation schedules (e.g., 20 Gy in five fractions, 17 Gy in 2-weekly fractions, 10 Gy in one fraction), which provide good symptomatic relief with fewer side effects, can be used for patients requesting a shorter treatment course and/or in those with a poor performance status (Rodrigues et al. 2011). The literature reports the successful use of radiotherapy for the control of bleeding from cancers of the bladder (Abt et al. 2013), vagina (Eleje et al. 2015), and rectum (Cameron et al. 2014).

4.11 Endoscopy

Endoscopy has been successfully used for the control of bleeding from upper gastrointestinal, lung, and bladder cancers. This approach allows the additional benefit of direct visualization of the bleeding site, enabling the endoscopist to undertake diagnostic biopsies and direct therapeutic interventions. Historically bleeding sites have been injected with ethanol, gelatin, and epinephrine. Bleeding from upper gastrointestinal tumors is most commonly cauterized by argon laser coagulation (Martins et al. 2016). For hematuria, the urologist may use cystoscopy when bladder irrigation has failed in order to inspect the bladder lining and cauterize any bleeding points identified. In cases of hemoptysis, bronchoscopy may be used to perform ice-cold saline lavages, balloon tamponade, laser phototherapy, or apply topical thrombin or fibrinogen to the bleeding site (Sakr and Dutau 2010).

4.12 Terminal Hemorrhage

Terminal hemorrhage is defined as a major hemorrhage, usually from an artery, which results in death. Death typically occurs within a period of time that may be as short as minutes, because of

the rapid internal or external loss of circulating blood volume. The incidence of terminal hemorrhage from published data varies from 3% in lung cancers, 6% in hematological malignancy, to 12% in head and neck cancers (Pereira and Phan 2004). Qualitative data reports terminal hemorrhage to be a distressing experience for both patients and staff although its management has historically been intuitive. A survey of UK palliative care teams suggested the management of patients considered to be at risk of terminal hemorrhage that would include the provision of what is known as "emergency" or "crisis" medication. Based on the understanding that a catastrophic bleed in a patient known to be at risk of exsanguination will be the terminal event, dominated by distressing symptoms, a consensus management is to administer high doses of sedatives with the intention of rendering the patient unconscious and unaware. However, a recent qualitative study of healthcare professionals' experiences of managing terminal hemorrhage directly challenges this approach on several levels (Harris et al. 2011). Firstly, the majority of patients experiencing terminal hemorrhage had not been identified as at risk, while those identified at risk of did not progress to bleeding. Secondly the average time from the initial bleed to loss of consciousness/death averaged at 60 s. In this context, if patients were administered emergency medication at the moment they bled, they would inevitably be unconscious before the sedative effects were realized. Finally, in circumstances where the emergency medicine was not kept close to the patient (i.e., in a controlled drugs cupboard), healthcare professionals may leave the patient to access the drugs, thereby leaving the patient dying alone.

In view of this data, while the principles of managing terminal hemorrhage remain the same, there is a greater emphasis on remaining with the patient and using supportive measures over the administration of crisis medication. Principles of managing terminal hemorrhage are identifying patients at risk of terminal hemorrhage, general supportive measures, and appropriate sedative medication (often termed as "emergency" or "crisis" medication). These principles are summarized in Table 6, and while they focus on carotid artery hemorrhage, also known as carotid blow-out, they can be applied to all forms of terminal hemorrhage.

Table 6 Management of terminal hemorrhage

Identifying patients at risk of terminal hemorrhage
For head and neck cancers, the main risk factors are surgery (e.g., radical neck dissection)
Radiotherapy (the most implicated risk factor), postoperative healing problems
Visible arterial pulsation
Presence of a pharyngocutaneous fistula
Fungating tumors with artery invasion
Other systemic factors
Age above 50 years
10–15% loss of body weight
Diabetes mellitus
Immunodeficiency
Generalized atherosclerosis
Malnourishment
General supportive measures
Ensure a nurse stays with the patient (if in hospital/hospice)
Provide psychological support to patients and their significant others
Call for nursing and medical assistance (if in hospital/hospice)
Apply pressure to external bleeding if possible
Use dark towels to camouflage blood loss
Use suction if possible
Place the patient in the lateral position
Administer oxygen
Use of sedative medication
Where possible, the drug should be given intravenously in order to get into the systemic circulation as quickly as possible. In the absence of venous access, the drug should be given intramuscularly rather than subcutaneous
Midazolam: 5–10 mg IV, IM, SC
Ketamine: 150–250 mg IV
Diamorphine: 10 mg IV, IM, SC

5 Section 2: Management of Venous Thromboembolism

Venous thromboembolism (VTE), comprising of deep vein thrombosis (DVT) and pulmonary embolism (PE), occurs in 1 in 1000 people per annum, affecting 6.5 million people worldwide (Cohen et al. 2007; Torbicki et al. 2008). Its

incidence is higher in cancer patients, occurring in up to 20% of patients during their lifetime. Cancer-associated thrombosis (CAT) is the commonest cause of chemotherapy-related death and the second commonest cause of cancer mortality overall (Khorana et al. 2007a). It also confers a significant symptom burden, both physical and psychological, which clinicians often find challenging to diagnose and manage (Johnson et al. 2012; Sheard et al. 2013; Johnson and Sherry 1997).

The symptoms attributable to VTE depend upon the location of the thrombosis and the volume of thrombus burden. An occlusive DVT may cause a spectrum of severity of symptoms including pain, swelling, and erythema. Untreated, a DVT risks propagating and ultimately breaking off and travelling to the pulmonary arteries causing a PE (Kakkar et al. 1969). Up to 80% of patients with pulmonary emboli report no symptoms suggestive of DVT. Therefore, the absence of DVT symptoms should not lower the index of suspicion of PE in a breathless patient (Meignan et al. 2000). As with DVT, the symptomatology of PE will vary from few, if any, attributable symptoms to severe dyspnea associated with chest pain, cardiovascular collapse, and death.

While the increased mortality due to VTE is considered to be of less relevance in the hospice setting, the symptom burden of fatal PE cannot be underestimated (Noble et al. 2008). Rather than being a sudden asymptomatic experience, the majority of fatal pulmonary emboli are associated with progressive "breathlessness dominated by tachycardia and fever" taking an average of 2 h to die (Havig 1977). In this cohort, only 10% of patients were diagnosed with a PE, the remainder being managed as heart failure, atrial fibrillation, and pneumonia. Breathlessness is often attributed to other pathologies without considering VTE as a diagnosis. These conditions may not only occur concurrently with VTE but also independently increase the VTE risk (Table 7).

Table 7 Attributable pathologies which mimic symptoms of pulmonary embolism

Attributable pathology	Can occur concurrently with PE	Increases risk of PE
Anemia	Yes	Yes: through release of erythropoietin or use of granulocyte colony stimulators
Pneumonia	Yes	Yes: pro-inflammatory condition
Left ventricular failure	Yes	Yes: venous stasis, increased viscosity with diuretic use and pro-inflammatory condition
Pulmonary metastases/ lymphangitis	Yes	Yes: cancer is prothrombotic
Malignant pleural effusion	Yes	Yes: cancer is prothrombotic

5.1 Epidemiology

It is highly likely that palliative care teams will see an increase in the number of patients with VTE, owing to the changing cancer population. Within the western world, people are living longer and a greater proportion of adults are being classed as obese. Both are independent risk factors for VTE, which along with people living longer with chronic illnesses establishes a highly thrombotic baseline risk. Specific to cancer patients, CAT rates have risen in parallel with increased chemotherapy use and are expected to grow further as people live longer with metastatic disease and receive ongoing cancer treatments until later in life (Khorana et al. 2007b).

The sequelae of VTE are not limited to the physical. Research has identified that patients who have been treated for VTE often go on to develop symptoms of post-traumatic stress disorder, and such complications are not limited to high thrombotic burden events (Noble et al. 2014; Bennett et al. 2016). Specific to CAT, research has suggested the symptomatic and psychological burden is such that some consider the experience more distressing than the cancer itself (Noble et al. 2014; Seaman et al. 2014). As such, a holistic approach to CAT is essential, particularly as these patients will also have needs within the context of their cancer journey (Noble et al. 2015b).

5.2 Treatment of VTE

The treatment and secondary prophylaxis of VTE in nonmalignant disease remains relatively straightforward; warfarin has been the mainstay of anticoagulants for decades but is likely to be superseded in most patients by the new direct-acting oral anticoagulants (DOACs) (Wells et al. 2014). However, there are some risks in the frail patient population where the bleeding risk is believed to be higher; DOAC elimination is reduced in renal impairment and should be avoided in those with creatinine clearance <30 ml/min.

Clinical guidelines for the treatment of CAT recommend between 3 and 6 months anticoagulation with weight-adjusted LMWH (Table 8). This is based on meta-analysis of randomized control trials, which have shown LMWH to reduce the rate of recurrent VTE when compared with warfarin, with no increase in bleeding rate. Additional benefits of LMWH are the lack of need for routine monitoring, absorption of the drug even in patients with vomiting, and few drug-drug interactions. Despite requiring a daily injection, qualitative data suggests that LMWH is acceptable within the context of the cancer journey (Seaman et al. 2014). Furthermore, warfarin's appeal as a tablet is undermined by its increased need for INR monitoring, which has been reported to lessen quality of life (Noble 2005). A recent study using conjoint methodology evaluated the preference of patients being treated for CAT (Noble et al. 2015a). Patients considered the most important attribute of their anticoagulant to be that it did not interfere with their ongoing cancer treatment. The second and third most important attributes were efficacy and safety, respectively, followed by the fourth most important attribute being a preference for a tablet over an injection. The authors concluded that patients saw themselves as cancer patients first and foremost, and their main concern was whether the VTE would affect or worsen their ability to receive the best cancer treatment possible. This is reflected in a single institution experience; patients will demonstrate considerable resilience to the side effects of their cancer treatments, in order to receive the best long-term outcome. Thus, they will also be willing to undergo similar inconvenience in the treatment of their CAT to ensure they receive the best treatment possible. Optimal compliance to LMWH is strongly improved by giving patients a full explanation of the importance of CAT treatment and the rationale for using LMWH (Noble et al. 2016).

5.3 Management of CAT when the Evidence Is Lacking

The heterogeneity of CAT goes beyond the different thrombogenicities and risk factors for VTE, conferred by each tumor type and chemotherapy regime. All of the LMWH studies in CAT had exclusion criteria: patients with poor performance status, life expectancy of less than 3 months, thrombocytopenia, increased bleeding risk, renal impairment, and weight less than 40 kg (Lee et al. 2003, 2015; Hull et al. 2006; Meyer et al. 2002). However, these patients are commonly seen by specialist palliative care teams, and up to 9% of patients receiving LMWH experience recurrent VTE, thereby requiring modification of their anticoagulation. Recurrent VTE is seen most commonly in those with advanced disease, in particular lung, ovarian, brain, and pancreatic cancer (Chee et al. 2014; Louzada et al. 2012). Up to 21% of CAT patients are managed outside of the standard treatment of weight-adjusted LMWH. These include patients with recurrent VTE despite anticoagulation, patient with thrombocytopenia, and those with bleeding complications. The management of such cases is covered in a guidance document recently published by the International Society on Thrombosis and Haemostasis Scientific Sub-Committee (ISTH SSC) for Malignancy and Haemostasis (Carrier et al. 2014). However, it is important to recognize that not all patients will be adequately managed with standard weight-adjusted LMWH, and such situations are summarized in Table 8.

The ISTH SSC makes only brief mention of using a twice day dosing of LMWH due to little supporting data. However, it is worth acknowledging a subgroup analysis of 149 cancer patients

Table 8 Management of challenging cases of CAT: ISTH SSC recommendations, Johnson et al. (2012)

Recurrent VTE despite anticoagulation
1. If on warfarin, switch to therapeutic LMWH
2. If already on LMWH, increase dose by 25% or increase back up to therapeutic weight adjusted dose if they are receiving nontherapeutic dosing.
3. If no symptomatic improvement, use peak anti-Xa level to estimate next dose escalation.
Management of CAT in thrombocytopenia
1. For platelet count $>50 \times 10^9\ L^{-1}$ give full therapeutic dose LMWH
2. For acute CAT and platelet count $<50 \times 10^9\ L^{-1}$
a. Full anticoagulation with platelet transfusion to maintain platelet count $>50 \times 10^9\ L^{-1}$
b. If platelet transfusion is not possible, consider retrievable IVC filter
3. For subacute or chronic CAT and thrombocytopenia (platelet count $<50 \times 10^9\ L^{-1}$)
a. Reduce therapeutic dose by 50% or use prophylactic dose for platelet count $25–50 \times 10^9\ L^{-1}$
b. Omit LMWH if platelet count $<25 \times 10^9\ L^{-1}$
Bleeding while anticoagulated
1. Assess each bleeding episode to identify bleeding source, severity, impact, and reversibility
2. Provide supportive measures to stop bleeding including transfusion where indicated
3. For a major or life-threatening bleeding episode: withhold anticoagulation
a. Consider IVC filter insertion in patients with acute or subacute CAT with a major or life-threatening bleeding episode.
b. Do not consider IVC filter insertion in patients with chronic CAT.
c. Once bleeding resolves: remove retrievable filter (if inserted) and resume/initiate anticoagulation

in a study of 900 VTE patients randomized to receive enoxaparin 1.5 mg/kg SC once daily or enoxaparin 1 mg/kg SC twice daily. The study showed a higher yet statistically nonsignificant rate of recurrent VTE in cancer patients dosed with enoxaparin 1.5 mg/kg SC once daily (6/49 patients, 12.2%) as compared to patients given enoxaparin 1 mg/kg SC twice daily (3/47 patients, 6.4%). Interestingly, the subgroup analysis also found that none of the 49 patients (0%) in the once daily arm died during the study, while 4/47 (8.5%) deaths were reported in the twice-daily arm.

5.4 Prevention of VTE

The prevention of VTE in hospitalized patients has gained increasing attention within clinical research and health policy. VTE prevention is a priority for quality improvement projects within many international health settings and has been covered in a myriad of clinical guidelines.

There has been considerable debate as to whether the data informing VTE prevention (Noble et al. 2008; Noble 2005; Noble and Finlay 2006; Pace et al. 2006; Noble and Johnson 2010; Ambrus et al. 1975) in a largely general medicine population can be applied to specialist palliative care units (SPCU), be it in hospital or hospice settings. In the past, patients admitted to hospices had a fairly short life expectancy and did not expect to be discharged. In this context, the majority of these patients would not benefit from primary thromboprophylaxis since any attributable symptoms could be managed with end of life, symptom control medicines. In more recent years, the population of patients being admitted to what have become SPCUs has changed. Now, patients are often admitted for a period of symptom control, earlier in their disease trajectory. It is not unusual for such patients to have a good performance status and have months or even years to live.

There are limited data pertaining to the prevalence and incidence of VTE in hospice inpatients. One study using light-reflection-rheography to detect obstruction to lower limb venous flow of 258 inpatients suggested findings consistent with the presence of DVT in 135 (52%; 95% confidence interval 46–58) (Johnson et al. 1999). This study acknowledged several limitations, while a highly sensitive test, light-reflection-rheography, is unable to identify the site or cause of obstruction to venous flow. However, the study identified changes consistent with bilateral DVT, and thus

potentially more extensive thrombosis, in 17% and 9% had VTE confirmed on imaging.

Practice in hospices has changed over the past 10 years, possibly due to increased awareness of the risks of VTE with advanced cancer (Noble and Finlay 2006; NICE 2018). Even so, the uptake of thromboprophylaxis remains relatively low in hospices despite qualitative data, which suggests that resistance to thromboprophylaxis does not lie with the patients (Noble et al. 2006). Reasons explaining this are complex but predominantly reflect a view that we do not have hard data pertaining to the true prevalence/incidence of VTE in the hospice/SPCU population or studies conducted in representative populations, reporting patient-relevant outcome measures (Noble et al. 2008).

Whatever the reasons for current practice, there appears to be a measurable prevalence of new symptoms attributable to VTE in patients admitted to SPCUs who would qualify for primary thromboprophylaxis if admitted through the medical on-call process. An audit of 1164 case notes from 5 UK hospices suggested that a temporary elevation of VTE risk factors was associated with a prevalence of VTE attributable symptoms in 21% of patients (Johnson et al. 2014). From a practical perspective, over 50% of SPCU admissions were identified as having contraindications to thromboprophylaxis. It is clear, therefore, that the impact of VTE in palliative care patients requires clarification with respect to prevalence, incidence, symptom burden, and impact on quality of life, before thromboprophylaxis guidance can be provided for clinicians caring for cancer patients in this setting (Noble and Johnson 2010). An outline of priorities for research that identifies these important issues has been suggested as follows:

- Identify the true prevalence and natural history of VTE in the palliative care setting.
- Develop appropriate outcome measures.
- Identify the clinical and symptom burden of VTE.
- Establish a consensus on what clinical/symptomatic outcome difference would be required to change thromboprophylaxis practice.
- Establish the clinical and cost-effectiveness of thromboprophylaxis.

At the time of writing, the Hospice Inpatient Deep vein thrombosis Detection Study (HIDDEN) is being conducted in order to establish the prevalence of VTE and evaluate the incidence of VTE during an inpatient stay. This study, in which hospice inpatients undergo a Doppler ultrasound on admission, and at weekly intervals, will provide data on the prevalence and incidence of VTE. These data, married with an appreciation of the symptom burden conferred by VTE, will help establish the need to evaluate the role of thromboprophylaxis. Until then, consensus recommends that hospice patients be considered on an individual basis. For patients admitted for terminal care, prevention of VTE is not a priority since symptoms attributable to VTE could be managed with end of life drugs. However, for the population of patients admitted for symptom control or rehabilitation, the prevention of VTE may be appropriate, especially in those with a longer life expectancy than days. For such patients, the strongest data still lies with LMWH.

5.5 New Anticoagulants and the Palliative Care Patient

The introduction of the oral factor IIa inhibitor (dabigatran) and the factor Xa inhibitors, i.e., rivaroxaban, apixaban, and edoxaban, offers an alternative to patients who would otherwise be treated with warfarin (Schulman et al. 2009; Prins et al. 2014; EINSTEIN Investigators et al. 2010; Agnelli et al. 2013; Hokusai et al. 2013). Collectively termed direct-acting oral anticoagulants (DOACs), they have demonstrated non-inferiority with warfarin for the treatment of conventional VTE, and some show a superior safety profile with respect to major bleeding. They require no monitoring or dose adjustments and have fewer drug-drug interactions than warfarin. As such, they have potential as an attractive alternative to current practice particularly in patients with nonmalignant disease. However, this assertion comes with certain caveats; to date it is not possible to accurately monitor their anticoagulation effect and no readily available reversal agent, should the patient bleed. Furthermore,

Table 9 Proportion of patients in clinical studies with metastatic disease

Study	LMWH (%)	Warfarin (%)	DOAC (%)
CLOT Lee et al. (2003)	66	69	–
LITE Hull et al. (2006)	47	36	–
CATCH Lee et al. (2015)	55	54	–
ONCENOX Meyer et al. (2002)	54	52	–
EINSTEIN DVT/PE Prins et al. (2014)	–	26	19
HOKUSAI VTE Hokusai et al. (2013)	–	22	24

all these drugs rely on the renal system for clearance and are contraindicated, or to be used with caution, in renal failure (creatinine clearance <30 ml/min). Finally, real-world data has suggested caution should be exercised with the use of DOACs particularly in the frail and elderly (Harper et al. 2012). While a case-by-case evaluation of their use in patients with advanced incurable illness is wholly justifiable, a working understanding of factors that increase bleeding risk is essential. Since increased bleeding with DOACs is associated with frailty, increased age, renal impairment, and polypharmacy, they are unlikely to become a vade mecum of anticoagulation to palliative care teams (Kundu et al. 2016).

Until recently, there has been limited data to inform the role of DOACs in the management of CAT, with the exception of the small proportion of cancer patients in the original DOAC VTE studies. A meta-analysis of all the cancer patient data from RE-COVER I and II, EINSTEIN DVT, and PE and Hokusai (but not AMPLIFY) demonstrated superiority of DOACs over warfarin, concluding they may offer an alternative to warfarin in CAT patients intolerant of LMWH (Schulman et al. 2009; Prins et al. 2014; EINSTEIN Investigators et al. 2010; Agnelli et al. 2013; Hokusai et al. 2013).

The pooled incidence rates of recurrent VTE were 4.1% (95% confidence interval [CI] 2.6–6.0) in cancer patients treated with DOACs and 6.1% (95% CI 4.1–8.5) in patients treated with warfarin (RR 0.66, 95% CI 0.38–1.2). The pooled incidence rates of major or nonmajor clinically relevant bleeding were 15% (95% CI 12–18) in cancer patients treated with DOACs and 16% (95% CI 9.9–22) in patients treated with warfarin (RR 0.94, 95% CI 0.70–1.3) (van der Hulle et al. 2014). However, it is important to note that VTE recurrence rates in both arms are low in comparison to other studies. A VTE recurrence rate of 6.1% in the warfarin arm is lower than the VTE rates in the LMWH arm of CLOT (9% LMWH vs 17% warfarin) (Lee et al. 2003), LITE (7% LMWH vs 16% warfarin) (Hull et al. 2006), and CATCH (7.2% LMWH vs 10.% warfarin) (Lee et al. 2015). However, this is not to infer that DOACs are as (or even more) efficacious than the LMWHs, since closer analysis of the data will reveal that the cancer patients in the DOAC vs warfarin studies are different to those in the LMWH vs warfarin ones. Table 9 summarizes the percentage of patients with metastatic disease in each arm of the LMWH vs warfarin CAT studies. Percentages of patients in each arm with metastatic disease, an independent risk factor for VTE, ranged from 47% to 66% in the LMWH arms and 36–69% in the warfarin arms. A subgroup analysis of the EINSTEIN studies has recently been published pooling data of 651 cancer patients (Prins et al. 2014). Recurrent VTE occurred in 16 (5%) of 354 patients allocated to rivaroxaban and 20 (7%) of 301 patients allocated to warfarin (hazard ratio [HR] 0·67, 95% CI 0·35–1·30). However, only 19% of patients in the rivaroxaban arm and 26% of those allocated to warfarin had metastatic disease. It is clear that the proportion of patients with metastatic disease were considerably less in the DOAC studies than the original LMWH studies. It would therefore be premature to infer that any of the DOACs have sufficient evidence to justify the first-line treatment of CAT. In particular, this current data is lacking in patients with advanced cancer and poorer performance status. Nevertheless, some

Table 10 Common drug-drug interactions with Direct Acting Oral Anticoagulants, based on (Lee and Peterson 2013)

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Interaction effect	P-glycoprotein	P-glycoprotein CYP3A4	P-glycoprotein CYP3A4	P-glycoprotein
Increases DOAC plasma levels[a]	Cyclosporine	Cyclosporine	Cyclosporine	Cyclosporine
	Tacrolimus	Tacrolimus	Tacrolimus	Tacrolimus
	Tamoxifen	Tamoxifen	Tamoxifen	Tamoxifen
	Lapatinib	Lapatinib	Lapatinib	Lapatinib
	Nilotinib	Nilotinib	Nilotinib	Nilotinib
	Sunitinib	Sunitinib	Sunitinib	Sunitinib
		Imatinib	Imatinib	
Reduces DOAC plasma levels[b]	Dexamethasone	Dexamethasone	Dexamethasone	Dexamethasone
	Doxorubicin	Doxorubicin	Doxorubicin	Doxorubicin
	Vinblastine	Vinblastine	Vinblastine	Vinblastine

[a]Drugs that inhibit P-GP or CYP3A4 can increase DOAC levels
[b]Drugs that induce P-GP or CYP3A4 can lower DOAC levels

clinicians use DOACs first-line for CAT, contrary to the recommendations of guidelines (Noble et al. 2015a).

At the time of writing, two RCTs have been reported, comparing a DOAC with LMWH in the treatment of CAT (Raskob et al. 2018; Young et al. 2018). The SELECT-D pilot study, comparing rivaroxaban with dalteparin for the treatment of CAT, has been presented at the 59th American Society for Hematology meeting in Atlanta. Over 400 patients were recruited with over 90% having locally advanced or metastatic disease and 83% receiving chemotherapy. The VTE recurrence rate at 6 months was 11% (95% CI 7–17%) for patients on dalteparin and 4% (95% CI 2–9%) for patients on rivaroxaban. Major bleeds were similar across trial arms [six bleeds from six patients (3%; 95% CI 1–6%) on the dalteparin arm and nine bleeds from eight patients (4%; 95% CI 2–8%) on the rivaroxaban arm]. There were more clinically relevant nonmajor bleeds (CRNMBs) on the rivaroxaban arm and 5 bleeds from 5 patients (2%; 95% CI 1–6%) on dalteparin compared with 28 bleeds from 27 patients (13%; 95% CI 9–19%) on rivaroxaban. In total, 11 patients (5%; 95% CI 3–9%) on the dalteparin arm had bleeds categorized as either major bleeds or CRNMBs compared to 34 patients (17%; 95% CI 12–22%) on the rivaroxaban arm.

The HOKUSAI VTE Cancer study was an open label non-inferiority trial, comparing 5 days LMWH followed by edoxaban 60 mg once daily with dalteparin at a dose of 200 IU/kg for 1 month followed by dalteparin 150 IU/kg in cancer patients with VTE. Treatment was given for at least 6 months with a primary outcome being a composite of recurrent VTE and major bleeding (Raskob et al. 2018). One thousand forty-six patients were included in the modified intention to treat analysis. Edoxaban demonstrated non-inferiority with dalteparin with a primary outcome event in 67 of the 522 patients (12.8%) in the edoxaban group with 71 of the 524 patients (13.5%) in the dalteparin group (hazard ratio, 0.97; 95% confidence interval [CI], 0.70–1.36; $P = 0.006$ for non-inferiority; $P = 0.87$ for superiority). Reviewing recurrent VTE and major bleeding events separately, it appears that edoxaban results in fewer recurrent VTE events, at the expense of more major bleeding episodes. Recurrent VTE occurred in 41 patients (7.9%) in the edoxaban group and in 59 patients (11.3%) in the dalteparin group (difference in risk, −3.4 percentage points; 95% CI, −7.0 to 0.2). Major bleeding occurred in 36 patients (6.9%) in the edoxaban group and in 21 patients (4.0%) in the dalteparin group and was predominantly due to gastrointestinal (GI) bleeding. Major bleeding was also higher in

particular cancers, namely, gastrointestinal (13.1%) and urothelial (7.9%). Based on this, it would seem unreasonable to use DOACs to manage CAT in these untreated/ active GI or urothelial cancers.

A final issue worthy of consideration lies with the potential for drug-drug interactions (Lee and Peterson 2013). DOACs, while subject to fewer interactions than warfarin, are particularly sensitive to medicines which inhibit P-glycoprotein or cytochrome P450 3A4 (CYP3A4). These are by no means insignificant, particularly in those receiving palliative chemotherapy, and are summarized in Table 10. Nevertheless, if patients are unable to take a LMWH, DOACs may be a better choice than warfarin. However, patients need to be aware of the limitations of data and the possible risks should they choose to take DOACs for the treatment of CAT.

6 Conclusion

Cancer-associated thrombosis remains a significant yet under-recognized issue for palliative patients, with the majority of practice based on low-quality evidence or data extrapolated from nonrepresentative populations. It is a problem that will become more prevalent over time, especially in those with metastatic disease. In an era of personalized medicine, where chemotherapy options are considered on the base of biomarkers and genetic mutations, it makes sense that an individualized approach to VTE management is also embraced by those clinicians caring for patients at the fringes of research-based data.

At present, the data supports LMWH first-line for the treatment of CAT. However, at the time of writing, non-inferiority randomized-controlled trials are being conducted to compare DOACs with LMWH, with first results expected in 2018. As with previous CAT studies, it is unlikely that these will reflect the patient population served by palliative care teams, but it may herald a change in clinical practice for the larger cancer population and consequently inform our practice.

Likewise, research is ongoing to define the true prevalence of VTE in hospice inpatients and the associated symptom burden. As such, the next 5 years are likely to see answers to several fundamental challenges in CAT management which will not only inform but also change the management of this underappreciated condition.

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Spinal Cord Compression

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_72

Abstract

Spinal cord compression, one of the most dreaded complications of malignancy, is usually caused by metastatic bone disease compressing the spinal cord and/or nerve roots. If not recognized and treated promptly, it can have potentially catastrophic outcomes. As patients live longer due to newer treatments, the incidence of malignant spinal cord compression may increase, and the types of presentation or behavior of tumors may change. Spinal cord compression must be considered in all patients who have a cancer diagnosis presenting with back or neck pain and/or neurological symptoms or signs. In this chapter, the terminology used in the diagnosis and treatment of spinal cord compression will be defined and the epidemiology and pathophysiology described. Given that spinal cord compression is a true emergency, it must be diagnosed and managed promptly by a multidisciplinary team. Early detection and effective treatment can make the difference between independent living and being bed bound. This chapter will explore the many factors that should be considered in determining the most appropriate care plan and highlight how the ultimate goals of care and care plan need to be continually reassessed to ensure the best outcome for the patient. Surgical intervention and radiotherapy treatment decisions are complex and will be explained in detail, within the context of these above considerations. Technical aspects and illustrations to clarify treatment options will be provided. Predicted outcomes will be discussed; however it is important to note that the best outcomes occur when the degree of premorbid neurological deficit is minimal and the diagnosis and treatment initiated within 24–48 h of presentation.

1 Introduction

Spinal cord compression is one of the most dreaded complications of malignancy usually caused by metastatic bone disease compressing the spinal cord and/or nerve roots, with potentially catastrophic outcomes. It affects up to 14% of patients with cancer and is a true emergency, which must be diagnosed and managed promptly by a multidisciplinary team, taking into account many factors to instigate the most appropriate care plan for that individual patient. Best outcomes occur when the degree of premorbid neurological deficit is minimal and the diagnosis and treatment initiated within 24–48 h of presentation.

2 Definitions

Within this chapter, it is necessary to define the common interpretation of the terms used. The term "spinal cord compression" in degenerative terms is just that; compression of the spinal cord alone by a structure such as bone or disc. In malignant parlance, it has a much broader definition, and it usually refers to compression of the spinal cord or cauda equina either directly from a malignancy or compression by a pathological fracture caused by a malignancy and its associated clinical findings. Malignant spinal cord compression also commonly involves the compression of nerve roots in the intervertebral foramina and is an integral part of the clinical picture in the symptom pattern (Fig. 1) (Cole and Patchell 2008).

It is best to maintain strict clinical and radiological definitions. "Malignant spinal cord compression" should only include compression of the spinal cord and conus, whereas "malignant cauda equina compression" is the compression of the lumbar nerve roots in the lumbar vertebral canal. "Malignant nerve root compression" is the involvement of the nerve roots, including within the intervertebral foramina. It is important to distinguish between the use of the term compression in relation to clinical syndromes. Compression is the mechanical compression of the spinal cord or nerve roots as defined radiologically. Therefore cauda equina compression is a radiological definition and should not be confused with "cauda equina syndrome," which is the clinical picture of nerve root signs, perianal sensory loss, and double incontinence. It is important to remember that a patient can have radiological compression without symptoms. This is termed "subclinical cord compression."

"Impending cord compression" is a loose term that should be avoided. It is used frequently to indicate a radiological finding that may progress to definite cord compression, either from tumor growth or bone fracture. Instead the term "at risk of spinal cord compression" should be used.

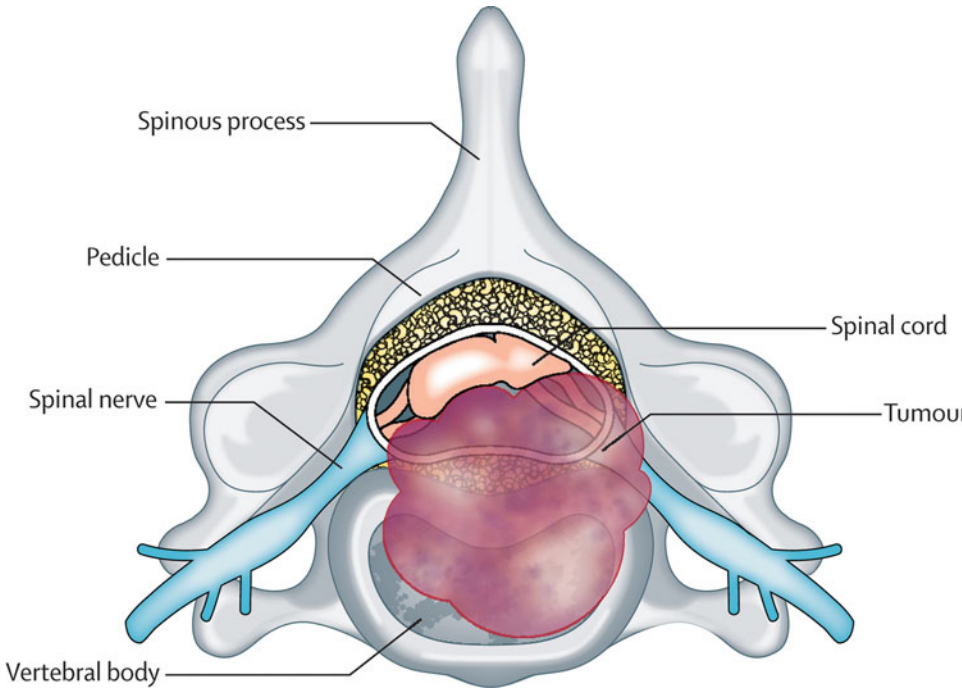

Fig. 1 Example of a tumor within a vertebral body, anterior to the spinal cord which is growing posteriorly into the vertebral canal to compress the spinal cord and/or nerve roots

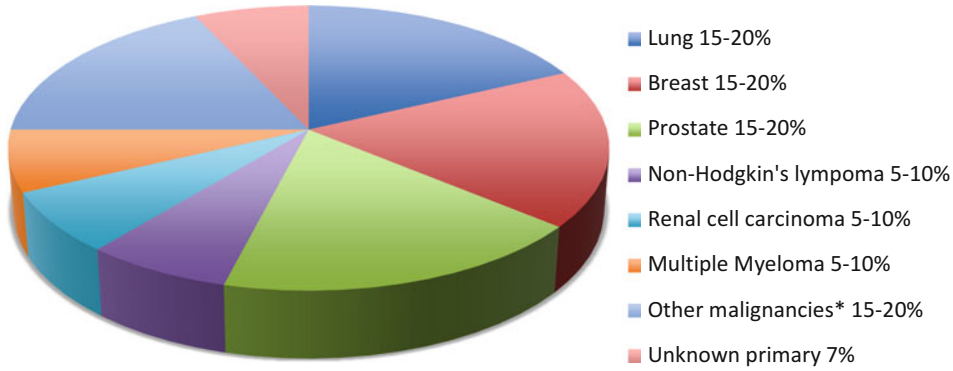

Fig. 2 Approximate proportion of primary tumors causing malignant spinal cord compression. *Other malignancies include colorectal carcinomas, sarcomas, melanomas, etc.

"Unstable fracture" in relation to malignancy indicates a vertebra that has developed a fracture and may possibly collapse further from loss of supportive elements. A "potentially unstable vertebra" is one that has lost a significant amount of its supportive elements and may go on to fracture.

3 Epidemiology and Pathophysiology

Estimates of the incidence of spinal cord compression from malignancy are variously quoted as between 5% and 14% of people with cancer (National Institute for Health and Clinical Excellence (NICE) 2008). In patients with bone metastases, approximately 60% will have metastases within the spine, and up to 10% of these patients will develop spinal cord compression (Spratt et al. 2017). With new treatments, patients with cancer are living longer, and it is likely that the incidence of spinal cord compression may increase. Of patients presenting with spinal cord compression, 77% have a known pre-existing malignancy. The remaining 23% have spinal cord compression as their first presentation of their malignancy (Levack et al. 2002).

Lung, breast, and prostate cancers are the commonest malignancies causing spinal cord compression and together account for over 50% of cases. Non-Hodgkin's lymphoma, renal cell cancer, and multiple myeloma each account for 5–10%, and most of the remainder of cases of malignant spinal cord compression are due to colorectal cancers, sarcomas, and melanomas (Cole and Patchell 2008). In 7% of patients, the site of primary tumor may remain unidentified (Fig. 2) (Levack et al. 2002).

The thoracic spine is most commonly affected with up to 70% of lesions. About 30% of lesions are within the lumbosacral spine and under 10% within the cervical spine (Helwig-Larsen and Sorensen 1994) (Fig. 3). Seventeen percent of patients have two or more levels of spinal cord compression (Levack et al. 2002).

Spinal cord and cauda equina compression can result from several different mechanisms. Direct growth of tumor (either from a vertebra or from paraspinal tissues) into the vertebral canal or intervertebral foramina is one mechanism. A pathological fracture with displacement of bone fragments is another. Often it is a combination of both. Malignant cells within the subarachnoid space may also result in neurological deficits caused by tumor deposits growing on the nerves or surface of the spinal cord within the vertebral canal. From a clinical perspective, it is helpful to consider any tumor in the subdural and subarachnoid space or within the spinal cord itself (compromising the spinal cord) as a cause of a patient's symptoms and signs and as lesions where a patient may benefit from treatment. Leptomeningeal disease is most commonly seen in patients with small cell lung cancer, melanoma, lymphoma, and tumors of the central nervous system, most commonly medulloblastoma.

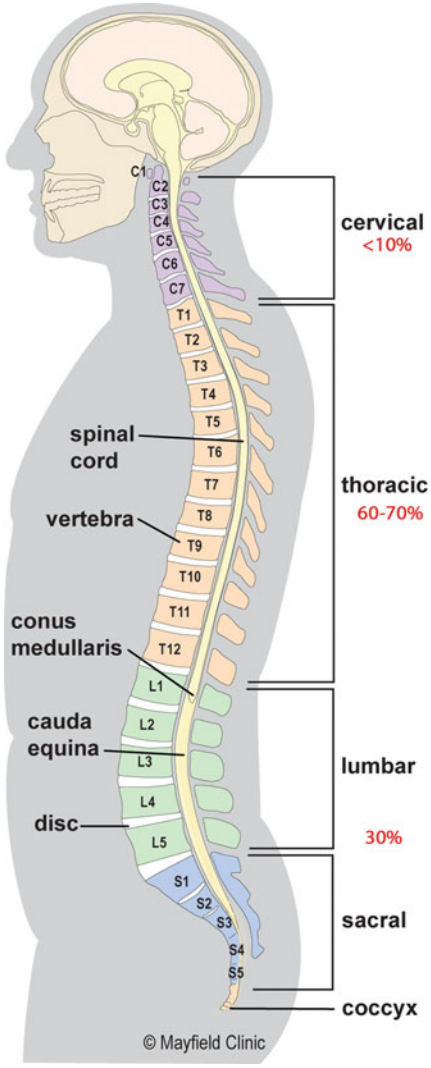

Fig. 3 Approximate distribution of the location of malignant spinal cord compression presentations. Percentages are given in red. 17% of patients have two or more levels of cord compression. (Illustration by Martha Headworth, printed with permission © 2016 Mayfield Clinic)

4 Clinical Features

Malignant spinal cord compression is one of the most dreaded complications of metastatic cancer. Its natural history, if untreated, is usually one of relentless and progressive pain, paralysis, sensory loss, and sphincter dysfunction (Loblaw and Perry 2005). These symptoms and signs can vary significantly between patients (Fig. 4), and therefore a detailed history and full neurological examination need to be performed and documented.

Back pain, the most common presenting problem in patients with spinal cord compression, may be sharp, shooting, deep, or burning. The pain can be localized to the back or may radiate in a band-like dermatomal distribution, if tumor compresses the nerve roots in or near the intervertebral foramina. Mechanical back pain is important to recognize, as it can be associated with spinal instability. An acute exacerbation of chronic back pain may be caused by a recent compression fracture.

In addition to pain, other common symptoms of spinal cord compression include motor dysfunction (weakness with associated reduction in mobility and/or sphincter disturbance with incontinence), sensory changes (paresthesia and loss of sensation), and autonomic dysfunction (urinary hesitancy and retention). At presentation patients tend to be more paraparetic than paralyzed and tend to be less aware of the sensory changes. Sphincter disturbance is usually a poor prognostic sign with regard to preservation or improvement of ambulatory status.

Patients with cauda equina syndrome usually present differently, with change in or loss of sensation over the buttock region, posterior-superior thighs, and perineal region. This is described as a "saddle distribution." Reduced anal tone and urinary retention, with overflow incontinence, are typically present.

A study (Husband 1998) of patients with malignant spinal cord compression found that more than half of the patients had lost further neurological function between the onset of symptoms and start of treatment. The majority of delays were attributed to lack of symptom recognition by the patient and diagnostic delay by the primary health provider or at the general hospital.

To prevent further deterioration and maximize the chances of neurological recovery, any new back pain or abnormal neurology that develops in a patient with a known malignancy needs to be investigated immediately, as the diagnosis of spinal cord compression warrants strong consideration.

Clinical symptom	Incidence in patients with spinal cord compression	Features
Back pain	83-95%	Localised or radicular Unilateral or bilateral Often worse at night Can be mechanical (worse with movement)
Motor deficits & difficulty ambulating	35-75%	Often described as 'heaviness or clumsiness' by patient Weakness on examination Can involve upper or lower motor neuron signs depending on level involved
Sensory deficts	50-70%	Change/loss of sensation typically begins distally and ascends as the disease advances
Autonomic dysfunction	50-60%	Bowel or bladder symptoms tend to occur late Rarely a presenting symtom

Fig. 4 Summary of the different clinical presentations of patients with malignant spinal cord compression (Cole and Patchell 2008)

Several studies have shown that patients with the slowest development of motor deficits before treatment had the best functional outcome compared with patients with faster development of motor deficits and that a greater interval from cancer diagnosis to the spinal cord compression independently predicted improved survival (Rades et al. 2002). Each of these factors probably reflects the presence of less aggressive tumors. Subclinical spinal cord compression (radiological evidence of cord compression in the absence of neurological deficits or pain) is also important to recognize as it represents a window for treatment with potentially the best clinical outcomes.

5 Radiological Diagnosis

5.1 Referral to Radiology

A low index of suspicion in a patient with a known malignancy is important. In a patient with the new onset of a neurological deficit, including bowel and bladder dysfunction or limb weakness, where malignant spinal cord compression or cauda equina syndrome is suspected, same-day magnetic resonance imaging (MRI) is important if the patient is deemed fit for treatment and this will be carried out in the same time frame. If a patient is not fit for treatment or would refuse any treatments offered, there is a little benefit in putting the patient through an MRI scan. The MRI scan can take up to an hour and can be an unpleasant experience for a patient, especially one who is in pain. Therefore if an MRI scan will not alter management, consider not referring the patient.

As a suspected spinal cord or cauda equina compression in a patient who is fit for treatment is a medical emergency, a personal phone call to the radiologist to expedite the radiological investigation is helpful. Discussion of the patient's underlying malignancy, symptoms, and signs assists the radiologist in determining the most appropriate imaging techniques and dedicated sequences, including extra sequences through the area of the spine that could be responsible for

the neurological abnormality, to answer the clinical question and to look for other causes of the patient's presentation. It is critical to good radiological investigation that the patient is examined thoroughly. While imaging should include the whole spine, a radiologist who is aware of the neurological findings may detect smaller lesions on the extra, dedicated sequences that would not necessarily be seen on standard sequences.

The referral (or request) should include information about:

- Nature of the known malignancy
- Neurological findings
- Allergies
- Renal function
- Contraindications to MRI (detailed below)

5.2 Patient Care and Optimization of Image Quality

These patients are often in pain and usually anxious. The MRI scanner table is hard and uncomfortable. An examination of the whole spine can take 1 h, and it is imperative that the patient does not move during the examination. Some MRI sequences can take over 8 min, and any movement during this time can result in non-diagnostic images. It is helpful for patients to understand what to expect: radiographers are good at explaining the technical side of MRI to patients but do not have the training or knowledge of the clinical situation to be able to provide a more holistic explanation. For patient comfort and better diagnostic results, it is helpful for patients to be prescribed an appropriate dose of a suitable analgesic prior to the scan, such as morphine. This should be administered when the radiographers call the ward to arrange transport of the patient to MRI.

5.3 Radiological Techniques

Magnetic resonance imaging (MRI) is the imaging technique of choice (Baur et al. 2002; Jung et al. 2003) (Figs. 5, 6, and 7). Its advantages include:

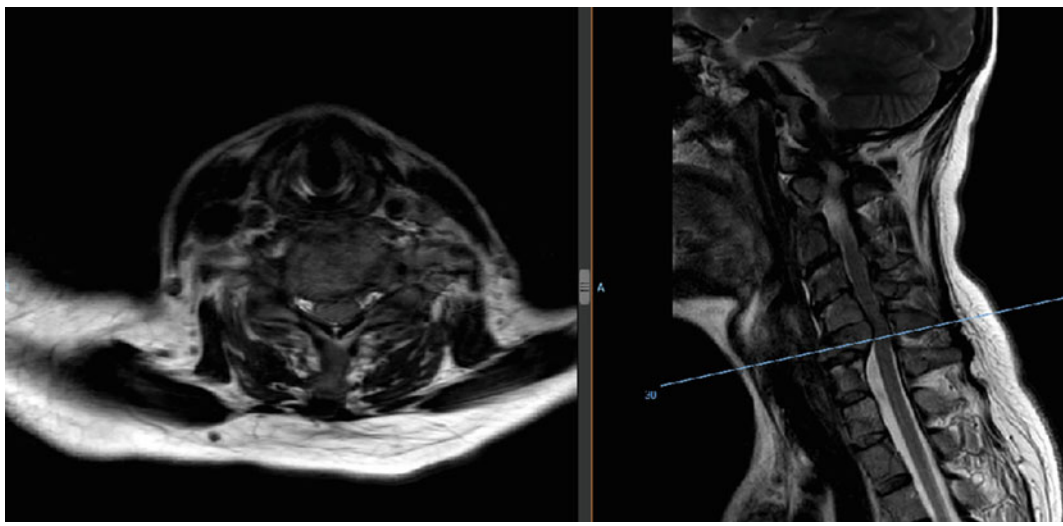

Fig. 5 A 50-year-old female with metastatic breast cancer to the bone only presented with neck pain/tenderness, increased upper limb reflexes, and urinary incontinence. Tenderness over the T5 level with associated bilateral radiating pain was also noted. An axial T2-weighted MR image (on left) through the C6 vertebra and a sagittal T2-weighted MR image of the cervical spine and upper thoracic spine (on right, with blue line demonstrating the level of the corresponding axial image). Confluent tumor at C5 and C6 levels replaces the vertebral bodies, with extension posteriorly into the vertebral canal, resulting in spinal cord compression. The signal return from the spinal cord is within normal limits

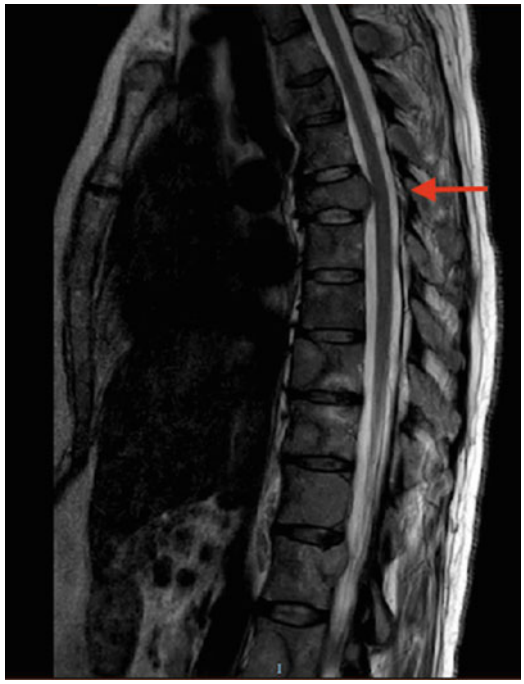

Fig. 6 A T2-weighted sagittal image of the thoracic spine of the same patient demonstrating a lesion in the T5 vertebral body extending into the anterior extradural space and abutting the ventral surface of the spinal cord (red arrow), without signal change within the cord. Numerous metastases involving the entire vertebral column were found on the whole spine images

- The ability to obtain images in any plane: usually at least two perpendicular planes and often three planes
- Good contrast between the relevant tissues including the spinal cord, nerve roots, cerebrospinal fluid, vertebrae, surrounding tissues, and tumor
- Good spatial resolution when the appropriate sequences are obtained and the patient is able to stay very still

There are, however, some disadvantages of MRI. These include:

- A long time required to acquire the imaging
- Patient discomfort if not adequately managed in advance
- Lack of access to MRI, especially for patients in rural locations or in departments where the MRI scanner is heavily booked (there are few opportunities to add in an extra patient with potential spinal cord compression, not least because of the long scanning time required for a full spine MRI)
- Difficulty monitoring patients when in the MRI scanner

MRI has a number of *absolute* contraindications. These include:

- Pacemakers: There are now some pacemakers that are MRI-compatible, but the majority are potentially lethal and without firm evidence of MRI compatibility; a pacemaker is an absolute contraindication.
- Defibrillators and other implanted stimulators.
- Aneurysm clips: The clips currently used by neurosurgeons are MRI-compatible, but many older clips are not. Placing a patient with an incompatible aneurysm clip in the MRI scanner can result in the clip twisting and tearing off the artery with fatal consequences. Unless there is definite proof that the clip type is safe, a patient with an aneurysm clip cannot be placed in the MRI scanner.
- Metal in the eye: Those who weld and grind metal can get metal fragments in the eye. If these have not been removed, then it is not safe to place the patient in the MRI scanner as the metal fragment may move, causing blindness.
- Some heart valves and intravascular stents are absolute contraindications. Definite proof of the nature of MRI-compatible devices is required prior to a patient being allowed in the MRI scanner.

Relative contraindications include:

- Being confused and/or unable to follow instructions. Communication problems can pose a risk with safety screening and an inability to understand the need to stay still for sufficient time to get diagnostic-quality images.
- Claustrophobia can result in a patient being unable to stay still in the MRI scanner or to stay in the scanner at all. Premedication with an anxiolytic can be helpful. The same effect may

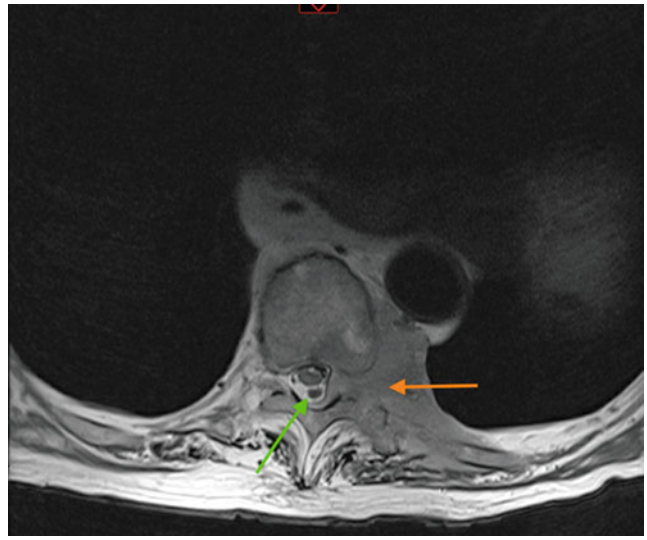

Fig. 7 This 93-year-old patient had metastatic angiosarcoma and presented with mid-lower thoracic radicular pain, radiating in a left T9–T10 dermatomal distribution. An axial T2-weighted MR image of the patient through the T9 level. There is nerve root compression from a left-sided paravertebral mass extending into the vertebral canal through the intervertebral foramen. The spinal cord is displaced to the right. Signal return within the spinal cord is normal (Orange arrow: tumor in the intervertebral foramen. Green arrow: tumor in the vertebral canal)

also be achieved by adequate analgesia with opiates.

- Recent operations with metal implants or clips. These items are problematic with recent operations (due to potential movement) and are considered safe after 6 weeks. Although it is safe to perform MRI after this period, as the prosthesis is fixed and stable, local tissue heating can occur. Patients are asked to let the radiographer know if they start to feel an area of heat. Metal in tattoo pigments can cause a similar effect.
- There is long checklist of other potential contraindications about which the radiographer and radiologist will need to be aware. The radiographer will complete this before an MRI scan can be performed. If the patient cannot speak English (or the language spoken in the country where he or she is being treated), an interpreter will be needed to complete the safety checklist.

If a patient is unable to undergo an MRI scan, then a CT scan and CT myelogram are appropriate imaging techniques. CT myelography is preferred as this more clearly demonstrates the effect of vertebral metastases on the spinal cord and intrathecal nerve roots. This is particularly helpful in the cervical and thoracic spine where a combination of artifacts from surrounding structures and little CSF surrounding the spinal cord can make it technically challenging to interpret a standard CT scan of the spine. Imaging patients with cauda equina syndrome can often be achieved with a CT scan alone. Myelography without a CT scan is no longer the standard of care. The lack of spatial and contrast resolution compromises clinical decision-making. On occasion a CT scan may assist a spine surgeon in planning treatment due to the better delineation of bony structures when compared with MRI. In this instance, the CT scan should be restricted to the region being treated.

The radiology report should always include a description of the extent and location of metastases, the effect (if any) on the spinal cord and nerve roots, any deformities of the spine, and any disease noted in adjacent tissues.

6 Goals of Treatment

The management options and decisions involved are complex for the team treating patients with malignant spinal cord compression. Perhaps the most fundamental question that must first be answered is as follows: *What are the goals of treatment*? The next question that follows is: *Are these goals actually achievable*? For example, the ultimate goal might be to regain the ability to walk, but the achievable goal may be to retain bed mobility and improve the patient's pain levels to enable easier transfers (from bed to chair). These treatment goals should be revisited at each decision point during a patient's management, ensuring that futile treatment is not recommended, and the "bigger picture" is kept in mind. Patients, their carers, and treating teams need to be open and honest about treatment goals.

To answer these questions relating to treatment goals, the key factors to consider are mobility, continence, analgesia, estimated prognosis of the patient, and patient preferences. Active treatments should be explored if ambulatory or sphincter function can be potentially preserved or recovered, or pain levels improved. These treatments include surgical interventions and/or radiotherapy. Best supportive care is imperative for all patients. The overarching treatment aim is always to improve the patient's quality of life.

7 Management Overview and Decision Process

Prompt diagnosis and instigation of appropriate treatment strongly affect the patient's ultimate outcome. The strongest prognostic factor for overall survival and the ability to ambulate after treatment is pretreatment neurological status and specifically motor function (Talcott et al. 1999). Therefore in a patient with known cancer, new back pain or abnormal neurological symptoms or signs should be investigated immediately. If the diagnosis of spinal cord compression is not consistent with the patient's known cancer biology, consideration should be given to arranging a biopsy. This will assist in excluding differential diagnoses, such as osteomyelitis.

Once the diagnosis of malignant spinal cord compression is confirmed, the treatment decisions need to be made quickly by the multidisciplinary team, comprising of the neurosurgeon, oncologists (both radiation and medical), palliative care physician, and community teams including the primary care provider. Urgent neurosurgical opinion should be considered for patients with symptomatic spinal cord compression, as evidence suggests that in selected patients, outcomes are better with decompressive surgery prior to radiotherapy (Patchell et al. 2005). Several national treatment guidelines and protocols suggest that treatment with surgery or radiotherapy ideally should be commenced within 24 h of *radiological diagnosis* for best functional outcome (National Institute for Health and Care Excellence (NICE) 2014; eviQ Cancer Treatments Online (Cancer Institute NSW) 2012), together with other studies confirming better outcomes if surgery is performed within 48 h of *initial presentation of symptoms* (Quraishi et al. 2013).

This initial multidisciplinary decision process may be performed utilizing a "virtual consultation" via telephone or the Internet, especially if the neurosurgical and oncology specialists are geographically distant from the patient. The treatment options can be divided into four categories (surgery, radiotherapy, systemic and supportive care) and will be detailed further in the next sections. Most patients require a combination of these treatments; however the decisions regarding sequencing can be complex.

There are many factors that the multidisciplinary team considers in developing a suitable treatment plan for each patient with malignant spinal cord compression. These can be divided into patient, tumor, and treatment factors (Fig. 8).

All of these factors are then synthesized together to choose the most appropriate treatment recommendation. For instance, for a patient with surgically appropriate disease, who has never received radiotherapy to the spine, with minimal burden of disease, and an excellent expected long-term prognosis, both surgical management and adjuvant radiotherapy would be recommended,

PATIENT FACTORS	Functional impact of symptoms (mobility & continence) Performance status (often measured as EGOG status) (Oken M 1982) prior to onset of syptoms/signs Pain levels Patient preferences Time elapsed since developing symptoms/signs Physical location of patient (distance to travel to hospital for surgery &/or radiotherapy delivery)) Any improvement with dexamethasone
TUMOUR FACTORS	Structural impact of disease (e.g. presence of bony compression and spinal instability) Levels within the spine involved Estimated prognosis • Bone only +/- visceral metastases • True 'oligo-metastatic' disease • Underlying cancer biology/progression
TREATMENT FACTORS	Predicted outcome from active treatments (i.e. potentially reverse or preserve function, or improve pain) Estimated length of time to achieve potential benefit from treatments Technical surgical factors Radio-responsiveness of tumour Response to systemic treatment options Previous treatments (neurosurgical interventions and radiotherapy in particular) Toxicities expected from treatments

Fig. 8 Factors to be considered by the multidisciplinary team in formulating a care plan for patients with malignant spinal cord compression

in addition to exploring aggressive systemic treatment with the best supportive care. For a patient with a poor performance status, previously treated spinal cord compression, who has a short prognosis and has exhausted systemic options, further surgery and/or radiotherapy may not be able to provide any potential benefit, and instead best supportive care alone is probably the best option. These factors will be explored further in the following section with respect to each treatment intervention, but it is important to further elaborate on a few general factors.

Given that the overall aim is to improve the patient's quality of life, it is extremely important to consider the premorbid level of function of the patient and what improvements are achievable. At best, interventions are able to reverse neurological abnormalities back to the patient's baseline level and eradicate pain. In practice this can be difficult to achieve, and therefore an honest and accurate estimation of "possible" versus "likely" benefit needs to be discussed with the patient and carers. Pain can be temporarily improved with steroid medication and analgesia, together with pressure care, insertion of indwelling urinary catheters, and other important supportive care measures. For more durable analgesia benefit, surgery and/or radiotherapy are the best options.

Estimated overall disease prognosis can be very difficult to predict accurately, despite many tools being developed (Krishnan et al. 2013), and probably deserves its own separate chapter. Essentially, if a patient has had a long disease-free interval (from diagnosis or last episode of disease progression to the development of spinal cord compression), has promising systemic options, or has oligo-metastatic disease, then they are likely to have a longer prognosis. Patients with particular tumor biologies (e.g., metastatic prostate cancer or receptor-positive breast cancer with bone-only disease) may also have better prognoses. The oncologist and palliative care physician who know the patient most closely are best placed to make this prognosis estimation.

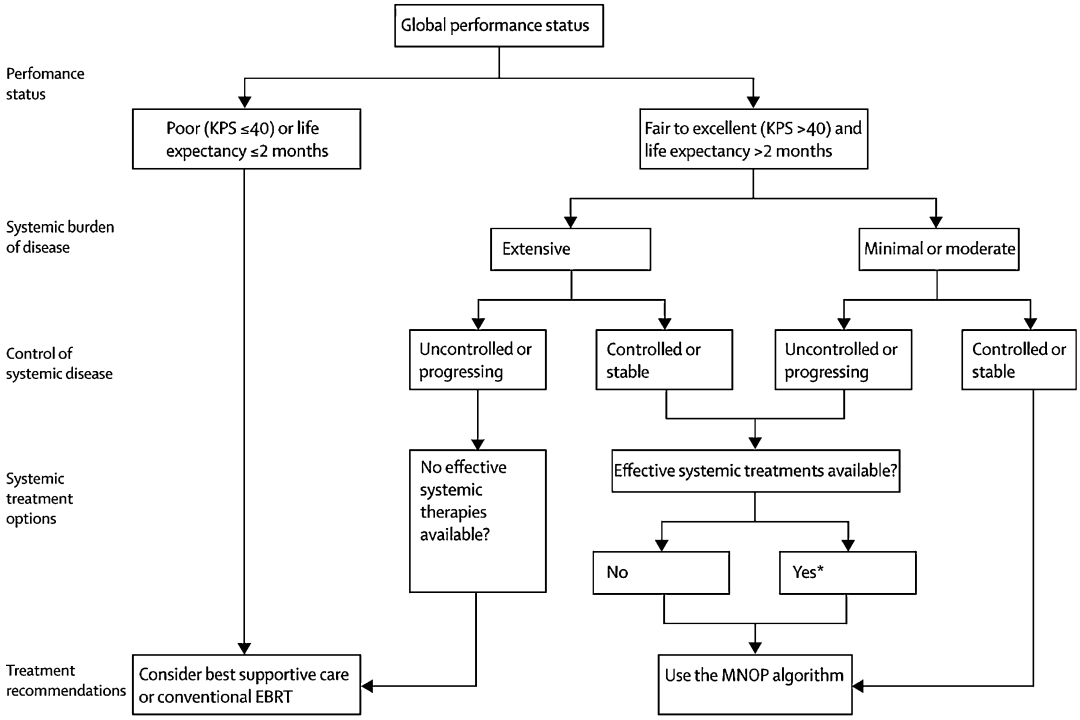

Fig. 9 Algorithm 1: initial assessment algorithm for patients with spinal metastases. *KPS* Karnofsky Performance status, *EBRT* external beam radiotherapy, *MNOP* mechanical, neurological, oncological, preferred treatment. *For selected patients with effective systemic therapy treatment options, systemic therapy without the use of radiotherapy might be most appropriate

For surgery and/or radiotherapy to achieve potential overall benefit, the predicted prognosis must be long enough to allow these treatments to be delivered, the toxicities managed, the patient to recover, and the best possible treatment outcomes realized. In the case of combined surgery and radiotherapy, a good rule of thumb is that if overall prognosis is less than 3 months, the patient may not live long enough to recover from the operation and anesthetic, proceed to radiotherapy (often five daily treatments over 1 week), heal from side effects, and await the 4–6 weeks it usually takes for maximal analgesia response and the initial consolidation of the structural benefit from radiotherapy. This has to be balanced by the patient's wishes and acceptance of potentially spending a prolonged period of time either in hospital or away from their usual place of residence, to receive these treatments.

Essentially the long-term benefits of an invasive, timely, or costly procedure might not manifest in patients with a short life expectancy. Furthermore, an overly aggressive treatment approach might cause more harm than benefit in patients who are frail and neurologically debilitated, or who are dying (Spratt et al. 2017). A number of algorithms have been developed to assist management teams in deciding appropriate treatment. The recent Lancet oncology review by Spratt et al. summarizes one such approach in patients with spinal metastases (Figs. 9 and 10) (Spratt et al. 2017). Spinal cord compression is detailed in the far-right portion (red box) of the MNOP (mechanical, neurological, oncological, preferred treatment) algorithm (Fig. 10).

8 Neurosurgical Intervention Overview

Surgical treatment in the management of malignant spinal cord or cauda equina compression remains controversial and difficult. It is not always an available option. The commonest treatment options are decompression, stabilization, or

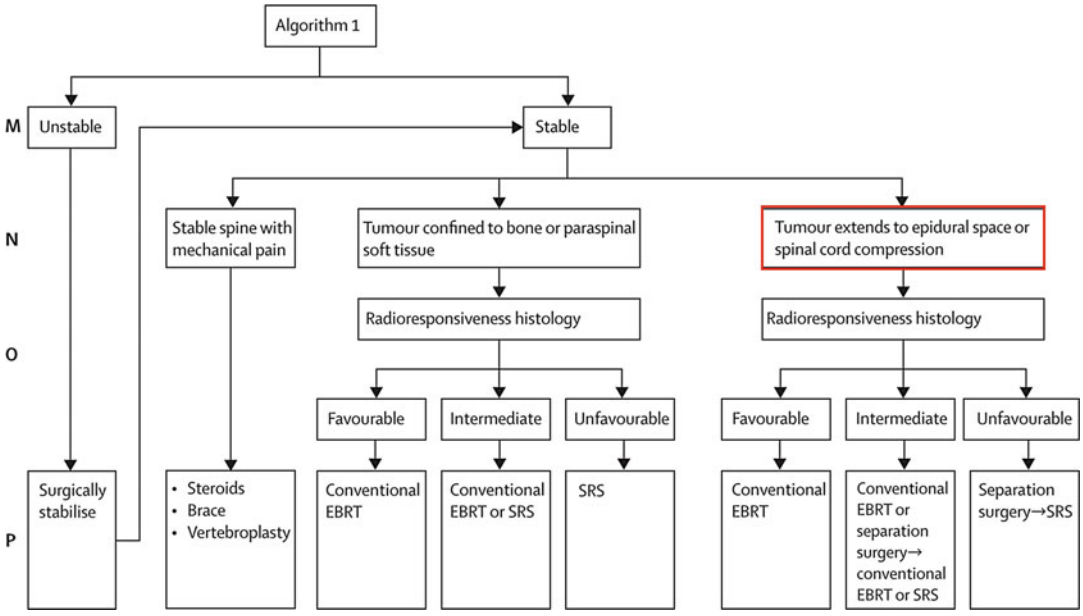

Fig. 10 MNOP algorithm for management of spinal metastases. Spinal cord compression is detailed in the far-right portion (red box). *MNOP* mechanical, neurological, oncological, preferred treatment, *EBRT* external beam radiotherapy, *SRS* stereotactic radiosurgery

both. The best-known studies showed that decompression alone produced a similar or worse outcome when compared with radiotherapy alone for malignant spinal cord compression, due to the destabilizing influence of the operation (George et al. 2015). For this reason, the majority of patients who now have surgery for spinal cord compression will have decompression combined with a form of stabilization. The preferred option is to make the decision and enact it, *prior* to the onset of major symptoms and signs. Prolonged paraplegia in a patient from malignant compression will generally not resolve with surgery.

The typical goals of surgery are:

1. Prevention of neurological deterioration
2. Restoration of neurological function
3. Treatment of pain from compression
4. Fracture stabilization for pain control and prevention of progressive deformity

The decision to operate needs to be based on the assessment of the value to the patient from the procedure. The questions that need to be asked are:

What does the patient want?

Patients will usually have an opinion in regard to what they are prepared to go through. This will depend on their expectations of the outcome. The potential outcomes must not be overstated. Surgery is going to be associated with a period of convalescence and likely rehabilitation, and the patient may not want to go through this.

Is surgery technically possible and what are the risks?

A surgical opinion with review of the radiology prior to discussion with the patient is invaluable, as many patients are not technically suitable for surgical intervention or the procedure will be too large considering the patient's condition.

Is the patient fit for any operation planned?

Surgery is precluded if the patient cannot have a prolonged anesthetic, is unable to stop any blood thinner medications, or is neutropenic or thrombocytopenic.

Is there a significant benefit to the patient from the surgery?

If the patient cannot walk prior to the surgery and has a predicted survival of less than 3 months, they are unlikely to walk again. If a patient has severe pain and has an unstable crush fracture, then stabilization should reduce the pain substantially which will significantly decrease medication requirements and hopefully supportive care measures, thereby improving quality of life.

What is the patient's life expectancy?

The only surgery that should be entertained in patients with short life expectancy is for the treatment of pain. If there is a long life expectancy, then it is appropriate to consider treatment early, as prevention of fractures and subsequent pain, kyphosis, and neurological deficit is ideal.

Rate of growth of the tumor and alternative treatment options?

In the palliative treatment of metastatic cancer involving the spine, it must be remembered that surgery is a temporary option, as the tumor will recur. If the lesion is radioresistant and there are no medical options, then even with surgical treatment, there is likely to be residual disease, and hence regrowth will occur at the known existing disease progression rate.

Should radiotherapy/radiosurgery be used perioperatively?

Conventional radiotherapy will affect tissue healing. If the patient has already had radiotherapy and subsequent surgery is planned, postoperative wound breakdown and infection will be much more likely. If stereotactic surgery to the tumor bed is planned, insertion of metal hardware may cause scatter of the radiation and affect the ability to plan the radiotherapy accurately. Preoperative radiosurgery, if time permits, may be a better and simpler option. If postoperative radiotherapy is planned, a period of at least 2 weeks is usually required for surgical healing, prior to fractionated radiotherapy.

9 Neurosurgical Procedures

9.1 Laminectomy

This involves the removal of a lamina from the back of the spine, thereby exposing the vertebral canal and allowing access to the spinal cord and any tumor around it. This is only suitable for patients who do not have any instability and predominately posterior and lateral extradural compression.

9.2 Stabilization Alone

This is usually a posterior procedure in the thoracic and lumbar spine. It involves the insertion of screws into the pedicles of the vertebral bodies and the linking of the screws to a rod that will cross an unstable segment of fracture. It can be imagined as an internal fixture or scaffolding. These are now usually constructed from titanium and, if done without other procedures, will be performed by a minimally invasive or percutaneous technique. Stabilization can be used in combination with external beam or stereotactic radiotherapy where tumor control would be adequate with radiation alone, but there is a risk of vertebral collapse.

9.3 Laminectomy with Posterior Stabilization

This is a combination of the above two procedures and allows for a more extensive bone removal and hence a wider decompression. In this combined procedure, the decompression may extend to involve the pedicles and part of the vertebra, which may then cause instability that needs to be treated with the stabilization. It may be a completely open procedure or combined with a minimally invasive technique.

9.4 Vertebrectomy with Stabilization

If the vertebra needs to be removed, this usually involves an anterior approach, but some surgeons will do certain levels from a posterior approach. The complexity and size of the operation increases from less complex in the cervical spine to much more complex in the lumbar spine. At most levels in the cervical spine, vertebrectomy with stabilization is relatively uncomplicated. Anterior surgery at vertebral levels C1 and C2 is not indicated in the palliative setting because of its complexity and risks. Similarly anterior surgery at vertebral levels T3–T5 is best avoided in the palliative setting. These levels are best treated from behind. If there is a high degree of instability either from the tumor or the operation, then an anterior decompression will be combined with posterior stabilization. Anterior surgical procedures in the lumbar and thoracic spine are less likely to be entertained in the palliative setting because of the risks.

10 Surgical Recovery and Length of Hospital Stay

Recovery from an operation will depend on the scale of the procedure undertaken and the preoperative state of the patient. An elective straightforward minimally invasive procedure over five thoracic vertebral levels with no preoperative deficit will typically involve a hospital stay of between 3 and 5 days in this patient group. A cervical vertebrectomy with anterior stabilization alone will be closer to 2 days.

11 Interventional Radiological Procedures

11.1 Vertebroplasty

Vertebroplasty is the fluoroscopically guided, percutaneous injection of bone cement into a vertebral body. Vertebroplasty will not relieve spinal cord compression; however, it can be helpful in relieving mechanical pain and stabilizing a vertebra at risk of fracture, particularly if the disease is within the vertebral body. As vertebroplasty is minimally invasive, it does not require a prolonged healing time before other treatments can be started.

11.2 Tumor Embolization

Very vascular tumors, such as renal carcinoma, may be rendered easier to treat surgically if embolized by a neuroradiologist and thereby made less vascular, prior to operation. Embolization can be performed using particles, coils, glue, or ethylene vinyl alcohol and may also contribute to reduction in a pain and neurological symptoms.

11.3 Image-Guided Tumor Ablation

There are a variety of radiological ablative techniques available, such as radiofrequency ablation, microwave ablation, thermal ablation, and cryoablation. These are typically used to treat painful metastases or as further treatment to areas previously irradiated. They are not used to treat acute spinal cord compression.

12 Radiotherapy

Radiotherapy is the mainstay of treatment for spinal cord compression and is given in combination with surgery, when appropriate. The main aims of radiotherapy are to reduce tumor bulk and pressure on the spinal cord and/or nerve roots, consolidate the mechanical benefit from surgery, and hopefully provide durable tumor control. Therefore, in a similar way to surgery, the overall goals with radiotherapy are to:

1. Prevent further neurological deterioration.
2. Restore neurological function.
3. Reduce pain.

It is important to note that even in the situation where any neurological improvement is unlikely,

radiotherapy can still potentially palliate symptoms of pain and improve quality of life. The maximal benefits from radiotherapy usually takes 4–6 weeks to occur, so this needs to be considered in making decisions.

There are two main types of radiotherapy: conventional external beam radiotherapy and stereotactic radiotherapy, which will be discussed in more detail below. Radiotherapy can be given as a single dose or fractionated into several smaller doses. Prior to starting radiotherapy, all patients should be considered for a full spine MRI, and commenced on corticosteroids (up to 16 mg dexamethasone a day in divided doses) as soon as the diagnosis is suspected. There is little evidence that higher doses are more effective (George et al. 2015; Loblaw and Mitera 2012), but serious adverse events are frequently higher with high-dose steroids, as expected. If the patient is receiving concurrent cytotoxic chemotherapy or immunotherapy, the potential increased risk of side effects with the radiotherapy needs to be considered and discussed with the patient and medical oncologist. Early radiotherapy-associated toxicities (e.g., esophagitis or erythematous skin reaction) tend to peak approximately 7–10 days after radiotherapy is completed and are specific to the area treated. They should be monitored and managed until resolution occurs. Late radiation reactions are rare in this setting.

12.1 Radiotherapy Simulation (Set-Up Position and Planning)

For radiotherapy to be effective, it needs to deliver the prescribed dose to the correct location within the body, with an accuracy of millimeters. This is achieved by ensuring the patient has adequate analgesia prior to simulation and each treatment and is able to lie in a comfortable and reproducible position. Often a patient-specific molded vacuum bag is used to help keep the patient immobilized in a comfortable position, together with small tattoo marks that are used to line the patient up in the correct position via laser beams on the treatment machine (Fig. 11a, b). A CT simulation image is usually acquired prior to starting treatment, and the radiotherapy is planned from this. In an emergency this process is simplified and often condensed to a single step.

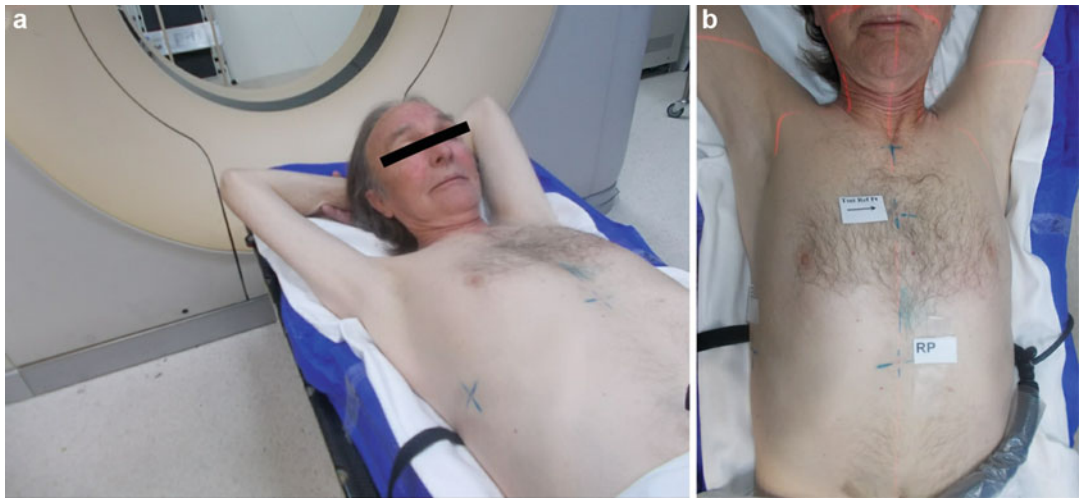

Fig. 11 (**a**) Patient lying supine on radiotherapy CT simulation couch for planning purposes. Blue vacuum bag is under patient. (**b**) Close-up photograph of treatment reference points (to be tattooed). This will assist with repositioning patient in the same position for radiotherapy treatment

12.2 Types of Radiotherapy

Conventional external beam radiotherapy is the most common technique used to treat spinal cord compression. It is a noninvasive method of delivering radiation to the tumor and surrounding structures (often the vertebral body above and below the level of concern) and is usually delivered using one to three radiotherapy beams (Fig. 12), depending on the location of the spinal cord or cauda equina compression. The radiation beams are shaped as they come out of the linear accelerator before they reach the patient to ensure they are directed at the tumor.

Stereotactic radiotherapy is another noninvasive technique but is more conformal using many smaller beams entering the body from a number of different angles. This means the radiotherapy dose distribution more closely matches the tumor and vertebral body (Fig. 13), avoiding nearby structures (particular organs at risk) compared with conventional external beam

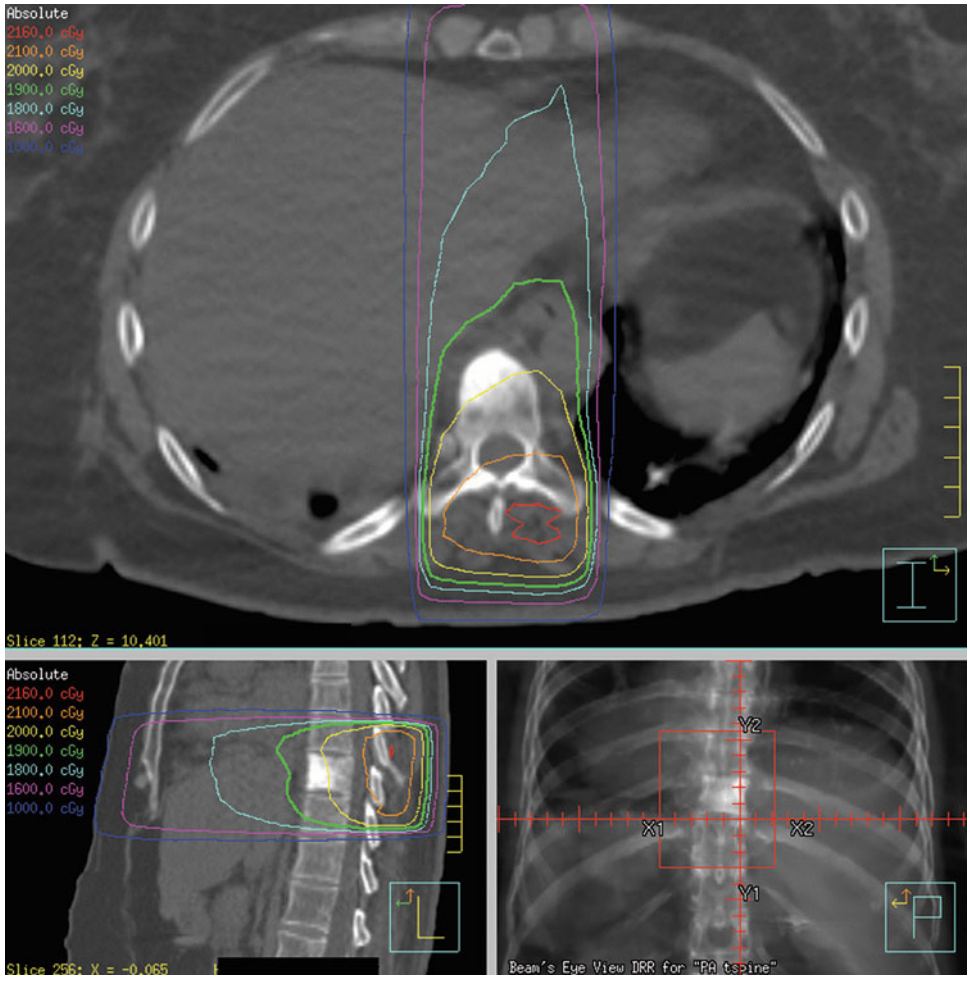

Fig. 12 Dosimetry of a conventional external beam radiotherapy plan for a patient with a single bone metastasis at T9 level. A single posterior beam is delivered, to a total dose of 20 Gy in five daily fractions. The green line is 95% of the prescribed dose. There is exit dose through the liver and stomach, potentially causing some mild temporary nausea

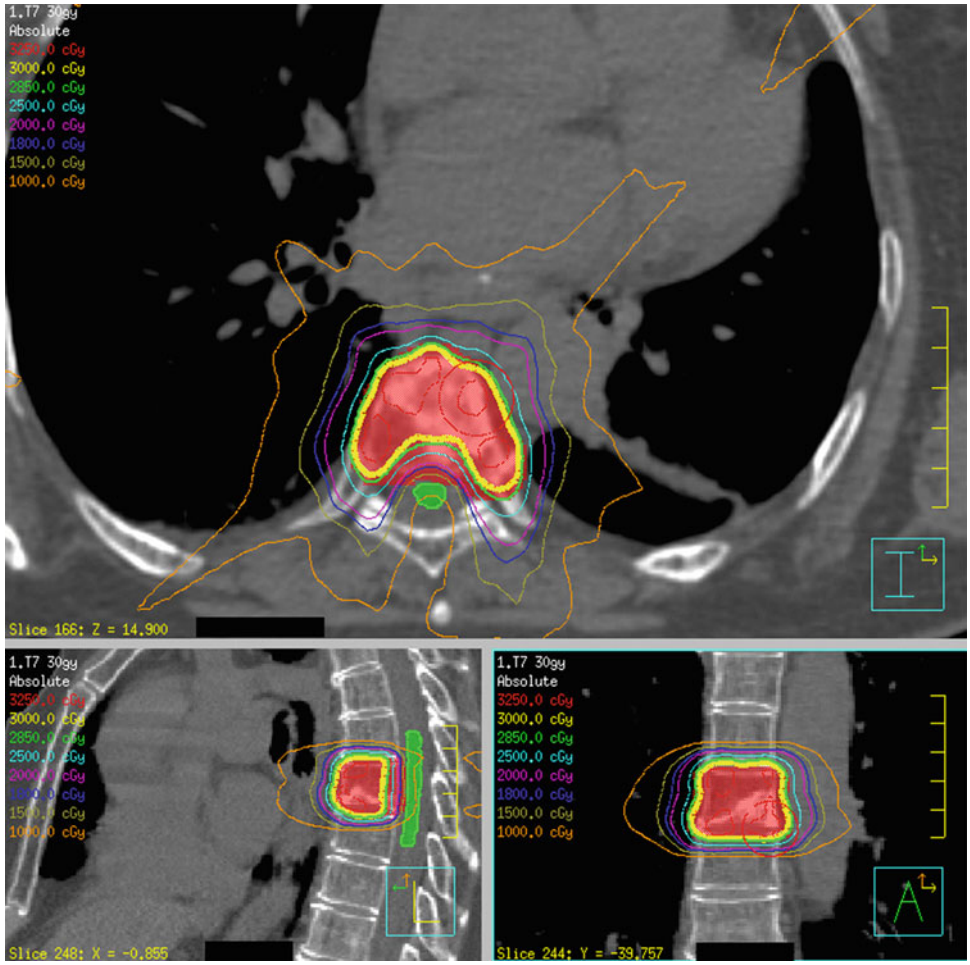

Fig. 13 Dosimetry of a stereotactic radiotherapy plan for a patient with a single bone metastasis at T7 level. Nine beams are delivered, to create a total dose of 30 Gy in four daily fractions. The yellow line is 100% of the prescribed dose and can be seen wrapping around (and therefore sparing) the spinal cord. There is minimal exit dose as the dose is highly conformal, therefore less toxicity to nearby organs

radiotherapy (Faculty of Radiation Oncology, The Royal Australian and New Zealand College of Radiologists 2017). Stereotactic radiotherapy is able to deliver a higher biological dose because it is better able to avoid normal healthy tissues and therefore requires tighter margins, a stricter set-up, and the patient to be very compliant and immobile during treatment planning and delivery. This higher biological dose may be particularly beneficial for tumor histologies (e.g., sarcoma, renal cell carcinoma, and melanoma) that have traditionally been regarded as relatively radioresistant.

While conventional external beam radiotherapy is widely available and easily delivered, stereotactic radiotherapy is more complex and may not be available in all situations. Stereotactic radiotherapy is unlikely to be used in an emergency situation because of the additional time required for planning and treatment verification. There are however two main advantages with stereotactic radiotherapy. Firstly, in a non-emergency situation for a patient with good prognosis disease, who has limited spinal metastases, the radiation oncologist may want to increase the radiotherapy dose to hopefully improve local

control in the longer term (Loblaw and Mitera 2012). This may be given preoperatively (prior to insertion of surgical hardware) so that the radiotherapy dosimetry and treatment verification are more accurate. The second benefit of stereotactic radiotherapy is for patients who have had previous external beam radiotherapy to the same spinal level and have a good performance status and a malignancy with a good prognosis. In this situation there may be an opportunity to offer re-treatment with stereotactic radiotherapy, with the advantage of sparing the spinal cord (avoid dose being deposited there) and a reduction in the treatment volume (therefore avoiding other normal tissues receiving additional dose). These are complex decisions and treatments requiring multidisciplinary discussion. Currently in the United States, the RTOG 0631 trial is comparing stereotactic radiotherapy with conventional external beam radiotherapy and includes patients with a limited (one to three) number of spine metastases, with or without minimal extradural compression (RTOG Foundation Inc 2016).

12.3 Dose Fractionation

The radiation oncologist chooses the "best-fit" radiotherapy dose and fractionation schedule, depending on the factors that were listed earlier in Fig. 8. The total dose and the number of radiotherapy treatment fractions (#s) vary widely (George et al. 2015). Various doses are acceptable for conventional external beam radiotherapy, including a single 8 Gy #, 16 Gy in 2 × 8 Gy#s delivered 1 week apart, 20 Gy in five daily #s delivered over a week, or 30 Gy in 8#s delivered over 2 weeks (4 days break in the middle of split course). Consideration should also be given to weekend treatment, especially early on in a fractionated course, or with the single doses. Higher doses may be considered for patients who are of excellent performance status, have limited disease, and have a long disease natural history. Stereotactic spine radiotherapy dose schedules also vary widely and include single 8–24 Gy fractions and multi-fraction dose schedules of 27–30 Gy in 3–5#s (Huo et al. 2017).

12.4 Efficacy and Outcomes

Radiotherapy is the most widely used treatment in the management of malignant spinal cord compression. A Cochrane Review (George et al. 2015) included six randomized trials ($n = 544$) of which Patchell et al. (2005) was the only trial to compare surgery with radiotherapy (RT) versus radiotherapy alone. This trial reported the following outcomes:

- Overall ability to walk after treatment was 84% (surgery + RT, RR 0.67, CI 0.53–0.86) vs. 57% (RT alone) (Patchell et al. 2005).
- Ability to walk was maintained by 94% (surgery + RT) vs. 74% (RT alone) ($p = 0.024$), with the median length of time able to walk being 153 days (surgery + RT) vs. 54 days (RT alone) ($p = 0.024$).
- Regaining ability to walk after treatment was achieved by 62% (surgery + RT) vs. 19% (RT alone) ($p = 0.01$), with non-ambulant surgical patients walking for a median of 59 days vs. 0 days (RT alone) ($p = 0.04$)
- Median survival was 126 days (surgery + RT) vs. 100 days (RT alone) ($p = 0.033$).
- Serious adverse effects (perforated gastric ulcer, psychosis, and death due to infection) were reported in 17% of patients receiving high-dose corticosteroid (96–100 mg dexamethasone) vs. 0% in moderate-to-low-dose (10–16 mg dexamethasone) patients (George et al. 2015).

This Patchell study excluded patients with poor prognosis (<3 months survival), multiple levels of spinal cord compression, and radiosensitive tumors (lymphomas, leukemia, multiple myeloma, and germ-cell tumors). It is important to note that patients with pathological fractures and spinal instability were included in the randomization, a situation which radiotherapy alone would not be expected to reverse and may have contributed to the poorer ambulatory outcomes in the radiotherapy-alone arm. A requirement of the trial was neurosurgical anterior decompression within 24 h of diagnosis, which may not be achievable in many settings. Again it is important

to note that even in patients with poor-prognosis disease, not suitable for surgery, or where neurological deficit reversal is unlikely, radiotherapy alone may still improve pain control and hence overall quality of life.

In terms of radiotherapy dose fractionation, the evidence suggests that single-fraction radiotherapy 8 Gy is just as effective as multiple fractions in patients with poor prognosis (<6 months survival) and no indication for primary surgery (diagnostic doubt, vertebral instability, bony impingement as the cause of spinal cord compression, or previous radiotherapy of the same area). No significant differences in overall survival, ambulation, duration of ambulation, pain response, and bladder control were reported in the two randomized controlled trials (Maranzano and Bellaviat 2005; Maranzano and Trippa 2009) comparing dose schedules (single versus multiple fractions) in these poor-prognosis patients.

For patients with a good prognosis, the use of surgery and radiotherapy should be considered where appropriate. Local tumor recurrence (within the radiotherapy field) may be more common, and consequently re-treatment rates higher, with a single dose, compared with higher-dose short-course radiotherapy schedules. Hence in patients who are expected to live longer, higher doses of radiotherapy are often prescribed, despite minimal evidence comparing radiotherapy schedules in patients with spinal cord compression and a good prognosis (George et al. 2015).

12.5 Early and Late Toxicities

Early radiotherapy toxicities are usually temporary, occurring midway during the radiotherapy course, peaking within 7–10 days of finishing, and usually resolving within approximately 4 weeks of radiotherapy course completion. These side effects will vary depending on the level of the spinal cord compression being treated (other organs/tissues within the RT field) and the dose delivered and may include:

- Esophagitis
- Nausea and vomiting (if the stomach in the radiotherapy field)
- Diarrhea (if bowel in the radiotherapy field)
- Alopecia (within the radiotherapy field only)
- Pneumonitis (if a significant volume of the lung is within the radiotherapy field)
- Skin reaction (includes itch, erythema, dry desquamation, but rarely moist desquamation at these lower doses) where the radiotherapy enters or exits the body
- Fatigue which is *independent* of the radiotherapy site and instead related presumably to cytokine release

Late radiotherapy toxicities are rare at these low palliative doses but may be permanent, usually occurring months to years after radiotherapy. Chronic progressive myelopathy is the main late side effect that must be considered. The estimated risk of myelopathy is low (<1%) for the conventional external beam radiotherapy dose schedules described above but may increase with dose-escalated stereotactic radiotherapy schedules (if spinal cord dose is not appropriately avoided) or in re-treatment settings (Kirkpatrick et al. 2010).

12.6 Re-treatment for Recurrent Spinal Cord Compression

Patients should be followed up clinically and/or radiographically to determine whether a local relapse develops. As with the first spinal cord compression diagnosis, prognosis, the probability of neurological recovery, and time to neurological recovery are highly dependent on pretreatment neurological status (Loblaw and Perry 2005). Patients should be considered for surgical decompression with or without radiotherapy first, because salvage rates seem to be better despite higher complication rates (Patchell et al. 2005). If a patient is not medically and surgically operable, radiotherapy with or without steroids should be given. Consideration needs to be given to the cumulative dosage of the combined radiotherapy courses, and therefore technique of radiotherapy

should be chosen to keep the cumulative dose of radiotherapy as low as possible to reduce the risk of myelopathy. Newer radiotherapy techniques such as stereotactic radiotherapy can be used to minimize cord dose (Loblaw and Mitera 2012; Ryu et al. 2010).

13 Systemic Treatments

A detailed explanation of all systemic agents that may be beneficial in patients with malignant spinal cord compression is beyond the scope of this chapter. Systemic agents include cytotoxic chemotherapy, immunotherapy, biological targets, hormonal therapy, and bisphosphonates. Each of these may have a role in different tumor subtypes, depending on the background performance status of the patient, burden of disease, previous systemic therapies received, and likelihood of benefit versus expected toxicities. However, these systemic agents are usually not suitable as primary treatment in the emergency setting for acute malignant spinal cord compression. Instead radiotherapy, surgery, or a combination of both is required.

For certain tumor biologies, the inclusion of systemic agents is of greater importance. In the case of multiple myeloma, although surgery and radiotherapy remain the primary approaches to treat malignant spinal cord compression, systemic therapy such as chemotherapy agents with steroids and either proteasome inhibitors or immunomodulatory drugs, with or without high-dose chemotherapy and stem cell transplantation, works rapidly and can be used instead of radiation in selected patients if there is minimal neurological deficit (Sen and Yavas 2016).

14 Supportive Care

Supportive care of all patients presenting with spinal cord compression is of utmost importance. This includes commencing corticosteroids, appropriate analgesia and aperients, exclusion/management of hypercalcemia, consideration of insertion of an indwelling urinary catheter, attention to pressure care, thromboprophylaxis, and referral to allied health and palliative care services if not already in place. The option of "best supportive care" without the active intervention of surgery and/or radiotherapy should always be considered and discussed with the patient and family if appropriate. Anxiety and depression are common in patients with cancer, and a referral to a psychosocial practitioner should be considered (eviQ Cancer Treatments Online (Cancer Institute NSW) 2012).

15 Conclusion

Spinal cord compression needs to be considered in all patients who have a malignancy and present with new or escalating back pain and/or abnormal neurology. Spinal cord compression is an emergency that must be diagnosed quickly, ideally with an MRI of the whole spine, urgent multidisciplinary input, and management instigated promptly. The best outcomes occur when the degree of premorbid neurological deficit is minimal and the diagnosis and treatment initiated within 24–48 h of presentation. Decompressive surgery with stabilization, followed by radiotherapy, in appropriately selected patients should be considered for best outcomes. Short courses or single fractions of radiotherapy (without surgery) are appropriate for patients with a predicted survival of less than 3 months, particularly if they are ambulant and have radiosensitive disease. Radiotherapy given to patients with very poor prognosis may still improve pain levels and quality of life, despite minimal improvement in neurological function.

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Superior Vena Cava Obstruction

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Belinda A. Campbell, John M. Troupis, and Jonathan Langton

Contents

Abstract

In the current era of increased availability and frequency of surveillance imaging for oncology patients, superior vena caval obstruction (SVCO) is often an incidental finding in asymptomatic patients. Less commonly, SVCO may present with advanced symptomatology, and in these cases the SVCO may represent rapid disease progression and/or the first presentation of malignancy. Contrast enhanced computed tomography (CT) is exceptionally useful for the diagnosis of SVCO, and often reveals extrinsic compression by mediastinal lymphadenopathy as the

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_73

more common mechanism for malignant SVCO. Non-small cell and small cell lung cancers constitute the more common histologies, with metastatic mediastinal lymphadenopathy or direct mediastinal invasion causing the SVCO. Radiotherapy is the traditional treatment of choice for patients with SVCO. For patients with severe symptoms, treatment of SVCO constitutes a medical emergency and requires urgent treatment with endovascular stenting to restore patency and produce rapid relief of potentially life-threatening symptoms.

1 Introduction

Superior vena caval obstruction (SVCO) is a changing entity in palliative care and oncology practice. The advent of improved radiological imaging, and its more widespread availability for the follow-up of cancer patients, has meant that SVCO is more frequently detected early while it is still asymptomatic. As such, the severe symptomatology that was not infrequently seen in the past is now a less common phenomenon in modern clinical practice. Nonetheless, left untreated, SVCO has the potential to cause significant symptomatology, undermining quality of life and potentially impacting on patient survival. In this chapter, the etiology, clinical features, radiological features, and management options of SVCO are discussed. For the purposes of this book, this chapter will focus on malignant etiologies of SVCO in the setting of palliative care.

2 Pathophysiology and Etiology

The superior vena cava is the major route for venous return to the heart from the head, arms, and upper torso. Despite the high flow volume, the superior vena cava is a relatively low pressure and thin walled structure that is readily compressible by adjacent masses arising in the superior or middle mediastinum. Slowly progressive SVCO allows for the development of a collateral blood-flow network, with enlargement of alternative draining pathways via the azygous, hemiazygous, intercostal, mediastinal, paravertebral, thoracoepigastric, internal mammary, thoracoacromioclavicular, and anterior chest wall veins. Therefore, in slowly progressive SVCO, this collateral venous network can alleviate the symptom development related to the venous congestion that is seen in more rapid onset SVCO.

SVCO may result from extrinsic or intrinsic luminal narrowing of the superior vena cava. In the current medical era, the most common cause of SVCO is due to luminal occlusion from malignant mediastinal masses (60–85% of cases of SVCO) (Lepper et al. 2011; Straka et al. 2016). However, as the utility of intravascular devices (e.g., catheters, pacemakers) increases, thrombus is an increasingly common, nonmalignant cause of SVCO. Infectious causes (e.g., tertiary syphilis) of SVCO are now rarely seen since the advent of antibiotic therapy.

The more common malignant causes for SVCO include non-small cell lung cancer (22–57%), small cell lung cancer (10–39%), and lymphoma (1–27%) (Straka et al. 2016). In these cases, obstruction may arise from extrinsic compression of the SVC by enlarged mediastinal lymph nodes or by direct invasion into the SVC. Of note, SVCO is the first presentation of malignancy in up to 60% of patients with a malignant SVCO (Lepper et al. 2011).

3 Symptoms and Clinical Features

The clinical features of SVCO are determined by the degree of increased venous pressure in the upper body. Typically, patients present with dyspnea and swelling of the upper body. Elevated venous pressure results in interstitial edema of the head, neck, arms, and upper thorax, and edema of the larynx or pharynx can cause hoarseness, cough, dyspnea, dysphagia, and stridor. On further examination, the jugular veins appear distended. Characteristically, visibly dilated veins are seen on the anterior chest wall, and are noncollapsing above the level of the heart, consistent with the venous distension of collateral

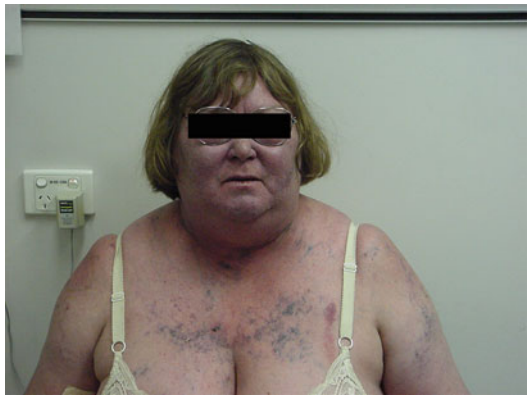

Fig. 1 Clinical photograph of a patient presenting with superior vena cava syndrome secondary to lung cancer with mediastinal lymph node metastases. Note the presence of visibly dilated veins on the anterior chest wall and upper arms, edema of the upper body, facial plethora, and cyanosis (Photograph kindly provided with permission to print by Professor David L. Ball, Peter MacCallum Cancer Centre, Australia)

vessels (Fig. 1). Facial plethora and cyanosis are less commonly presenting signs. Rarely, the patient may present with symptoms of cerebral edema, a serious and life-threatening consequence of SVCO, with headache, confusion, dizziness, and altered conscious state.

As previously mentioned, the severity of symptomatology depends not only on the degree of SVC compression, but also the rate of onset. Slowly progressive SVCO allows for the development of collateral venous channels, and thus the classically recognized symptomatology of SVCO may not be seen. A classification scheme for the grading of SVCO symptomatology was proposed by Yu et al. in 2008 (Table 1), patterned after the Common Terminology Criteria for Adverse Events (CTCAE) v3.0 of the National Institutes of Health (Yu et al. 2008). In this proposed grading system for SVCO, a grade of 0 to 5 is defined based on the severity of signs and symptoms attributable directly or indirectly to the underlying SVCO. An important distinction is the acknowledgment and differentiation of nonsevere, severe, and life-threatening situations. The majority of patients with SVCO are likely to present with mild or moderate symptomatology (75%); the remaining patients are likely to be asymptomatic (10%) or experience severe (10%) life-threatening (5%) or fatal (<1%) symptoms (Yu et al. 2008).

4 Radiological Features

4.1 Anatomy

The superior vena cava (SVC) is responsible for returning blood to the right heart from the upper limbs, neck, and head. It is formed from the confluence of the right and left brachiocephalic veins and drains into the right atrium and courses along the right side of the middle mediastinum, adjacent to the trachea and ascending aorta, which are both to the left. In healthy adults, free of cardiopulmonary disease, it has been assessed with high-resolution electrocardiography (ECG) – gated computed tomography (CT) angiography as measuring between 1.08 and 4.42 cm in cross-sectional area (Lin et al. 2009).

Inferiorly, the azygos vein, which extends from the abdomen, right and anterior to the thoracic vertebrae, inserts into the SVC after passing over the right tracheobronchial angle at the level of the carina. The azygous vein connects with the distal SVC from the posterior aspect.

Further smaller tributaries include esophageal, pericardial, and mediastinal veins (Gray 1918). Most draining veins are connected by smaller plexuses that are normally not well appreciated on routine cross-sectional imaging.

When the SVC is obstructed, the brachiocephalic veins, mediastinal venous plexus, and the tributaries dilate as a means of creating collateral venous circulation.

4.2 Imaging Modalities and Features of SVCO

Imaging modalities vary considerably in their clinical utility for sensitivity and specificity in the diagnosis of SVCO.

4.2.1 Chest X-ray

Chest radiography may demonstrate widening of the upper right mediastinal border suggesting

Table 1 Proposed grading system for superior vena cava syndrome (Yu et al. 2008) (Permission to reprint kindly provided by Elsevier and Dr. Frank Detterbeck, Yale Cancer Center, USA)

Grade	Category	Estimated incidence (%)	Definition[a]
0	Asymptomatic	10	Radiographic superior vena cava obstruction in the absence of symptoms
1	Mild	25	Edema in head or neck (vascular distention), cyanosis, plethora
2	Moderate	50	Edema in head or neck with functional impairment (mild dysphagia, cough, mild or moderate impairment of head, jaw or eyelid movements, visual disturbances caused by ocular edema)
3	Severe	10	Mild or moderate cerebral edema (headache, dizziness) or mild/moderate laryngeal edema or diminished cardiac reserve (syncope after bending)
4	Life-threatening	5	Significant cerebral edema (confusion, obtundation) or significant laryngeal edema (stridor) or significant hemodynamic compromise (syncope without precipitating factors, hypotension, renal insufficiency)
5	Fatal	<1	Death

[a]Each sign or symptom must be thought due to superior vena cava obstruction and the effects of cerebral or laryngeal edema or effects on cardiac function. Symptoms caused by other factors (e.g., vocal cord paralysis, compromise of the tracheobronchial tree, or heart as a result of mass effect) should not be considered as they are due to mass effect on other organs and not superior vena cava obstruction

SVC dilatation or a mediastinal mass. In the setting of a peripherally inserted central catheter (PICC), frontal and lateral radiographs are the primary imaging tools for assessment of the position of the catheter, with the tip expected to be either 85% of the distance from the sternoclavicular junction to the carina or 9 mm above the carina (Dulce et al. 2014).

4.2.2 Ultrasound

Ultrasound (US) may offer indirect evidence of central venous obstruction as direct visualization of the SVC is challenging due to both adjacent lung and bone overlay. Monophasic waveforms or lack of normal respiratory phasicity in the brachiocephalic, internal jugular, or subclavian veins at Doppler US and echocardiography are considered useful indicators for SVCO. Although direct visualization of the SVC is limited, there has been a recognized limited role in the assessment of the proximal SVC by utilizing the suprasternal and right supraclavicular windows (Khouzam et al. 2005).

4.2.3 Computed Tomography (CT)

Computed tomography (CT) imaging without contrast enhancement may demonstrate indirect findings of SVCO such as abnormal PICC or central venous catheter (CVC) position, or calcifications along the SVC that could be caused by calcified thrombi, fibrin sheaths, or retained lead fragments.

Contrast enhanced CT is considered exceptionally useful for the diagnosis of SVCO (Fig. 2). Although dedicated protocols have been developed (Lin et al. 2009; Bae et al. 2008; Kim et al. 2003), the SVC can be assessed both with and without dedicated protocols. Using diluted contrast material combined with optimal vascular window settings may minimize streak artifact. Additional delayed imaging beyond 50 s may be useful when thrombus is a possibility.

There is a high correlation between the CT imaging appearances of SVCO and the presenting clinical symptoms and signs (Plekker et al. 2008). The most commonly visible collateral venous circulation includes the azygous-hemiazygous-accessory hemiazygous system, the vertebral and subscapular plexuses, the mediastinal venous plexus, esophageal venous plexus, diaphragmatic venous plexus, lateral thoracic plexus, and superficial thoracoabdominal venous plexus (Gosselin and Rubin 1997). The appearance on contrast enhanced CT can vary depending on the exact location of the SVCO. If the obstruction is above the azygous arch, antegrade flow from the azygous to the right atrium will be demonstrated. However, if the obstruction is below the arch,

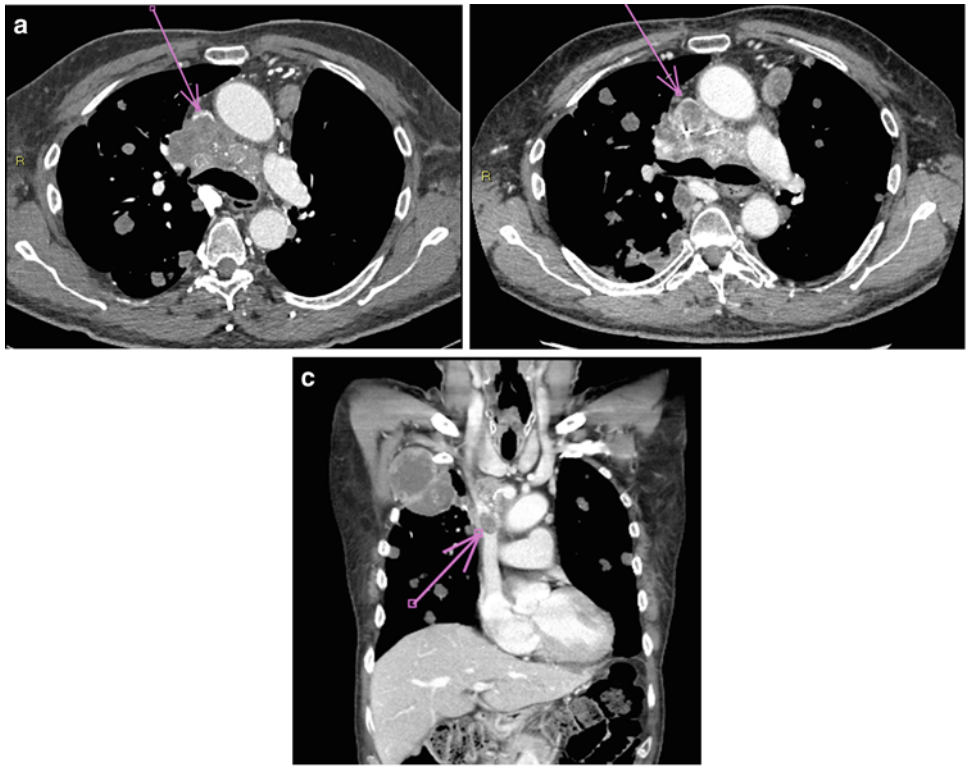

Fig. 2 A 63-year-old male with colorectal carcinoma metastases and SVCO secondary to malignant mediastinal nodal mass. (**a**) Axial image with purple arrow demonstrating an intrinsic filling defect within the central and posterior superior vena cava. (**b**) Axial image slightly more inferiorly than (**a**) with purple arrow demonstrating/highlighting the contrast outlining the tumor. (**c**) Coronal image with purple arrow highlighting the well-demonstrated tumor mass occupying the lumen of the superior vena cava

the entire azygous and hemiazygous veins will be heavily opacified due to the blood re-routing via this pathway to the inferior vena cava (IVC). Further variations may include demonstration of the paravertebral, intervertebral, and epidural veins where blood extends via the ascending lumbar veins to the azygous system. Chest wall and breast collateral veins may also dilate and intensely enhance (Lawler and Fishman 2001), as might abdominal venous collaterals in the abdominal wall or in the liver manifesting as perfusion anomalies.

4.2.4 Magnetic Resonance Venography

MR venography, utilizing Gadolinium-enhanced MR venography (gadobenate deglumine [MultiHance; Bracco Diagnostics, Milan, Italy], 0.1–0.2 mmol/kg), can include static high-resolution first-pass, time-resolved, or steady-state acquisitions (Kim and Merkle 2008). Furthermore, nonenhanced MR venography with three-dimensional (3D) steady-state free precession (SSFP) has been shown to be a useful tool for evaluation of the SVC (Tomasian et al. 2008) .

4.2.5 Radiographic Venography

Venography with the assistance of dynamic radiographic imaging (conventional venography) has numerous advantages for demonstrating strictures including extent and location, with further assessment of collateral pathways, thrombus, and relative functional (partial or complete) obstruction. Conventional venography has the advantage of allowing the procedure to extend into intervention to assist with either alleviation or resolution of the obstruction.

5 Management Options

Management is aimed at alleviating symptoms caused by the SVCO, and also at treating the malignant tumor that is causing the obstruction. Therefore, deciding on the optimal management pathway for SVCO will depend on the severity of the symptoms, the diagnosis of the underlying obstructing tumor, the stage of the malignancy, and the likely responsiveness of the tumor to treatment. Yu et al. published a proposed management algorithm based on these factors (Fig. 3) (Yu et al. 2008). Also to be considered are the previous treatments, comorbidities, and overall prognosis of the patient. Early involvement of the multidisciplinary team is strongly advisable for optimal patient care.

Life-threatening SVCO is uncommon, but notably requires emergency medical management. Positioning the patient in a seated position may help to reduce some of the pressure in the upper half of the body and may provide some degree of symptom relief. Oxygen, diuretics, and corticosteroids are traditional medical treatments that may also be helpful in providing some symptomatic relief in this situation, although there is a paucity of published evidence to support or quantify the benefit of these interventions. In the uncommon situation of stridor and airway compromise, intubation and airway management is required. Radiological imaging, including venogram, is performed to confirm the SVCO, and followed by urgent intravascular stenting that is aimed to achieve rapid relief of the obstruction. If there is associated thrombosis, then anticoagulation and/or direct thrombolysis should also be considered. Of note, SVCO slows venous return from the upper body, and therefore intravenous and intramuscular administration of drugs into the upper limbs should be avoided.

In patients with undiagnosed malignancy and nonemergency SVCO, it is advisable to first organize for prompt tissue biopsy and staging

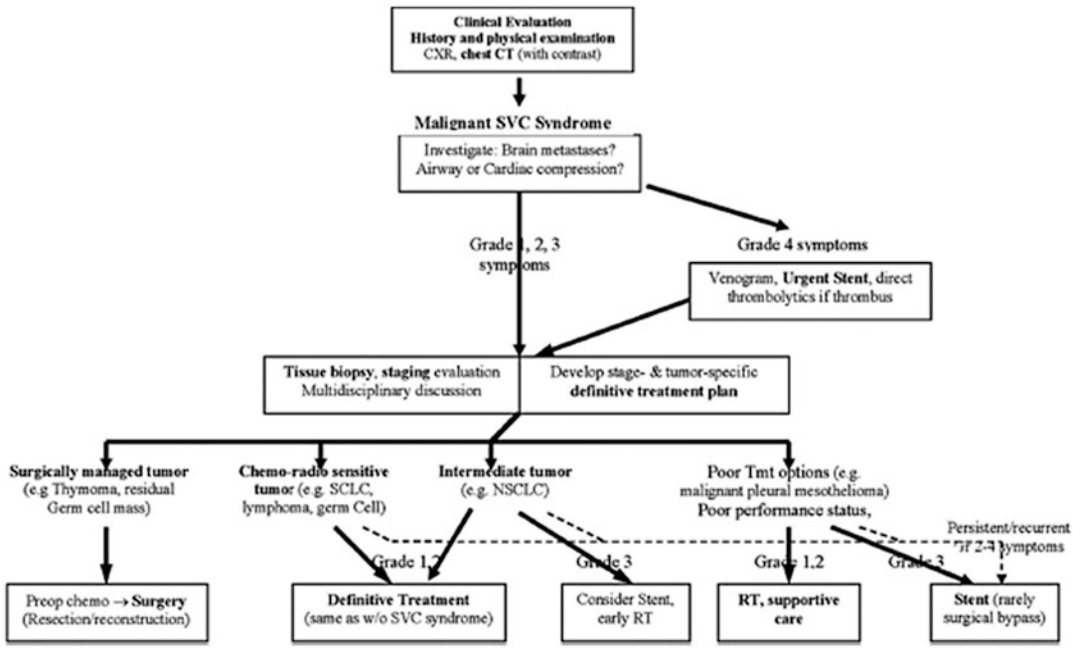

Fig. 3 Proposed management algorithm (Yu et al. 2008) (Permission to reprint kindly provided by Elsevier and Dr. Frank Detterbeck, Yale Cancer Center, USA)

evaluation, as this will allow for optimal management of the underlying tumor. These investigations will be important to determine if the patient is to be treated with curative- or palliative-intent, and will influence the choice of treatment modalities based on the expected responsiveness of the tumor (Fig. 3). Tissue biopsy may be obtained by endoscopic bronchial ultrasound of the mediastinal mass and offers a less invasive alternative to mediastinoscopy. Alternatively, in patients with more disseminated disease, a disease site that is more readily accessible to biopsy may be identified on the staging investigations.

5.1 Choice of Treatment Modality

For malignant causes of SVCO, the two most commonly practiced treatments are endovascular stenting and external beam radiotherapy. Less commonly, chemotherapy may be considered for chemo-sensitive tumors, or surgery may be considered for resectable tumors.

There are several factors to be considered in the choice of treatment modalities for SVCO. For patients with SVCO caused by malignancy, it is generally accepted that radiotherapy achieves a slower onset of response than stenting. Thus, stenting is often considered the treatment of choice for symptomatic patients requiring urgent intervention. For patients with severe SVCO, stenting offers an effective and rapid treatment for the relief of symptoms, with relief of headache occurring virtually immediately, resolution of facial edema within 24 h, and edema of arms and trunk within 72 h (Rowell and Gleeson 2002). Whereas in patients receiving radiotherapy for SVCO, the rapidity of response can generally be expected to take up to 1–2 weeks following treatment. On the other hand, the main advantage of external beam radiotherapy over stenting is that radiotherapy is a noninvasive technique. Unfortunately, there are no published randomized data to reliably compare quality of life outcomes or durability of response, and nonrandomized reports are subject to potential selection bias between the cohorts.

5.2 Role of Endovascular Stenting

5.2.1 Endovascular Stenting: Indications

Acute SVCO secondary to malignancy often responds to external radiation and steroids. However, if the SVCO is complicated by life-threatening symptoms, extensive thrombus, or is refractory to radiotherapy, then catheter-based treatments or surgery should be considered as the treatment of choice. Furthermore, the rapid relief of symptoms achieved by endovascular techniques makes SVCO extremely rewarding to treat. Whenever possible, stent placement should be considered at the onset of clinical symptoms, before the development of a tight stenosis, occlusion, or extensive chronic thrombus (Mauro et al. 2014).

5.2.2 Endovascular Stenting: Technique and Technical Considerations

The primary aim of treatment is to ensure relief of symptoms, which can usually be achieved by restoring inline drainage from one jugular vein to the right atrium (Kaufman and Lee 2004) (Fig. 4). A secondary consideration is the preservation of venous access sites, by minimizing the number of large caval tributaries occluded by stents, preventing future catheterization.

First, thrombus has to be cleared prior to stenting. Techniques to achieve this include the use of local thrombolysis or pharmachomechanical thrombectomy. A plasminogen activator (for example, tPA, rtPA, urokinase) is infused directly into the thrombus (Tzifa et al. 2007). Aspiration techniques and mechanical adjuncts accelerate the process. Low dose anticoagulation therapy is always given simultaneously, usually through a peripheral line.

Stenoses can usually be crossed with relative ease by an interventional radiologist, but more advanced techniques may have to be applied in the setting of occlusion and transmural invasion of the SVC. Combined femoral axillary or bilateral axillary approaches may be required to cross an occlusion (Massmann et al. 2016). The use of stiff

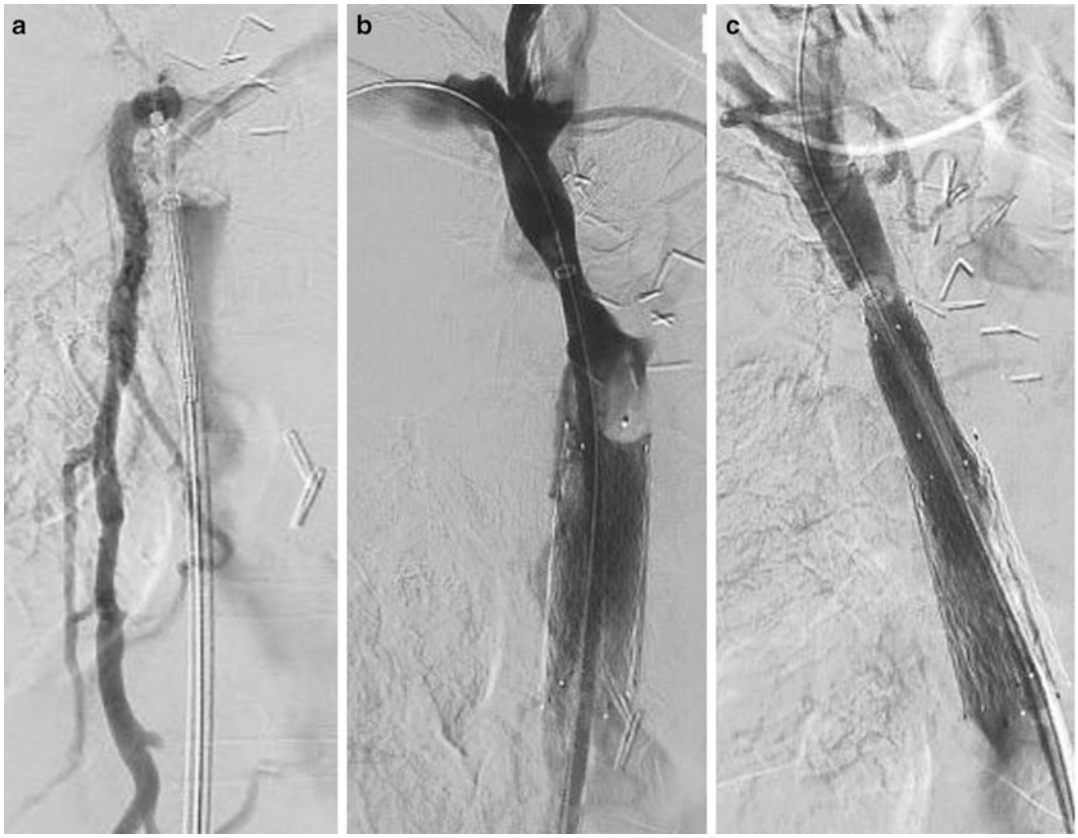

Fig. 4 Sequential stenting of the SVC. (**a**) SVC stenosis with alternate drainage of contrast via the azygos system. (**b**) Initial stent deployed in the distal portion of the SVC, residual filling defects requiring further stenting. (**c**) Inline stenting of the right innominate vein, restoring return of blood from the ipsilateral jugular vein to the right atrium

catheters, and even transjugular intrahepatic portosystemic shunt (TIPS) needles to cross tumor and regain access to the caval system, increases the likelihood of complications and requires careful intraoperative monitoring for cardiac tamponade.

Stent selection is an important aspect of the procedure. Large diameter (10–14 mm) bare metal stents are typically used, except in venous perforation or transmural tumor invasion, where covered stents would be deemed more appropriate (Fig. 5). If stent thrombosis occurs rapidly after placement, then the cause must be determined and treated appropriately with balloon plasty or additional stent placement (Fig. 4), after local thrombolytic therapy.

In cases where immediate and full restoration of flow is achieved across an SVC stenosis, in the absence of thrombus, then heparinization may not be required. Local thrombolysis should be considered in patients with residual thrombi adherent to the stent or vessel wall. It is usual practice to follow heparin therapy with oral anticoagulants for several months, to allow neo-endothelium to cover the stent (Mauro et al. 2014).

5.2.3 Endovascular Stenting: Patient Selection

Patient cooperation during any interventional procedure is imperative. Some patients with severe SVCO syndrome may have difficulty lying flat. If this is the case, then the procedure should be performed under a general anesthetic (Kaufman and Lee 2004).

Stenting of the airway should always precede management of caval obstruction in patients who

Fig. 5 Covered and uncovered stents. Covered stents are comprised of a fabric, such as polytetrafluoroethylene (PTFE), covering a metal stent (left). Applications for covered stents included sealing iatrogenic perforations or ruptures and exclusion of aneurysms

present with synchronous tracheobronchial narrowing secondary to mediastinal disease burden.

Contraindications to the use of thrombolytic agents include: active bleeding, brain metastases, and intracranial or intraspinal trauma within 2 months. These factors would preclude venous stenting in the setting of extensive venous thrombosis. Other relative contraindications, such as anatomy predisposing to severe technical difficulties, transmural tumor invasion, and advanced disease in preterminal patients, are important to consider. It is also important to note that transmural invasion is not an absolute contraindication, but would require the use of a covered stent.

5.2.4 Endovascular Stenting: Complication Risk

Complications related to venous stenting are relatively few and only seen in 5–7% of procedures (Ganeshan et al. 2009). Usual puncture site complications apply and include: venous thrombosis, arteriovenous fistula, venous pseudoaneurysm, and pneumothorax (jugular punctures). Stent related complications include misplacement or migration, fracture or fragmentation, especially if the stent inadvertently crosses the thoracic outlet. Misplaced stents crossing the thoracic outlet fracture from repeated compression between the clavicle and first rib. Rates of stent infection, bacteremia, and septicemia are minimized with strict aseptic technique. Extremely rare complications include caval perforation and pericardial tamponade.

5.2.5 Endovascular Stenting: Outcomes

In malignant SVC obstruction, the main aim of endovascular stenting is to achieve immediate relief of symptoms. About 68–100% of successful SVC stent deployments result in almost instant complete or significant improvement of symptoms, sustained to a follow-up of 16 months (Mauro et al. 2014). Patients report relief of tension in the face and neck within minutes of stent expansion and restoration of flow in the SVC. Edema in the face and neck resolves after 1–2 days and by day three in the scapula region and upper limbs. There is limited data on long-term patency, but in survivors re-occlusion of the SVC occurs in up to 40% (Mauro et al. 2014; Ganeshan et al. 2009). Previous thrombosis and smaller final stent diameters are associated with the highest rates of re-occlusion (Fagedet et al. 2013).

In conclusion, percutaneous, endovascular stenting of malignant SVCO syndrome offers a high initial success rate and rapid relief of symptoms, avoiding the morbidity associated with invasive surgery. Early detection and endoluminal treatment, before the full symptoms of SVC occlusion develop, are key in facilitating the best patient outcome.

5.3 Role of Palliative Radiotherapy

5.3.1 Radiotherapy: Principles of Treatment

Historically, radiotherapy was the mainstay of management of SVCO due to malignancy, and

today remains an important component in the management of nonsevere or asymptomatic SVCO (Yu et al. 2008). Depending on the underlying tumor type and stage, radiotherapy may be delivered with either palliative or curative intent. The primary principles of palliative radiotherapy are to (i) deliver a dose of radiotherapy that is sufficient to adequately de-bulk the tumor to allow for un-occlusion of the SVC and therefore alleviate the symptoms of the SVCO, while (ii) minimizing the potential morbidity from radiotherapy-induced side effects that are more commonly associated with higher doses of radiotherapy. On the other hand, curative-intent radiotherapy involves delivering a higher dose of radiotherapy with the aim of achieving long-term sterilization of the tumor cells, and in this scenario, it is often reasonable to accept a higher risk of acute side-effects as a trade-off for more durable tumor control. In making this decision, it is vital for the clinician to pay careful attention to the relevant patient factors (i.e., comorbidities, performance state, patient wishes) and tumor factors (i.e., histological diagnosis, stage, alternative treatment options). Discussion in a multidisciplinary tumor board meeting is strongly recommended.

5.3.2 Radiotherapy: Efficacy of Treatment

The use of palliative radiotherapy to relieve SVCO has evolved over the preceding decades and is now an established treatment in clinical practice; however, the true efficacy of radiotherapy is not well reported in the literature. Rowell and Gleeson conducted a Cochrane systematic review of the effectiveness of SVCO treatments in patients with lung cancer (Rowell and Gleeson 2002). The investigators discovered that, in general, the included studies failed to define objective criteria for relief of SVCO, had variable definitions of treatment response, and lacked measurements of symptoms or quality of life (Rowell and Gleeson 2002). Considering these limitations, the authors of the systematic review reported that the response rate to radiotherapy was 94% in patients with no prior treatment for lung cancer, versus 74% in patients who had previously received treatment for lung cancer (Rowell and Gleeson 2002). The effectiveness of radiotherapy for SVCO did not appear to be related to any particular radiotherapy fractionation regimen (Rowell and Gleeson 2002).

5.3.3 Radiotherapy: Treatment Dose and Delivery

For palliative patients, external beam radiotherapy offers a noninvasive treatment option for the management of SVCO caused by malignancy (Fig. 6a and b). Depending on the patient's symptoms and performance state, radiotherapy may be delivered as an outpatient or an inpatient. In general, palliative courses of hypofractionated radiotherapy are delivered in daily fractions, 5 days per week, over 1–3 weeks. Standard fractionation schedules for the palliative treatment of SVCO include 20 Gy in five fractions (20Gy/5F) delivered over 1 week, 30 Gy in 10 fractions (30Gy/10F) delivered over 2 weeks, or 36 Gy in 12 fractions (36Gy/12F) delivered over 2½ weeks. Higher dose radiotherapy fractionation schedules may be considered for patients who are expected to have longer life expectancies, as it is thought that higher dose of radiotherapy may achieve more durable local disease control and reduce the risk of SVCO recurrence. This includes patients with good performance state, limited burden of disease, and with tumor histologies that are known to have a more indolent pattern of behavior. For patients who are suitable for curative-intent treatment, high doses of radiotherapy are often required for disease eradication; for example, for patients with non-small lung cancer who are suitable for curative-intent radiotherapy are usually treated to 60Gy in 30 fractions over 6 weeks, with concurrent radiosensitizing chemotherapy to further improve tumor control.

5.3.4 Radiotherapy: Side Effects of Treatment

As a noninvasive and localized treatment modality, external beam radiotherapy offers a generally well-tolerated treatment for palliative patients with SVCO. Common, acute side effects include localized esophagitis, localized skin erythema, and fatigue. In patients receiving higher dose

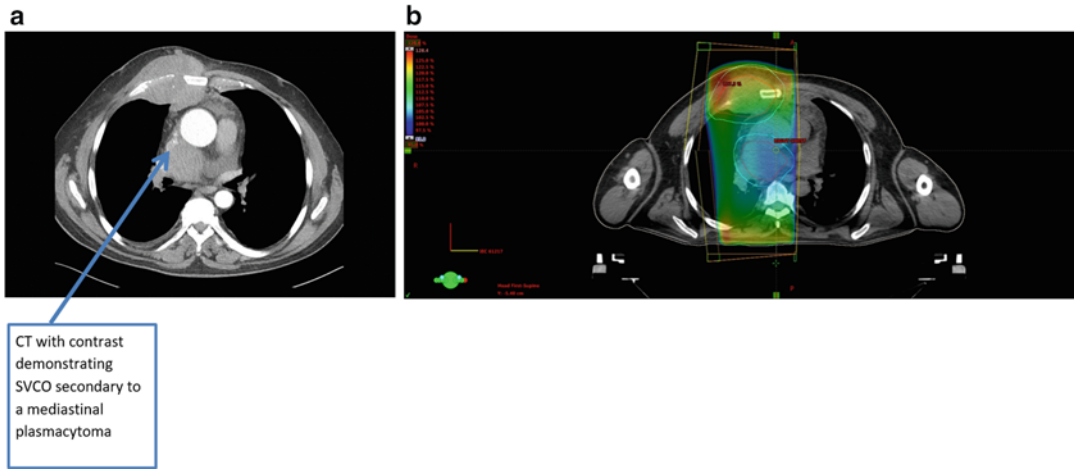

Fig. 6 Palliative radiotherapy to treat an asymptomatic SVCO caused by a mediastinal, extraosseous plasmacytoma in a patient with known chemo-refractory multiple myeloma (a rare cause of SVCO). Durable symptom control was obtained in these sites following radiotherapy; the patient succumbed to multiple myeloma 5 months later. (**a**) CT with contrast demonstrated the incidental finding of the asymptomatic SVCO, secondary to an extraosseous plasmacytoma in the mediastinum. This CT scan was originally performed to investigate the patient's anterior chest wall pain and deformity, caused by a large osseous plasmacytoma of the rib. (**b**) Dosimetry for the palliative radiotherapy plan to treat the symptomatic rib plasmacytoma and the asymptomatic mediastinal plasmacytoma causing the SVCO. The gross tumor volume is marked in red, and the planning target volume is marked in pale blue. The patient was treated with parallel-opposed 6MV photon beams, to a total dose of 20 Gy in 5 fractions, delivered over 5 consecutive days

fractionation schedules, the severity of these symptoms increases and patients may require analgesia and a soft food diet to manage the esophagitis. These acute side effects frequently peak in intensity approximately 10 days after completion of treatment.

For patients being treated with curative-intent radiotherapy, the longer-term toxicity profile must also be considered. Subacute side effects include risk of radiation pneumonitis, which characteristically presents approximately 3–6 months after radiotherapy, with symptoms of cough, fever, and breathlessness, and is best managed via early intervention with a short course of oral steroid therapy. Radiation pericarditis is a less commonly seen subacute side effect following radiotherapy for upper mediastinal tumors, but is also best treated early with oral steroid therapy. In cancer patients treated with curative-intent radiotherapy, long-term toxicity risks from thoracic radiotherapy may also include pulmonary fibrosis, esophageal stricture, spinal cord myelopathy (rare), and radiation-induced second malignancy (rare).

5.4 Role of Chemotherapy

Less commonly, SVCO may be caused by chemosensitive malignancies. These include small-cell lung cancer, mediastinal lymphomas, and mediastinal germ-cell tumors. These tumors usually respond well to appropriate chemotherapy regimens and symptoms of SVCO are quickly relieved. Depending on both patient and tumor factors, chemotherapy may be delivered with either curative or palliative intent; therefore, careful tumor staging and discussion in a multidisciplinary meeting is recommended prior to embarking on treatment.

6 Conclusion

SVCO is a changing entity in modern medical practice. In the current era, malignancy is the most common cause of SVCO; however, it is often detected while the patient is still asymptomatic. This is due to the increasing availability and

sensitivity of medical imaging modalities and the increasing frequency of imaging in the follow-up of oncology patients; as such, patients rarely present with life-threatening symptoms of SVCO. It is recommended that all oncology patients with SVCO are discussed in a multidisciplinary meeting with review of the available imaging and pathology, prior to treatment. The optimal selection of medical treatment will depend on the severity of symptoms caused by the SVCO, the etiology of the obstructing lesion, the histology of the underlying malignant process, the stage of the disease, response to previous treatments, and patient comorbidities and performance state. The more frequently used treatment modalities include endovascular stenting and external beam radiotherapy, with chemotherapy and surgery having less common roles. In the uncommon scenario of severe or life-threatening SVCO, urgent endovascular stenting is the treatment of choice for rapid relief of symptoms from obstructing lesions.

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Acute Cancer Pain Syndromes in Palliative Care Emergencies

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Sophia Lam, Leeroy William, and Peter Poon

Contents

Abstract

Acute pain syndromes in palliative care are predominantly malignant in origin. These are often emergencies due to the severity of the pain, its meaning to the patient, the disruption of ongoing curative treatment, and the resultant erosion of quality of life. A prompt accurate pain assessment is a vital component of clinical management, followed by analgesic intervention and attention to the physical, psychological, social, and spiritual aspects of pain. Clinicians should develop excellent communication skills to support patients,

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_79

their families, and also other healthcare professionals in the delivery of optimal care. Pain will not always be managed according to the expectations of others, and so how we deliver care and explain the limitations of treatment is important.

Acute cancer pain that is not managed well can become chronic in nature. The development of chronic pain can greatly reduce the functional ability and mood of patients over time. As with all symptoms, managing the acute presentation should lead to an investigation of causative factors, mechanism of pain, and potential therapeutic interventions. Acute pain syndromes can be approached via two causative mechanisms: treatment-related pain and pain directly related to the cancer process. A multimodal and multidisciplinary approach to treatment is often required to not only help the patient, but also to support the family during an uncertain and unsettling period of care.

1 Introduction

The symptom of pain is likely to occur in 20–50% of people with cancer (Fischer et al. 2010), at multiple sites (Gutgsell et al. 2003), and for those with advanced disease about 80% will have moderate to severe pain (Bruera and Kim 2003). The negative impact of pain on functional status and quality of life (Kroenke et al. 2010; Porter and Keefe 2011) has driven efforts to improve pain management over a number of decades. A systemic review of the literature, covering the period between September 2005 and January 2014, aimed to look at pain prevalence and pain severity. Unfortunately, it revealed that cancer pain is still poorly controlled with a prevalence of 39.3% following curative treatment; 55% in people undergoing anticancer treatment; and 66.4% in people with advanced, metastatic, or terminal disease. Moderate to severe pain scores were also found in 38.0% of all patients (van den Beuken-van and Hochstenbach 2016).

Even the promotion of "pain as the fifth vital sign" by the American Pain Society in 1995 and its focus upon the numerical pain scale (NRS) has been questioned. The idea was to raise the awareness of pain as a priority healthcare issue; however, the campaign may have inadvertently contributed to the current opioid epidemic in the USA (Levy et al. 2018). Pain therefore remains a feared symptom by patients and their families, and adequate pain management is affected by barriers that are patient-related (e.g., reluctance to report pain and poor compliance to analgesics); clinician-related (e.g., insufficient knowledge of cancer pain management, and inadequate pain assessment skills); and societal-related (e.g., opiophobia and the stigma of opioid addiction) (Cipta et al. 2015; Pargeon and Hailey 1999).

The particular significance of pain, and the fear that accompanies it, in people with cancer should not be underestimated. Increasing pain is often perceived to be associated with progressive disease, or a shorter prognosis. Many patients choose to defer the use of regular opioids for a time in the future when they believe the pain will become more severe, or when they are closer to death. They also fear addiction to opioids and how opioids will affect their lives. Importantly, the resistance to adequate analgesia can be a barrier to ongoing curative treatment, causing breaks in therapy. Treatment breaks are common in cancer therapy, due to disease progression or toxicity from therapy, e.g., mucositis, radiation enteritis, or neutropenic sepsis. Pain may also coexist, adding to the picture of a more debilitated patient. Without the adequate assessment and treatment of pain, clinicians may assume that disease progression or treatment toxicity is responsible for functional deterioration and reduced quality of life. Hence, treatment may be modified in strength or even ceased under a false perception of deterioration. On the other hand, explaining this possible curtailment of oncological treatment can often motivate patients to accept and comply with prescribed analgesia.

Palliative care utilizes the concept of total pain, i.e., that pain is comprised of physical, psychological, social, and spiritual components. Therefore, the optimal management of pain addresses all these domains and promotes a multidisciplinary team approach. It is also important

to plan for potential pain crises, via the use of breakthrough pain medications and supportive care plans. These considerations allow patients to have control and manage their pain while living their lives.

In this chapter, we aim to cover the management of acute cancer pain syndromes from the perspective of a palliative care emergency. Acute noncancer pain syndromes and chronic pain syndromes are not discussed here, as they would usually be managed by acute pain and chronic pain services, respectively. Palliative care services still predominantly see cancer patients, who invariably present with cancer pain. We will discuss the rapid assessment of patients and timely interventions for stabilization, alongside the holistic approach to care. Acute cancer pain syndromes will then be discussed considering the underlying cause of the pain. Firstly, pain caused by the treatment of the cancer, and then secondly the pain caused directly by the cancer itself.

2 Acute Cancer Pain Syndromes

2.1 Definitions

The classification of acute pain was recently reviewed by an expert panel involving the Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTTION), American Pain Society (APS), and American Academy of Pain Medicine (AAPM). A multidimensional approach has now been adopted to the new definition (Kent et al. 2017):

"Acute pain is the physiological response to and experience of noxious stimuli that can become pathological, is normally sudden in onset, time limited, and motivates behaviours to avoid potential or actual tissue injury."

Acute pain can last up to 7 days, but may be prolonged to 30 days, and the duration is indicative of the mechanisms and severity of the causative process. Subacute pain has been defined by acute pain prolonged beyond 30 days, but less than 90 days (Kent et al. 2017). Although acute pain plays an important protective role in our recovery from an insult, it should be managed promptly to prevent neuronal remodeling and sensitization that commonly occurs in cancer and lead to chronic pain (Carr and Goudas 1999).

Chronic pain usually persists for more than 3–6 months and involves permanent or persistent tissue damage, alongside potential behavioral changes in coping with the pain and daily activities. There may be acute episodes of pain on a background of chronic pain, but treatment targeted at the underlying disease process can help both acute flares of pain as well as the baseline chronic pain.

Cancer pain has become more chronic in nature due to the successes of cancer therapies. Patients are living longer with their malignancies, contributing to an increasing chronicity of pain due to the cancer itself or as part of survivorship. However, acute events may increase pain, e.g., fractures, hemorrhages, and plexopathies. Furthermore, acute pain may occur from treatment of the cancer, e.g., peripheral neuropathy, mucositis, and radiotherapy.

3 General Cancer Pain Management

The World Health Organization (WHO) Analgesic Ladder has underpinned cancer pain management since 1986, and involves three steps in dealing with mild, moderate, and severe pain. Using the visual analogue scale (VAS), a mild pain equates to a score of 1–2/10, a moderate pain 3–6/10, and a severe pain 7–10/10. The first step involves the use of nonopioids, e.g., paracetamol and NSAIDs; the second step adds in weak opioids if the pain is not controlled, e.g., codeine, dihydrocodeine, and tramadol; and similarly, the third step involves the addition of strong opioids, e.g., morphine, fentanyl, and methadone. Adjuvant analgesics may be used at any time (WHO 1987). Over the years, the WHO ladder has been found to provide adequate analgesia for 45–100% of people with cancer pain (Azevedo et al. 2006). However, criticisms of the WHO ladder do exist, e.g. the second step is perhaps redundant due to the severity of cancer pain (Vadalouca et al. 2008);

the approach used does not evaluate the cause of the pain to guide analgesia (Ashby et al. 1992); and a modified version has included a fourth step to redress the omission of interventional analgesia (Vadalouca et al. 2008; Vargas-Schaffer 2010). Finally, the total pain approach promotes the nonpharmacological and multidisciplinary benefits to managing pain, in addition to the WHO ladder. These options should not be forgotten, even in the trying to control acute pain. Reassurance and support for patients in a pain crisis, as well as their families, can help until the analgesia becomes effective.

A pain assessment should include a review of the pain to explore the following: intensity, location, quality, interference on quality of life, emotional component of the pain, temporal pattern, treatments, duration, pain beliefs, pain history, exacerbating, and relieving factors (Hølen et al. 2006). Consideration of the mechanism of pain, as per Ashby et al., is essential and if used to determine the choice of first line analgesia may also prevent a delay of adequate pain control (Ashby et al. 1992). Nociceptive pain involves injury to somatic and visceral structures. Somatic pain affects the skin (superficial or cutaneous somatic pain) and other deeper structures, e.g., bone, muscle, and tendons (deep somatic pain). Visceral pain is seen in internal organs, e.g., lungs, liver, bowel, and heart). Neuropathic pain may be due to nerve compression or nerve injury (affecting central nerves, peripheral nerves, or sympathetically maintained nerves). Although pain may be nociceptive or neuropathic, in many malignant cases, a mixed picture with moderate to severe pain is common in clinical practice. Hence, the use of the WHO ladder in cancer pain may result in a delay in adequate pain control, due to the sequential step process (Maltoni et al. 2005; Forbes 2011).

Acute pain in the emergency setting, outside of palliative care, may involve intravenous morphine or fentanyl protocols that use small doses of opioid titrated to the pain, with frequent reviews to monitor for toxicity. Sedation and respiratory rate are carefully reviewed during the titration process, with the use of naloxone to counter opioid overdose. However, in a palliative care setting, subcutaneous opioids are usually titrated to effect as they provide a lower peak concentration and longer duration of action compared with intravenous delivery. Subsequently, naloxone is rarely required, but if needed small doses are used to avoid reversing analgesia. The appropriate team should manage nonmalignant causes of the acute pain, e.g., a nonmalignant fracture may require orthopedic surgery, and the perioperative analgesia would be best managed by the acute pain service. In these instances, a collaborative working relationship facilitates a smooth transition between acute interventions and palliative care for the patient. Postoperatively, the acute pain team can handover care to palliative care services where appropriate.

If patients are opioid-naïve on presentation with acute pain, opioids can be titrated using regular small doses as required. In some instances, the pain may be unresponsive to opioids, or partially opioid responsive, e.g., colicky abdominal pain from malignant bowel obstruction, or pathological fractures, hence the importance to consider the mechanism of pain. In these cases, adjuvants may be useful to achieve pain control, e.g., hyoscine butylbromide for colicky abdominal pain, and steroids or NSAIDs for pathological fractures. Interventional adjuvants may also be appropriate, and sometimes the optimal management, but require time to organize, e.g., orthopedic management of pathological fractures, stenting of mechanical bowel obstructions, or radiotherapy for bone metastases. For patients who are not opioid-naïve, the management requires a different approach. There are few consensus guidelines for acute cancer pain management in this scenario; however, a recent eight-step approach has been suggested (Fadul and Elsayem 2016):

1. Assessment of the pain syndrome, including pain location, severity, onset, and exacerbating and relieving factors
2. Holistic assessment of factors potentially affecting the pain
3. Calculate the total morphine-equivalent daily dose (MEDD)

4. Prescribe 10–15% of the MEDD as the rescue dose
5. Assessment of the pain response within 15 min of giving the first analgesic rescue dose. Dose can be repeated if pain relief is not satisfactory
6. Assessment of the functional ability of the patient, correlated with pain
7. Adjustment of the basal opioid dose either by adding the rescue doses needed over the past 24 h or an incremental increase by 30%
8. For patients whose pain is refractory to these initial steps, prompt consultation with pain or palliative care experts, if available, is recommended

There are further options in management provided by the expertise of the specialists involved in step 8. These may include the commencement of patient-controlled analgesia (PCA), continuous subcutaneous infusions (CSCI), or opioid rotations with the introduction of co-analgesics specific to the pain mechanism, as discussed above. In an older study, Mercadante et al. used the titration of morphine 2 mg intravenously every 2 min to effectively manage acute, severe cancer pain in less than 10 min for palliative care patients. Once control was achieved, conversion to oral morphine was possible (Mercadante et al. 2002). For patients with large background opioid doses, the use of ketamine may be useful due to its antiinflammatory effects and reduction of central sensitization (Matthews et al. 2018). As mentioned earlier, the other elements of multidisciplinary care should not be forgotten, as the patient-centered approach is likely to provide most benefit to the patient (Luckett et al. 2013).

There are well-described cancer pain syndromes that can cause acute pain. These can be divided into those induced by treatment and those related to disease (Portenoy and Lesage 1999).

4 Treatment-Induced Acute Pain Syndromes

Treatment-induced acute pain syndromes can be broadly divided into those arising from:

1. Diagnostic and therapeutic procedures
2. Surgical management
3. Chemotherapy, hormonal therapy, and immunotherapy
4. Radiation therapy
5. Mucositis

4.1 Acute Pain due to Diagnostic and Therapeutic Procedures

(a) Thoracocentesis and pleurodesis are therapeutic procedures for the palliative management of breathlessness due to malignant pleural effusion. Thoracocentesis can also be a diagnostic and recurrent procedure. Access to the pleural space is gained via a large bore tube to remove fluid. Pleurodesis involves the chemical or mechanical induction of pleural inflammation to adhere the visceral and parietal pleura, thereby eliminating the space for air of fluid to accumulate. The procedure is better for recurrent malignant pleural effusions and is attempted days after a thoracocentesis has completely drained the effusion. Talc is the most common agent used in pleurodesis. Both tube insertion and pleurodesis are acutely painful processes due to surgical skin incision and pleural irritation but involve local anesthetic during the procedure. Such pain can subsequently be managed with opioid and NSAIDs analgesics (Rahman et al. 2015).

(b) Lumbar punctures are frequently performed for diagnostic purposes and as a means of delivering therapeutic treatment. Headache is a common post procedural occurrence. Supine position, hydration, simple analgesia, opioids and antiemetics are used for management of mild to moderate symptoms. Rarer and with more severe consequences are spinal subdural hematomas, presenting with severe low back pain, radicular pain, sensory loss, or paraparesis in the hours or days post-lumbar puncture. Management options include blood patch, epidural saline, epidural dextra 40, and oral and intravenous caffeine. Decompressive laminectomy may be required (Ahmed et al. 2006).

(c) Embolization is an endoluminal procedure used to occlude a vessel for therapeutic benefit. There is a plethora of possible sites for intervention and a number of agents used; consequently, a wide spectrum of side effects and complications exist (Bilbao et al. 2006). Transarterial chemo embolization (TACE) is useful in the palliative management of primary hepatocellular cancer and less commonly in hepatic metastases from neuroendocrine or gastrointestinal malignancies. A common (up to 86%) Post-embolization Syndrome (PES) of fever, right hypochondrium pain, nausea, vomiting, and a rise in transaminases can occur 48–72 h post procedure and is felt to be due to a combination of liver capsule distension and parenchymal necrosis. Treatment is symptomatic, with steroids reserved for severe cases (Rammohan et al. 2012).

(d) Percutaneous nephrostomy tube insertion is a frequently performed procedure to relieve urinary obstruction. Major complication rates are low but vary depending on size of catheter introduced (large is 28F–30F), approach (subcostal vs. intercostal), and amount of intrarenal manipulation required (Hart and Ryu 2002). Mild peritube insertion nociceptive pain is to be expected in the immediate postoperative period with use of anxiolytics and local anesthesia at time of insertion, and simple opioid analgesia post insertion. Occurrence of more severe complications such as periorgan (bowel, spleen, liver) damage, infection, and abscess formation can result in more intense pain, requiring surgical intervention, intravenous antibiotics, and strong opioids.

4.2 Surgical Management: Acute Postoperative Pain

Curative and diagnostic surgical intervention is common in the management of cancer. Acute pain is an expected part of the postoperative experience in these procedures that remove affected primary sites of malignancy. Untreated or undertreated pain can lead to persistent pain in up to 50% of individuals, up to 20% of whom will have severe chronic pain or development of chronic postsurgical pain syndromes (Wu and Raja 2011). Acute postsurgical pain is nociceptive in nature from skin, soft tissue, and muscle interruption and/or neuropathic from nerve damage. Severity and presentation depends on location and extent of surgery. Effective management to prevent the long-term sequelae of a chronic pain syndrome usually requires a multimodal, multidisciplinary approach in the perioperative period.

(a) Acute postmastectomy pain

Acute postmastectomy pain is usually due to intercostal brachial nerve injury. Injury to this nerve is almost unavoidable if axillary dissection is required, although some approaches can minimize the sensory symptoms. Pain can present acutely or up to 6 months post procedure, as a neuropathic pain distributed across the medial upper arm, axilla, and anterior chest wall. A combination of intra- and perioperative analgesic interventions can minimize progression to a chronic pain syndrome. Intraoperative techniques which result in better pain outcomes are: minimizing surgical trauma, nerve preservation, and minimally invasive staging techniques leading to less axillary dissection. Perioperative pain management that reduces severity and duration of acute pain involves use of multireceptor analgesic agents (NSAIDs, neuropathic agents, opioids, and NMDA receptor antagonists) as well as recognizing and addressing psychological distress earlier.

(b) Thoracotomy pain

Thoracotomy is associated with a high risk of severe and long-lasting acute postoperative pain. Pain is due to intercostal nerve injury during rib separation with or without rib resection. It presents as an aching sensation along the incision and can be associated with sensory and autonomic changes. Persistence of this pain beyond 2 months is termed the Post-thoracotomy Pain Syndrome (PTPS). Multimodal peri- and intraoperative

analgesia is recommended for acute pain management. This includes the use of regional anesthesia and intravenous ketamine postoperatively. Regional anesthesia techniques employed are mostly thoracic epidural anesthesia (TEA), thoracic paravertebral block, and secondarily, pleural infusion or intercostal nerves block. A mixture of opioids and local anesthetic agents are used. Ketamine preoperatively as an epidural and intravenous intra- and postoperatively appears to lessen the nociceptive process causing severe pain (Della Corte et al. 2012).

(c) Acute postnephrectomy pain

Acute postnephrectomy pain is primarily nociceptive from tissue damage with some contribution from parietal and nerve damage. The symptoms are aching deep back pain and incision pain on mobility, which relate to the pathophysiology is of tissue inflammation, spinal pain mechanism activation, and reflexive muscle spasm. Laparoscopic approaches can cause neuropathic pain due to trochar injury to neural structures. Severe postoperative pain and neuropathic pain are associated with the development of a chronic postoperative pain syndrome (Oefelein and Bayazit 2003).

(d) Limb amputation pain

Limb amputation is always followed phenomena associated with the missing body part. Two of the well-described syndromes can present with acute pain; stump pain and phantom pain. Both are common, arising in over 50% of cases. Stump pain occurs in the immediate postsurgery phase and is the acute nociceptive pain arising from the site of tissue injury. It usually resolves within a few weeks and is managed with simple analgesia and opioids. Phantom pain most commonly presents within a few weeks of amputation, but onset can be delayed for up to years. It is described in multiple terms such as shooting, burning, cramping, and aching, characteristically located at the distal end of the affected limb. The precise pathophysiology is unknown, but postulated theories all describe abnormal sensory processing although at different levels. In the absence of well-studied effective management, a multidisciplinary, multimodal approach to treatment is advisable. There is some evidence but not enough to support the use of preoperative epidural pain relief. Short-term postoperative pain control has been shown to be achievable with the use of strong opioids, sciatic, or posterior tibial nerve blocks intra- or postoperatively; intravenous salmon calcitonin; and transcutaneous electrical nerve stimulation TENS. No trials were able to show improvement in the long-term outcome of preventing phantom limb pain (Jackson and Simpson 2004).

4.3 Acute Pain due to Chemotherapy, Immunotherapy, and Hormonal Therapy

There are numerous acute pain syndromes caused by treatment with chemotherapy, immunotherapy, hormonal therapy, and growth factors. There are those associated with infusion technique; those due to specific drugs; and those due to drug toxicity. Most are self-limiting and ameliorated with slowing infusion rates, dose reductions, or drug cessation. Patient education prior to initiation of the causative cytoreductive agent allows early recognition of the acute pain syndrome and prompt initiation of the appropriate symptomatic therapy.

4.3.1 Acute Pain Syndromes Associated with Infusion Technique

(a) Intravenous infusion pain

Venous spasm, chemical phlebitis, vesicant extravasation causing extreme pain, anthracycline-associated localized skin flare reaction (Portenoy and Conn 2009).

(b) Hepatic artery infusion pain

While the portal vein contributes 70% of the hepatic blood supply and the hepatic artery delivers 30%, almost 100% of the

blood supply to primary and metastatic cancer is delivered via the hepatic artery. Taking advantage of this anatomy, direct infusion of chemotherapy such as floxuridine with dexamethasone, or with mitomycin, into the hepatic artery via an implanted pump is sometimes utilized. Side effects include generalized abdominal pain, gastric ulceration, and cholangitis. Pain usually resolves with cessation of infusion (Cohen and Kemeny 2003).

(c) Pain from intraperitoneal chemotherapy

Administration of chemotherapy directly into the intraperitoneal space is used to treat cancers of the abdominal region. Intraperitoneal chemotherapy is given either as Hyperthermic Intraperitoneal Chemotherapy (HIPEC) as an intraoperative procedure, or as a course of up to six cycles delivered via a port. Abdominal pain during and after administration is a common side effect that can limit the ability to tolerate a full course of chemotherapy. This pain can be improved by adjusting the fill volumes in line with the individual patient's physique (Zeimet et al. 2009). Catheter-associated problems such as positioning, kinking, and infection can also cause pain. The repeated dose regimen is associated with a higher likelihood of all side effects including pain (Blinman et al. 2013).

(d) Intrathecal chemotherapy

The central nervous system is a unique location of malignant disease due to the inability of many standard oral and intravenous chemotherapeutic drugs to penetrate the blood-brain barrier. Administration of therapy directly into the leptomeninges via intrathecal infusion is therefore employed. An Ommaya reservoir is an intraventricular catheter system which can deliver drugs or be used for aspiration of cerebrospinal fluid. It is placed to facilitate intrathecal chemotherapy and improve flow. Along with the side effects associated with lumbar puncture already mentioned, there are additional potential neurotoxicities from the drugs more commonly used which can cause pain (Kerr et al. 2001). Methotrexate and cytarabine can both cause an acute chemical arachnoiditis, presenting with symptoms of headache, nuchal rigidity, back pain, vomiting, fever, and CSF pleocytosis. This is usually self-limiting (Jacob et al. 2015).

4.3.2 Acute Pain due to Specific Drug Reaction Syndrome

(a) Paclitaxel

Paclitaxel, most commonly used in treatment of breast cancer, is associated with a particular set of symptoms known as the Paclitaxel Acute Pain Syndrome (P-APS). Onset of symptoms is 24–96 h after dosing, most commonly with a diffuse aching discomfort, most often in the legs, hips, and lower back, although it can be widespread. Resolution of symptoms is over 24–96 h. Symptoms can recur at greater or less intensity with repeated dosing and can evolve to develop into a sensory peripheral neuropathy, with greater initial intensity a predictor for this (Loprinzi et al. 2011). P-APS can be managed with dose reduction and analgesics, but no methods of prevention are known. Aggressive treatment of P-APS may prevent development of the chronic sensory neuropathy.

(b) 5-Fluorouracil

5-Fluorouracil, commonly used in the treatment of gastrointestinal malignancies, has well-described potential cardiotoxicity mediated by coronary vasospasm. The cardiotoxicity manifestation ranges across a wide spectrum from ECG changes to angina pain to cardiogenic shock. Treatment of angina is in accordance with standard cardiac pain protocols.

(c) All-Trans-Retinoic Acid

All-Trans-Retinoic Acid is used in the treatment of acute promyelocytic leukemia. Headache is a common side effect. A less common side effect is development of pseudotumor cerebri with severe headache (Tallman et al. 1997).

(d) Hormonal therapies

Hormonal therapies are used to suppress tumor progression in malignancies which are hormone responsive. The use of estrogens, antiestrogens, androgens, and gonadotrophin-releasing hormone (GnRH)

agonists is associated with a tumor flare syndrome and thus has implications in the management of breast and prostate cancer. Initiation of these agents in the treatment of breast cancer can be accompanied by one or more of the manifestations; acute bony pain; hypercalcemia; or rapid increase in size of tumor foci causing pain and swelling. Onset of these symptoms within days to weeks of initiation and spontaneous resolution differentiates the symptoms of tumor flare syndrome from disease progression (Margolese et al. 2003). Treatment is symptomatic. Tumor flare after initiation of GnRH agonists in prostate cancer can be biochemical and/or clinical with potential significant adverse effects. Onset is within 1–2 weeks of commencing androgen deprivation therapy and the most common manifestation is bony pain although ureteral obstruction, urinary retention, spinal cord compression, lymphedema, and death have been reported. Tumor flare from a GnRH agonist can be prevented or minimized with antiandrogenic agents such as cyproterone acetate, diethylstilbestrol, flutamide, nilutamide, or ketoconazole (Thompson 2001).

(e) Colony-stimulating factors

Colony-stimulating factors are associated with a range of constitutional symptoms and a diffuse aching bone pain is the most frequently reported adverse effect (Vial and Descotes 1995).

(f) Intravenous steroid

Acute perineal pain due to intravenous steroid has been described in the literature. It is immediate, brief (seconds to minutes), and self-resolving. Pain is burning and shooting in nature, localized to the perineal area and severe in intensity. Pathophysiology is unknown (Neff et al. 2002).

4.3.3 Acute Pain due to Chemotherapy Toxicity

(a) Many chemotherapy agents are neurotoxic and thus associated with peripheral neuropathy sequelae which are usually a polyneuropathy and rarely mononeuropathic. Agents with a higher incidence of polyneuropathy are vinca alkaloids, platinum drugs, taxanes, thalidomide, and bortezomib (Wolf et al. 2008). Presentation can be acute, with paresthesias and dysesthesias commonly in the fingers and toes. Other sites are also described such as the pharygolarnygeal spasm of oxaliplatin. More commonly, the onset is gradual, with increasing pain intensity with repeated administrations. Dose reductions and cessation of the agent can resolve the symptoms, but a chronic residual neuropathy can develop. Vincristine is associated with a rare mononeuropathy causing acute orofacial pain due to trigeminal or glossopharyngeal nerve toxicity (McCarthy and Skillings 1992). Several preventative and ameliorating approaches are used, including dose modification and delays. Symptomatic treatment is with neuropathic agents and behavioral modifications.

(b) Palmar-plantar erythrodysesthesia syndrome is a well-described toxicity reaction to a number of chemotherapy drugs. Most commonly implicated are capecitabine, doxorubicin, cytarabine, and fluorouracil. Symptoms include erythema, swelling, pain, paresthesia, dysesthesia, and desquamation. Onset, extent, and severity of symptoms are variable, but appear to increase with prolonged exposure or high dose exposure to the causative agent. Management is supportive with emollients, analgesia, and limiting exposure to noxious environments. The reaction is essentially self-limiting and responds to dose modification and drug cessation (Lokich and Moore 1984).

(c) Gastrointestinal Mucositis (see below)

4.4 Acute Pain due to Radiation Therapy

(a) Radiation therapy (nonmucosal)

Radiation therapy to breast, lung, and head and neck cancers pose a risk to proximate critical structures such as the brachial plexus. The syndrome of radiation-induced brachial plexopathy (RIBP) is one of the possible late effects of radiation. It most commonly

presents months after the radiation but can occur years later, making diagnosis difficult (Amini et al. 2012). A rare, early transient RIBP syndrome has also been described, presenting during or within 3 months of treatment (Metcalfe and Etiz 2016). There is a spectrum of symptoms with pain, numbness, paresthesia, and motor deficits that can be extremely debilitating. RIBP is thought to be due to demyelination leading to irreversible axon loss and symptomatic treatment is difficult. Balancing the tolerance of the brachial plexus with the risk of treatment failure during radiation planning is complex.

(b) Oral Mucositis (see below)

4.5 Mucositis

Mucositis may cause acute pain via a number of modalities: chemotherapy, radiation, or hemopoietic stem cell transplant-induced oral and gastrointestinal (GI) mucositis.

Oral and gastrointestinal mucositis is the most common side effect causing pain in the treatment of malignancies. Up to 100% of patients undergoing high dose chemotherapy and hemopoietic stem cell transplant (HSCT) suffer from oral and GI mucositis. Up to 80% of patients receiving radiation therapy for head and neck cancers suffer from oral mucositis. Between 5% and 15% of patients receiving chemotherapy agents are affected by GI mucositis although 5-fluorouracil treatment has a 40% incidence rate with doxorubicin and methotrexate, the other most common causes of oral mucositis (Sonis et al. 2004).

Oral mucositis is the result of injury to the submucosal tissue by radiation or chemotherapy. This damage initiates a cascade of events beginning with free radical generation causing DNA damage, followed by an inflammatory state, then an ulceration phase, and finally a healing phase. Full thickness mucosal damage is present during the ulcerative phase that often occurs at the same time as neutropenia and is exacerbated by bacterial colonization. This phase is most likely associated with the pain of mucositis.

Gastrointestinal (GI) mucositis has a similar pathophysiology, with differences in function accounting for the differences in symptoms and morbidity when compared to oral mucositis. GI mucositis is more common in chemotherapy due to the large numbers of rapidly dividing cells.

Symptoms of oral mucositis are of oral pain, swelling, difficulty eating, speaking, and swallowing, with onset 2–5 days after radiation or chemotherapy and lasting 7–14 days. Symptoms of GI mucositis are abdominal pain, bloating, and diarrhea between days 3 and 7 following chemotherapy. Morbidity can be severe with significant treatment limiting and delay implications, although mucositis is a self-limiting process (Rubenstein et al. 2004).

Management of oral mucositis consists of prevention strategies, educating patients on basic oral care, and pain control with systemic opioids, coating agents, and topical anesthetic/analgesics. Patient-controlled analgesia for oral mucositis in HSCT has level 1 evidence (Pillitteri and Clark 1998).

5 Disease-Related Acute Pain Syndromes

Most acute cancer pain syndromes occur in relation to investigations and treatment, i.e., iatrogenic causes. Acute pain syndromes due to the cancer itself are limited by comparison, e.g., pathological fractures, spasms, or perforations due to malignant bowel obstructions, and bleeding into tumors. Cancer pain due to disease usually has a more chronic duration with acute exacerbations and encompasses invasion into visceral, somatic, and neural tissue. The most common presentation of cancer pain is of a mixed nature, where a number of tissues may have been affected, e.g., spinal cord compression in relation to malignant invasion of bone and neuropathic tissues.

Management of the underlying disease process can provide analgesia via controlling the disease and its complications. Hence the consideration of the pathology and disease biology of cancers is important in optimizing analgesic interventions. As treatment for the underlying malignancy

continues, it can be easier to recognize more chronic pain states that develop over time.

In this section, we discuss the tumor-specific causes of acute cancer pain syndromes.

5.1 Tumor-Specific Acute Pain Syndromes

Acute pain syndromes that are directly related to the tumor necessitate urgent treatment of the underlying lesion, in addition to aggressive pain control. The degree to which the lesion is treated often depends upon the goals of care for the patient in question, i.e., curative, restorative, palliative, or terminal goals of care.

(a) Pathological fracture

Bone pain is the commonest type of pain caused by cancer, with skeletal metastases in 30–69% of cancer patients, especially from advanced breast, lung, and prostate cancers (Li et al. 2014). Malignant bone disease may be asymptomatic, but growth within the bone may cause moderate to severe pain and lead to acute pathological fractures (Zhu et al. 2015). Patients describe the sudden onset of back or limb pain, with or without any particular trauma of note. There may be pain that worsens on movement, i.e., incident pain, with a background of localized bone pain which is tender on palpation.

Incident pain can be a marker of vertebral instability and is often poorly managed due to the lack of attention to the temporal nature of the pain. It has a quick onset with movement, a high intensity and a short duration of seconds to minutes. Immediate-release opioids take 20–30 min to act and therefore may not be ideal for incident pain. Vertebral pain is often only partial opioid responsive, i.e., opioids alone will not provide adequate analgesia. Baseline long-acting opioids should first be optimized, in conjunction with the use of analgesic adjuncts such as nonsteroidal or steroidal antiinflammatories and a holistic approach. The incident pain may resolve enough to be tolerable and nonpharmacological approaches, e.g., a brace to support the back, may allow adequate analgesia. Where pain continues to be problematic, then rapid-onset opioids (ROOs) can be used, e.g., fentanyl lozenges and fentanyl sublingual/buccal tablets. When ROOs are used, they are titrated to efficacy using the recommended dosing regimen, and not dosed according to a proportion of the baseline opioid.

In severe cases of vertebral instability, urgent neurosurgery may be warranted in order to provide rapid stabilization and reduce the risk of associated neurological impairment. Surgical stabilization of long bone fractures, if feasible and consistent with the overall goals of care, may relieve pain and should be considered. In addition, a femoral nerve block can provide regional anesthesia, e.g., for a neck of femur fracture or osteosarcoma (Pacenta et al. 2010) Similarly, sacral bone pain from metastatic disease can be aided by a sciatic nerve block (Fujiwara et al. 2015). Surgery should also be considered if there is no fracture, but the cortex of the bone is at risk of being breached from malignancy.

Radiation therapy is usually considered for all pathological fractures post surgery and often augments pain control over a maximal period of 6–8 weeks. If surgery is not part of the management of the fracture, and pain cannot be managed adequately with medications, then radiotherapy is also warranted. A pain flare may occur during or post radiotherapy, where the addition or increase of steroids is likely to be of benefit.

Vertebral collapse may be treated conservatively with analgesics, e.g., opioids, NSAIDs, and/or steroids. As discussed, radiotherapy may be considered but another option is vertebral augmentation, i.e., vertebroplasty or kyphoplasty, especially in osteolytic lesions. These techniques are best performed for fractures that are less than 6 weeks old. They may also avoid the potential deterioration of the fracture post radiotherapy if the cancer is so radiosensitive that it causes

vertebral instability after responding to the radiotherapy. Vertebroplasty involves the infiltration of the vertebral body with cement, to strengthen the bone, ablate the cancer deposit, and reduce the pain. Kyphoplasty involves the same injection of cement, except a balloon is inflated into the vertebral body to create the space for the cement. These are usually day case procedures, with local anesthetic and minimal sedation, with rapid resolution of pain and functional ability (Chandra et al. 2018).

Vertebral augmentation requires careful selection of patients, with absolute contraindications listed as: spinal column infection or other active systemic infection; uncontrollable bleeding; inability to tolerate a prone procedure with sedation or general anesthesia; significant myelopathy due to cord compromise at the site under consideration, because of epidural tumor extension or fracture retropulsion; and known bone cement allergy. For sacroplasty patients, i.e., sacral augmentation, sacral decubitus ulcers are an absolute contraindication to avoid osteomyelitis and implant infection. The main complications of these procedures are: subcutaneous and/or paraspinal hematoma; fractures (of rib, pedicle, vertebral body, or sacrum depending on treatment level); infection (osteomyelitis, epidural abscess); cement leakage; nerve or spinal cord damage resulting in paralysis or bowel/bladder dysfunction; pulmonary embolus (secondary to cement or fat emboli); hypotension or depressed myocardial function (secondary to free methyl methacrylate monomer or fat emboli); pneumothorax (for thoracic vertebroplasty and kyphoplasty); and worsened pain or failure to treat (Chandra et al. 2018).

(b) Hemorrhage into a tumor

A sudden hemorrhage into a tumor can lead to acute pain, e.g., bleeding into tumors of the brain and liver, in both primary and metastatic disease. The hemorrhage may be due to clotting abnormalities, erosion into blood vessels, or rupture of vasculature of the tumor. Opioids are the mainstay of treatment. In cases of bleeding into organs with a capsule, e.g., the liver or spleen, distension of the capsule leads to acute pain. NSAIDs and steroids can provide analgesia in conjunction with opioids in such capsular pain. Hemorrhages can be a life-threatening complication of cancer and clinical interventions may include transfusions, analgesia, and sedation, according to the goals of care. In some cases, if appropriate, more urgent action to control the bleeding may be needed, e.g., trans-arterial embolization, but if unsuccessful, emergency surgery may be required.

(c) Obstruction/perforation of a hollow viscus

Acute pain can occur when a hollow viscus is obstructed, increasing the risk of a potentially fatal perforation. Pancreatic cancers may cause right upper quadrant pain from biliary duct obstruction. In patients with a poor prognosis, stenting of the biliary tree or the duodenum may provide symptomatic relief. The options of bypass surgery require careful consideration, given the median survival of 6.5 months for those eligible for surgery (Sohn et al. 1999).

Prostate, bladder, and pelvic cancers can cause ureteric obstruction, as can lymphadenopathy and retroperitoneal fibrosis via direct invasion or extrinsic compression. In patients with a good prognosis, retrograde stenting of the ureter or percutaneous nephrostomy can be considered. The acute pain may be relieved, but these procedures can also cause pain. One-third of patients will have a failed stent within 6 months, and coupled with the risk of infection or displacement, the management can be frustrating for patients and their families. For patients in whom retrograde stenting is impossible, the option of percutaneous nephrostomy and/or anterograde stent insertion is available but carries the same management problems.

Malignant bowel obstruction can be managed conservatively, via a syringe driver and in some instances a nasogastric tube. Hyoscine butylbromide can help with colicky abdominal pain and the reduction of large bowel fluid. Octreotide has an antisecretory

effect on the upper small bowel, and therefore has usually been reserved for multilevel or malignant small bowel obstructions. Constipation is a common dilemma in the management of patients with malignant bowel obstruction. Hyoscine butylbromide can relieve colicky abdominal pain, to spare opioid uses and reduce somnolence. Steroids can also help to reduce peritumoural edema, at a dose of 4–8 mg daily. These patients may also benefit from decompressive procedures, stenting, or occasionally surgery.

Bowel perforations are generally fatal, but may also be small and become walled off, to allow for some repair of the injury and better prognosis. The presentation of an acute abdomen usually warrants a review for urgent surgical intervention, but in palliative care, this is invariably inappropriate. The goal of care becomes symptom management and preparation for a potential death. Opioids, benzodiazepines, and antipsychotics may all be used, according to the agitation and distress that exists. Often a syringe driver will be needed with appropriate breakthrough medications. The need for review is important, to ensure that adequate symptom control is being achieved and that the syringe driver can be changed if needed.

(d) Spinal cord compression

The urgent management of spinal cord compression is discussed in the relevant chapter of the Palliative Care Emergencies section.

(e) Thrombosis and acute pulmonary embolism

The urgent management of venous thromboembolism is discussed in the relevant chapter of the Palliative Care Emergencies section.

6 Summary

Acute pain in palliative care is always an emergency to assess and manage the pain appropriately and in a timely fashion. This may involve leading the care or collaborating with other healthcare professionals in the management. Acute interventions may be required, e.g., with fractures, but the patient needs review to determine if the emergency treatment is appropriate for the goals of care. Acute pain management may also require the involvement of acute pain services.

We have discussed common acute cancer pain syndromes to highlight the diagnosis and consider management accordingly. Acute pain can occur independently, or as an episode of pain on a background of chronic pain. The development or worsening of chronic pain states drives the urgency for treatment, which invariably is best provided in a multimodal fashion, via a multidisciplinary team.

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Acute Dyspnoea

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Contents

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_80

Abstract

Acute (or episodic) dyspnoea is a debilitating symptom that induces fear and anxiety in patients and family/carers alike. Management focuses on addressing the underlying cause where this can be identified. In addition to addressing reversible causes, management of acute dyspnoea or a dyspnoea crisis will be discussed. Evidence for both pharmacological and non-pharmacological management strategies is outlined, with discussion of how these can be incorporated into a comprehensive, individualized management plan. Involvement and education of the wider interdisciplinary team across healthcare settings is essential. This chapter will also cover some of the more specific causes of acute dyspnoea such as anxiety or breathing pattern disorders, stridor or upper airway obstruction, bronchospasm, and the sensation of choking with a focus on neuromuscular diseases.

1 Introduction

This chapter will focus specifically on acute dyspnoea, more commonly described in the literature as episodic breathlessness. At times, episodic breathlessness may lead to a dyspnoea crisis, an important feature to recognize and actively manage. Information regarding chronic breathlessness syndrome is featured elsewhere in this textbook, as is the management of massive hemoptysis and superior vena cava obstruction. Specific information about palliative care in lung disease is detailed in a separate chapter.

Assessment and management of acute dyspnoea will depend on the stage of the patient's disease, their ability and willingness to undergo investigation, and the support available to them in their place of care. While this chapter covers some reversible causes of acute dyspnoea, the appropriateness of investigating and managing potentially reversible causes of decline need to be assessed on an individual basis. Many patients experience repeated episodes of acute dyspnoea, and this experience can be drawn upon to initiate and negotiate a care plan in advance – such as an advance care plan, advance directive, or breathlessness management plan – especially important since patients are usually unable to relate their wishes to healthcare professionals when acutely dyspnoeic. Many patients report feeling that their breathlessness is unrecognized by healthcare professionals (Gysels and Higginson 2011) despite the significant impact this symptom has on quality of life.

The aim of this chapter is to give health professionals an overview of:

- Acute (or episodic) dyspnoea and the recent research that is helping to define this symptom
- The assessment of an acutely dyspnoeic patient
- Investigations and treatments for certain clinical conditions or emergencies
- Non-pharmacological and pharmacological management strategies for a dyspnoea crisis
- Individualized dyspnoea crisis management plans

2 Episodic Breathlessness and Breathlessness Crises

Acute dyspnoea is a common, under-researched symptom that has a significant impact on both carers and patients. Retrospective studies have shown that in 3 months prior to death, 50% of patients referred to a palliative care service experienced no dyspnoea, falling to 35% at the time of death. Dyspnoea severity is higher in those with noncancer diagnoses (Currow et al. 2010). More recent research has focused on the type of dyspnoea, classifying breathlessness as continuous, episodic, or both. Episodic breathlessness has been further defined via a Delphi consensus method:

> Episodic breathlessness is one form of breathlessness characterised by a severe worsening of breathlessness intensity or unpleasantness beyond usual fluctuations in the patient's perception. Episodes are time-limited (seconds to hours) and occur intermittently, with or without underlying continuous breathlessness. (Simon et al. 2014)

Episodic breathlessness may occur without continuous breathlessness, but the opposite is rarely described (Simon et al. 2013a).

Episodic breathlessness was studied in 82 patients with chronic obstructive pulmonary disease (COPD) or lung cancer (Weingartner et al. 2015) and was reported in 71% of patient interviews, most often in COPD. The majority of episodes lasted less than 20 min. In other work, the duration of episodes has been described as 2–10 min (Reddy et al. 2009) and 1–5 min (Weingartner et al. 2013). Episodes could occur several times a day and are defined by a beginning and an end, with peak severity being worse in patients with a diagnosis of COPD (Weingartner et al. 2015). A systematic review found the prevalence of episodic breathlessness to be 81–85% in one lung cancer study (Simon et al. 2013b) or 61% in a second study (Reddy et al. 2009).

Simon et al. (2013c) has further described subtypes of episodic breathlessness in patients with lung cancer, COPD, heart failure, or motor neuron disease. These are detailed below. Types 3, 4, and 5 are less predictable and more likely to induce a panicked response.

1. Triggered episodes with normal levels of breathlessness (e.g., heavy exertion)
2. Triggered episodes with predictable response (e.g., talking, emotion)
3. Triggered episodes with unpredictable response (e.g., climbing stairs)
4. Non-triggered, unpredictable, attack-like episodes
5. Triggered or non-triggered wavelike episodes in COPD (more gradual onset, severe)

Episodic breathlessness is important to consider for two reasons. The first is that the sensation of breathlessness is intimately linked to panic and fear, more so when the dyspnoea becomes acutely worse for an unknown reason. However, even predictable episodes of breathlessness can have a significant impact on the individual due to the second reason – trigger avoidance. Breathlessness triggered by a known cause, such as exertion, leads to avoidance of that trigger and consequent deconditioning with a resultant increase in overall breathlessness (Janssens et al. 2011). High dyspnoea-related fear is associated with impaired quality of life and worse dyspnoea during exercise but also responds more positively to interventions such as pulmonary rehabilitation.

Episodic breathlessness, especially subtypes 3, 4, and 5 described above, may precipitate a "dyspnoea crisis." This has been defined as:

> sustained and severe resting breathing discomfort that occurs in patients with advanced, often life-limiting illness and overwhelms the patient and caregivers' ability to achieve symptom relief. (Mularski et al. 2013a)

Little is known about the incidence and prevalence of dyspnoea crises, the theoretical components of which were proposed during an American Thoracic Society Workshop. A survey of members of the American Thoracic Society performed prior to this workshop obtained 109 responders, 75% of whom had encountered outpatients in a palliative phase of their illness with acute crisis dyspnoea resulting in a 911 call or attendance at an emergency department (ED). Responders had encountered this situation weekly (19%), monthly (41%), or yearly (38%) (Mularski et al. 2013b).

The three required components for a dyspnoea crisis are:

- A worsening in dyspnoea
- A biopsychosocial/spiritual patient response
- An overwhelmed caregiver/environment

The workshop suggested that in order to manage the breathlessness crisis, all of the above components need to be assessed and actively managed on an individual basis. Only 9.6% of responders in the above survey indicated that their practice had any local policy or guideline on the management of acute crisis dyspnoea (Mularski et al. 2013b).

2.1 Impact on Patients

The impact of episodic breathlessness on patients is significant. Terms used by patients include frightening, panic (Gysels and Higginson 2011),

smothering, choking, couldn't get air, deathly sick, fighting for breath (Parshall et al. 2001), fear of choking, drowning, and suffocating (Simon et al. 2013c). Many patients fear that they will die suddenly of suffocation or choking during an attack or when asleep (Giacomini et al. 2012). Bailey described the dyspnoea–anxiety–dyspnoea cycle, a circular relationship with ever-escalating symptoms until the cycle is somehow broken. However, patients also describe that heightened emotion is an indicator of increasing breathlessness and may be the first sign of an impending crisis (Bailey 2004). While it is possible for patients to develop their own strategies to deal with the panic that arises during episodes, in one qualitative study, only 8 of 51 patients described having learnt to do so (Simon et al. 2013c). Many patients describe having never received health professional advice on how best to manage their breathlessness (Gysels and Higginson 2011).

2.2 Impact on Families and Caregivers

The impact of episodic dyspnoea and breathlessness crises on families and lay caregivers cannot be underestimated. During episodes, caregivers express a sense of helplessness and fear. There is significant relief and a sense of security once help is sought (Bailey 2004). Heightened vigilance leads to disturbed sleep, due to the unpredictability of episodes and the need to "sleep with one eye open" (Hearson et al. 2011). In COPD, relatives are repeatedly called to the hospital to "say goodbye" during acute exacerbations, only for the patient to survive and the cycle to recur again at some undetermined point in the future. Many relatives of patients with COPD fear that the dying process will be as prolonged as the disease course itself. However, in retrospect these relatives described the death as peaceful and calm, as if sleeping, as opposed to what the patient had most feared (Ek et al. 2015).

As described above, the family/caregiver plays a pivotal role during a dyspnoea crisis. During this time, the patient may be unable to self-manage their increased breathlessness, and the assistance of a family member or lay carer is therefore essential. Management of acute dyspnoea not only requires impeccable assessment of the patient but also of the family members or lay caregivers concurrently.

3 Causes of Acute Dyspnoea

When an episode of dyspnoea does not resolve or return to baseline, this requires further assessment in order to optimize management. Even for those at the very end of life, this can be worthwhile as simple strategies may be effective. Patient and caregiver distress is likely to be heightened. Taking the time to explore with the patient and their carer the change in their dyspnoea is an important acknowledgment of this symptom and validation of their concerns.

When assessing acute dyspnoea, it is important to identify those causes with a potentially reversible component. Progression of the underlying disease tends to occur over weeks or months and is a less likely cause of an acute dyspnoea episode. Commonly, the cause of the acute episode is due to a new diagnosis or complication, e.g., aspiration pneumonia. While anxiety can cause a dyspnoea crisis, this is a diagnosis of exclusion. Table 1 outlines causes of dyspnoea that have a relatively rapid onset and relevant investigations.

The degree to which these investigations are pursued will depend on the patient, the stage of their disease, and their wishes around management. Conversations around this can be difficult to negotiate during a crisis and should ideally have been anticipated in advance. For some, a change in location of care may be appropriate if a more supported environment is required to manage the dyspnoea, even if further investigation of the underlying cause is not pursued.

4 Assessment

As always, a clinical history is a vital component of the assessment of acute dyspnoea. In patients with a background of continuous dyspnoea,

specific qualities of the dyspnoea itself may be difficult to tease out. Despite this, patients (or carers) may be able to describe the degree of functional impairment compared to baseline (e.g., normally I can walk to the bathroom; today I can't get out of bed). The impact of the acute dyspnoea on the psychological state of the patient and their carers is an important component of the history. As outlined above, increasing anxiety may be either a consequence of acute dyspnoea or the initial symptom of an acute episode. The psychological state of the patient and carer will impact on their ability to cope with the acute episode and therefore the management strategy that is put in place. Specific questions may need to be directed at what happened immediately prior to the episode of acute dyspnoea, individual triggers, and management strategies that have or have not helped previously.

Dyspnoea has many components and subtypes, just as pain can be neuropathic or pleuritic in nature. Terms that have been consistently used by patients to describe their dyspnoea can be grouped under the headings "air hunger or unsatisfied inspiration," "work/effort," and "tightness" (Parshall et al. 2012). Other descriptors include heavy/fast, shallow, or suffocating. The term "tightness" when used by patients has been consistently associated with a diagnosis of asthma, but other qualities of dyspnoea are not reliably associated with a specific condition. In patients with high anxiety scores, terms such as frightening or awful are more frequent, as is the term "shallow" in patients with interstitial lung disease (Chang et al. 2015).

Associated symptoms may be present, such as cough, fever, production of purulent sputum, facial pain or postnasal drip relating to sinus infection, chest pain, peripheral edema, calf tenderness, paroxysmal nocturnal dyspnoea, or orthopnea.

In the respiratory system, clinical examination can help to narrow a differential diagnosis, is noninvasive, and easily performed at the patients' location of care. Many of the causes of acute dyspnoea in Table 1 have distinct clinical examination findings that can be picked up at the bedside. For example, abnormal pulse rate and rhythm can suggest arrhythmia, expiratory wheeze suggests bronchospasm, and stridor suggests upper airway obstruction.

Patient observations can be very helpful in refining the differential diagnosis, such as temperature, oxygen saturations, pulse, and blood pressure. However, a caveat is that in many patients with advanced lung disease, their baseline figures for these observations may be abnormal. For example, a patient with COPD may have a baseline oxygen saturation of 90% on room air and a heart rate of 100 beats per minute. It is therefore the *change* in the observation value that is most useful during assessment of an acute episode.

Table 1 Causes of acute dyspnoea and onset and investigations

Onset usually minutes or hours	Relevant investigations	Onset usually days	Relevant investigations
Acute MI	ECG, serial troponins	Cardiac tamponade	Echocardiogram
Diabetic ketoacidosis	Blood glucose, ABG	Congestive cardiac failure	BNP, CXR
Arrhythmia	ECG	Pneumonia	CXR
Sepsis	Blood culture	Exacerbation of COPD	FBC, CRP, CXR
Bronchospasm	Auscultation Peak expiratory flow in asthma	Upper airway obstruction	CXR, CT neck/chest or endoscopy
Pulmonary embolism	CTPA or V/Q scan	Anemia	FBC
Pneumothorax	CXR or USS chest	Pleural effusion	CXR or USS chest
Anxiety	ABG	Superior vena cava obstruction	CT chest with contrast

MI myocardial infarction, *ECG* electrocardiogram, *ABG* arterial blood gas, *CTPA* computed tomography pulmonary angiogram, *V/Q* ventilation perfusion scan, *CXR* chest x-ray, *USS* ultrasound scan, *BNP* brain natriuretic peptide, *FBC* full blood count, *CRP* C-reactive protein, *CT* computed tomography

5 Investigations

Whether or not to perform investigations for acute dyspnoea will depend on a number of factors, including the stage of the illness and patient's goals of care. Many of the investigations in Table 1 will require admission to a hospital or similar facility. Patients may have suffered many episodes of acute dyspnoea and will often be guided by previous experiences.

The clinical suspicion of a pulmonary embolism (PE) often brings difficult decision-making, as definitive diagnosis requires a computed tomography pulmonary angiogram (CTPA) or V/Q scan. The D-Dimer test is routinely used in ruling out a pulmonary embolism but has most utility in patients with a low probability of PE. The majority of cancer patients or those with advanced, life-limiting nonmalignant disease will not fall into a low probability group according to Wells' criteria, which makes the D-Dimer test less useful in this group. Consideration should be given to proceeding directly to definitive imaging in those where there is a high clinical suspicion of PE (Linkins and Takach Lapner 2017).

Pleural ultrasound is a relatively new, noninvasive technique that can be applied at the bedside to diagnose cardiogenic pulmonary edema, pleural effusion, pneumothorax, or consolidation in trained operators. It is increasingly being used by emergency physicians to aid in narrowing a differential diagnosis for patients presenting with breathlessness. While the interobserver and intraobserver variability has been reported as low in skilled operators, the main limitation of its use lies in operator training and experience (Wimalasena et al. 2017).

6 Management of Specific Conditions

The management of massive hemoptysis and superior vena cave obstruction is covered elsewhere in this textbook. Discussed below are management strategies for several causes of acute dyspnoea that commonly cause distress.

6.1 Anxiety or Breathing Pattern Disorders

Anxiety as a cause of acute dyspnoea or dyspnoea crisis is a diagnosis of exclusion, when organic causes have been ruled out. In some patients, a more chronic breathing pattern disorder can occur, such as hyperventilation syndrome or periodic deep sighing. These conditions are more common in those with underlying respiratory disorders, most commonly asthma. They are difficult to diagnose but should be suspected when chronic changes in breathing pattern result in dyspnoea, in excess of that expected for the underlying disease, plus non-respiratory symptoms resulting from hypocapnia such as dizziness or tingling of the extremities. The Nijmegen questionnaire is helpful in identifying individuals with this diagnosis, and evidence of hyperventilation on an arterial blood gas is also suggestive. Identification of a breathing pattern disorder is important as physiotherapy-directed breathing techniques can be effective in managing this condition. In the acute setting, rebreathing is no longer recommended; reassurance and time are usually sufficient to allow symptoms of an acute attack to settle (Boulding et al. 2016).

6.2 Stridor or Upper Airway Obstruction

Stridor can be defined as an "abnormal high-pitched musical sound caused by an obstruction in the trachea or larynx" (Harris et al. 2014). Stridor may be accompanied by drooling or inability to swallow secretions. Causes in the palliative setting are usually malignant, most commonly due to lung cancer (Guibert et al. 2016) but can include more benign causes such as foreign body aspiration. Rapid deterioration can occur if swelling, secretions, or bleeding narrows the airway lumen further. The management of stridor will depend greatly on the goals of care for the individual and range from emergency intubation or tracheostomy to palliative sedation in the last days of life.

For those patients not appropriate for intubation or surgical airway management, initial treatment will include supportive care with positioning (usually in the upright position), attention to secretion management with gentle suction as required, and oxygen for those who are hypoxemic. Nebulized adrenaline has been used in this setting with anecdotal benefit in case reports (Flockton et al. 2007). Doses recommended are adrenaline 1:1000 made up to 5 ml with 0.9% saline and delivered via nebulizer up to four times a day, though doses used for croup in the pediatric setting can be much higher than this. Reported side effects are tachycardia, tremor, hyperactivity, and hypertension.

Heliox, a mixture of helium and oxygen gas, has been reported as beneficial for patients with acute upper airway obstruction (Smith and Biros 1999). Room air is mainly a mixture of nitrogen and oxygen; when nitrogen is substituted for helium, the overall gas density is reduced, and laminar airflow is restored, a theoretical advantage in those patients with large airway obstruction causing turbulent airflow. Helium is inert, with an excellent safety profile in humans. There are no evidence-based guidelines around the use of heliox in acute upper airway obstruction, but a trial of therapy should be considered as a bridge to definitive treatment. Numerous case reports describe clinical improvement following heliox in patients with upper airway obstruction due to lymphoma, cancer, or radiation therapy (Smith and Biros 1999; Diehl et al. 2011).

Depending on the likely cause of the upper airway obstruction, steroids may be indicated. Dexamethasone is usually the drug of choice due to its potent anti-inflammatory effects. Due to the nature of action of dexamethasone, full benefit may not be seen for several days. Steroids should therefore be initiated early in conjunction with other management strategies as mentioned above.

Interventional bronchoscopy is a developing field and is available in many centers worldwide. For malignant tumors causing central airway obstruction in the trachea, main bronchus, or bronchus intermedius, interventional techniques may provide palliation of symptoms. Between 20% and 30% of lung cancers will cause central airway obstruction, either from endoluminal blockage, extrinsic compression, or a combination of both (Guibert et al. 2016). Bronchoscopic techniques that can allow rapid reversal of central airway obstruction include thermocoagulation with electrocautery, argon plasma coagulation or Nd–YAG (neodymium-doped yttrium aluminum garnet) laser. These techniques are contraindicated in patients requiring supplementary oxygen with a FiO_2 exceeding 0.4 due to the risk of combustion. Once the airway lumen has been enlarged, an endoluminal stent may be placed to prevent recurrence. For extrinsic compression, stenting may be the only bronchoscopic option available. A registry study of therapeutic bronchoscopic procedures quotes technical success rates of over 90% but with improvements in dyspnoea scores and quality-of-life (QoL) scores of 48% and 42%, respectively. It was noted that those patients with higher dyspnoea scores and lower QoL pre-procedure gained most benefit in terms of relief of symptoms. The overall complication rate was 3.9% with a 0.5% procedural mortality rate (Ost et al. 2015). In summary, interventional bronchoscopic techniques may be appropriate for selected patients with central airway obstruction, which is causing significant dyspnoea or impaired QoL and who do not require high-flow oxygen.

6.3 Bronchospasm

Bronchospasm can be defined as "an excessive and prolonged contraction of the smooth muscle of the bronchi and bronchioles, resulting in an acute narrowing and obstruction of the respiratory airway" (Harris et al. 2014). It is usually reversible. Precipitants include underlying asthma or COPD, allergic reactions such as anaphylaxis, or pseudoallergic reactions such as a drug reaction. Pseudoallergic reactions can occur on first exposure to a drug, such as the histamine release induced by morphine. This side effect of morphine is generally described when given intravenously, often during general anesthesia, but can cause itching, bronchospasm, and vasodilatation.

Other drugs such as aspirin, nonsteroidal anti-inflammatory drugs or beta blockers may cause bronchospasm, particularly in those with underlying diseases such as asthma.

Increasingly, nebulized therapy is being utilized in many areas of medicine, e.g., nebulized saline for troublesome secretions or nebulized lignocaine for intractable cough. Any nebulized treatment has the potential to cause bronchospasm, especially in those with risk factors such as asthma. In practice, if there is clinical concern that bronchospasm may occur, then serial spirometry performed before and after administration of the drug in question may be helpful; in many centers a 200 ml or 12% drop in FEV1 readings post-administration would be considered significant. In those patients unable to perform spirometry, premedication with a beta agonist may be required.

Treatment of acute bronchospasm involves the use of bronchodilator medication. This falls into two groups, beta agonists and muscarinic antagonists. In the acute setting, inhaled, short-acting beta-2 agonists are the drug of choice. Beta-2 agonists act on bronchial smooth muscle to affect rapid bronchodilation, acting within 3–5 min with a peak effect at 15–20 min. When short-acting beta-2 agonists such as salbutamol are delivered via metered dose inhaler (MDI) and spacer device by appropriately trained personnel, they can be as efficacious as a nebulizer device. However, nebulized short-acting beta-2 agonists may be appropriate for those who are unable to use an MDI (e.g., incoordination, poor technique, unable to activate device), and many patients express a preference for nebulized therapy. The increased risk of transmission of airborne infection limits the use of nebulizers in the hospital setting. Side effects of beta-2 agonists include tremor, nervousness, tachycardia, and rarely paradoxical bronchospasm (Cates et al. 2013).

Short-acting muscarinic antagonists such as ipratropium can be considered as additional treatment for those not responding to beta-2 agonists and are available in both MDI and nebulized forms. Side effects include dry mouth, nausea, headache, and rarely paradoxical bronchospasm.

Both beta-2 agonists and muscarinic antagonists are available in long-acting formulations, evidence for their use centers around chronic management of asthma or COPD. With the exception of formoterol, their onset of action is too long to be of use in the management of an acute dyspnoea crisis and should not be used in this setting. In asthmatics, use of a long-acting beta agonist without concurrent use of inhaled steroid should be avoided.

6.4 Choking Episodes

Choking episodes are uncommon in patients with life-limiting illness but cause significant anxiety and distress. They are particularly common in those with neurological disorders affecting swallow, such as motor neuron disease (MND). Choking episodes can also occur in those with malignancies affecting the upper airway or lower respiratory tract due to excessive secretions, particularly bronchoalveolar cell carcinoma of the lung which can occasionally produce a high volume of secretions (or bronchorrhea) (Remi et al. 2016).

Much of the evidence around choking episodes centers on MND, where bulbar dysfunction affects between 20% and 30% of patients (Banfi et al. 2015). While many patients with MND are worried about choking to death, retrospective studies have shown that this does not occur in reality (Neudert et al. 2001). In one review, 7% of patients experienced episodes of choking on saliva or mucous within the last 24 h prior to death, with 4% experiencing coughing. A further study comparing coughing or choking episodes in patients with MND to healthy controls revealed that the majority of MND patients experienced coughing or choking episodes, ranging between 1 and 50 episodes over a 3-day period. Twenty-seven percent of patients described the episodes as moderate or very distressing, and 32% described shortness of breath or inability to breathe during episodes (Hadjikoutis et al. 2000).

Much of the management of choking episodes focuses on chronic management of secretion production. Secretions may either be “thick” and

cause problems with difficultly expectorating sputum or "thin" due to excessive saliva production and inability to swallow saliva or bronchorrhea. It is essential that the type of secretion problem be assessed carefully; in one study 40% of MND patients described thin secretions, 23% thick secretions, and 37% both. Overtreatment of thin secretions can cause thick secretions to become a problem (McGeachen et al. 2017a).

Chronic management of thin secretions includes the use of anticholinergics such as hyoscine butylbromide, tricyclic antidepressants, atropine (eye drops, used sublingually), glycopyrronium, and nasal anticholinergics such as propantheline or ipratropium (used sublingually). For thick secretions, medications such as carbocisteine or 0.9% saline via nebulizer may be of benefit, in addition to conservative measures such as fruit juices (e.g., grape or pineapple) and attention to hydration (McGeachen et al. 2017a).

Acute management of choking episodes is less evidence-based. These episodes should be anticipated in advance in those at risk, and an action plan developed with the patient and carer may reduce anxiety and distress. Attention should be paid to positioning (sitting upright, use of mechanical aids to allow easy change in position, or turning to the contralateral side if bed-bound). Gentle suction can be helpful, particularly for those with thin secretions. Carer education is essential, for example, in the use of devices such as suction machines and nebulizers or performing manually assisted cough in those with poor respiratory muscle function.

Thick secretions can be challenging to manage in an acute choking episode; saline nebulizers may be helpful as well as manually assisted cough (McGeachen et al. 2017b). For those with tracheostomies, suction is essential but is of more limited use for those with an intact oropharyngeal airway and gag reflex.

7 Management of the Dyspnoea Crisis

As described above, a dyspnoea crisis can be defined as:

> sustained and severe resting breathing discomfort that occurs in patients with advanced, often life-limiting illness and overwhelms the patient and caregivers' ability to achieve symptom relief. (Mularski et al. 2013a)

The majority of these episodes are short-lived, up to 10 min duration (Reddy et al. 2009) and mainly occur in the patients' place of care, such as their own home. Such a crisis may have an acute, reversible underlying cause, but many episodes resolve spontaneously or with measures targeted at relieving the dyspnoea itself. Despite this, acute on chronic breathlessness has been shown to be responsible for at least 5.2% of all presentations to the ED in one study. In this study population, only one in five patients had a GP or paramedic involved in the decision to attend the ED, with patients and family/friends most frequently initiating the decision to present. Although patients rated their shortness of breath as "severe" at the time of the decision to attend, the rating had reduced to "mild" by the time of assessment in the ED itself, supporting the fact that the episodes are generally short-lived (Hutchinson et al. 2017). For some patients, where a dyspnoea crisis is sustained or severe, it may be appropriate to seek medical assessment for consideration of investigation or treatment. This will depend on the patient and families' goals of care, which can be impossible to discuss during an acute episode.

7.1 Non-pharmacological Measures

Management of chronic refractory dyspnoea is detailed in ▶ Chap. 11, "Palliative Management of Breathlessness" and will not be reiterated here. Most of the measures described can be applied in some way to episodes of acute dyspnoea or a dyspnoea crisis. Non-pharmacological measures may provide simple, effective means of managing a dyspnoea crisis with little or no side effects; however evidence to support this is lacking, with most research focusing on chronic refractory dyspnoea. While many non-pharmacological measures can be easily put into practice during a crisis, such as switching on a handheld fan or adjusting position, others are less easily utilized.

Relaxation and breathing control techniques in particular cannot be learnt in a state of heightened anxiety and panic and must be taught when the patient is in a more stable condition. These techniques require practice and reinforcement to utilize them effectively, meaning that a degree of planning must take place before a dyspnoea crisis occurs.

7.2 Pharmacological Measures

More recently, research has focused on the utility of pharmacological measures to manage a breathlessness crisis or episode of acute dyspnoea. Because of the short duration of breathlessness episodes, an ideal drug is one which is absorbed swiftly, with a rapid onset of maximum effect and short duration of action. For this reason, the transmucosal, intranasal, or nebulized routes of drug administration are particularly attractive. Since a systematic review of opioids in the management of dyspnoea failed to show any beneficial effect of nebulized opioids over nebulized saline, this route has fallen out of use (Jennings et al. 2002), and with the advent of oral transmucosal drug delivery systems, such as fentanyl citrate, research has been focused on this area.

Depending on the preparation, the onset of action of oral transmucosal fentanyl citrate is between 5 and 10 min with a bioavailability of between 50% and 90% (Cabezon-Gutierrez et al. 2016). Similarly, intranasal medications such as midazolam have been reported to have a median time to maximum effect of 10–14 min with bioavailability of 50–83% (Hardy et al. 2016). Drugs with a short half-life, such as fentanyl or midazolam, would seem ideally suited to the management of an acute episode of dyspnoea to tailor the duration of effect as closely as possible to the duration of the crisis.

Fentanyl has been the most studied opioid for the management of an acute episode of dyspnoea or dyspnoea crisis. However, most trials to date have been small or nonrandomized; therefore evidence of significant benefit is currently lacking. A systematic review by Simon et al. in 2013 identified only two randomized controlled trials (one of which included only two patients), with several case studies and before–after studies, totalling 88 patients. A variety of routes of administration were described, including oral transmucosal and intranasal. All studies reported successful relief of breathlessness after fentanyl application, but the only randomized controlled trial failed to demonstrate a statistically significant difference compared with placebo (Simon et al. 2013d). A further non-systematic review by Cabezon-Gutirriez of opioids for the management of episodic breathlessness identified 4 clinical trials and several case series, totalling 204 patients. Drugs studied included oral transmucosal fentanyl, intranasal or subcutaneous fentanyl, morphine and/or midazolam, and oral or subcutaneous hydromorphone. While these studies reported an improvement in dyspnoea, the heterogeneity of the study design makes it difficult to ascertain efficacy of any one intervention. Side effect reporting was low and limited to somnolence and dizziness, suggesting that opioids for the treatment of episodic dyspnoea are safe in the majority of patients (Cabezon-Gutierrez et al. 2016). Further trials are underway at the time of writing.

Despite the lack of evidence for the use of benzodiazepines for managing chronic, refractory breathlessness, these medications are commonly used. As described above, a dyspnoea crisis overwhelms the ability of the patient and/or caregivers' ability to cope, often due to the anxiety and panic caused by severe shortness of breath. Intuitively, therefore, use of a short-acting anxiolytic agent, such as midazolam, could modify this anxiety and break the dyspnoea–anxiety–dyspnoea cycle. Evidence is limited however. A randomized, double-blind trial of intranasal midazolam for chronic refractory dyspnoea showed no benefit over placebo (Hardy et al. 2016). Evidence specifically in episodic dyspnoea is very limited, and to date no clear benefit has been shown (Simon et al. 2016). A pragmatic approach should be taken until further research can guide the use of benzodiazepines in this setting. Medications with more robust evidence for the palliation of dyspnoea should be used first-line, with reservation of

benzodiazepines as second- or third-line therapy for those patients where there is a significant degree of anxiety or panic during dyspnoea crises. To minimize harms, an individualized (or n-of-1) trial should be undertaken, with a short-acting benzodiazepine initiated at low dose and titrated upward.

Oxygen is commonly used during episodes of breathlessness. Patients with chronic breathlessness or frequent episodes of acute dyspnoea requiring emergency medical assessment are often familiar with the use of oxygen during an emergency. High flows of oxygen are applied immediately on arrival of the paramedic or at the ED. While in reality multiple interventions are occurring for the patient during this time, many patients recall the initiation of oxygen as having a positive effect on reducing their breathlessness. Evidence for this is lacking, however, particularly in the group with maintained oxygen saturations of greater than 90% on room air. In chronic, refractory breathlessness, a large randomized double-blind trial showed no beneficial effect of oxygen over room air when delivered by gas concentrator for 16 h or more per day. A significant number of patients declined to continue therapy at the end of the trial, as the burdens were felt to outweigh the benefits by those individuals (Abernethy et al. 2010). Evidence for ambulatory oxygen, for those with exertional oxygen desaturation, is similarly lacking with a large trial in COPD showing no benefit on quality of life or walking distance (LOTT Group 2016). Domiciliary oxygen is not without harms and is contraindicated in active smokers. For this reason, oxygen should not be used first line as an intervention for breathlessness crises but trialed on an individual basis as part of a comprehensive management plan.

7.3 Palliative Sedation

For some patients with overwhelming distress, sedation may be required. The aim of sedation may vary from transient (for a period of hours until the current episode has resolved) to palliative sedation for a patient in the last days of life experiencing intolerable suffering due to dyspnoea. Where it is anticipated that sedation may be required, it is important to recognize, plan for, and discuss this with the patient and family prior to an event occurring. Many patients and families consent to transient sedation during a breathlessness crisis where symptoms cannot be controlled by other means. It is important to emphasize the goals around this and expectations regarding the duration and depth of sedation. This is usually delivered by bolus medications on an "as required" basis.

Palliative sedation in the last days of life involves continuous administration of sedating medications to render the patient unaware of the symptom that is causing intolerable suffering, i.e., dyspnoea. Palliative sedation in this setting has not been shown to hasten death (Godbout et al. 2016). The decision to commence palliative sedation can be difficult and ideally should involve engagement with the wider healthcare team as well as family/carers, with preemptive education and opportunity for discussion. This can be impossible to achieve in the setting of a dyspnoea crisis, where decision-making is usually rapid. Where possible, this option should be discussed in advance with patients at risk of requiring palliative sedation or who disclose fears about control of breathlessness in the last days of life.

7.4 Advance Care Planning

Advance discussions around the goals of care for an individual are imperative when managing a breathlessness crisis. During an episode, most patients are unable to communicate their wishes effectively; they are usually too breathless or too panicked to be able to engage in a complex discussion about their wishes for treatment. Similarly, most family members or carers will be focused on managing the distress of their loved one a rather than specific treatment options. It is therefore important to recognize discussions around the goals of care as essential to managing those at risk of a dyspnoea crisis and for these conversations to occur during a time of relative stability.

Repeatedly in the literature, patients express a wish to know their future prognosis but wait for their healthcare practitioner to initiate this conversation. Components of the discussion should focus on a shared understanding of the disease process, expected complications, and prognosis, with a strong focus on the goals of the individual in the time ahead. Once goals are established and agreed upon, treatments can be considered that may or may not achieve these goals, such as invasive ventilation or cardiopulmonary resuscitation. For some patients it can be difficult to make advance decisions, particularly in diseases where the course of events is less certain, such as COPD (MacPherson et al. 2012). For this group, advance conversations can still add value by identifying a surrogate decision-maker and preparing the patient for *how* decisions may be made in the event that a crisis occurs.

The value of these discussions lies in the conversations between the patient, their loved ones, and the treating healthcare practitioner. Many patients will choose to write down advance decisions to assist with transparency over multiple healthcare settings and to avoid future conflict or uncertainty. This can be done via an advance directive, advance care plan, or other format such as Physician Orders for Life-Sustaining Treatment (POLST) form.

7.5 Individualized Dyspnoea Crisis Management Plans

Since the majority of episodes of dyspnoea crisis occur outside of healthcare settings, self-management is essential. Despite this, few guidelines are available for either healthcare professionals or patients/carers with regard to self-management of breathlessness episodes. A review of internet-based guidelines for patient self-management of chronic breathlessness found multiple websites of varying quality. Specific guidance for breathlessness crises suggested attending the ED immediately, rather than subsequent to implementing incremental management strategies; none offered support for goal setting. Website content for carers was limited, and compliance with American Medical Association benchmarks for quality were low (Luckett et al. 2016).

An American Thoracic Society workshop in 2009 on the assessment and management of dyspnoea crisis proposed a customizable self-management patient/caregiver plan, incorporating the management strategies described above (Mularski et al. 2013a). While there is little evidence for the effectiveness of such plans as yet, such a multicomponent intervention is difficult to assess. Management plans for a dyspnoea crisis involve utilizing interventions that the patient and caregiver have previously found beneficial for their breathlessness, in a specified order. It is therefore imperative that specific techniques or medications, such as a fan or opioids, have been trialed individually before a comprehensive plan can be created. Individual components may be assessed by patient/caregiver report or a symptom control diary. Each plan should be individualized and may involve multiple members of the interdisciplinary team in its creation. Plans should be fluid enough to adapt to the patient experience; reviews should be scheduled regularly. Vital to the plan is identification of who to call for help should the end of the management cascade be reached, as well as transparency as to the goals of care and indications for transfer to an alternative place of care, such as the ED.

An example of a management plan cascade is below. The order of specific therapies will depend on the patient. In general, non-pharmacological therapies are used first, but in some patients with a significant anxiety component to their dyspnoea crises, medications may need to be administered early as panic limits the ability to engage with therapies such as relaxation techniques.

- Call or signal for help.
- Attend to positioning and environmental factors, e.g., switch on a fan or open a door.
- Distraction – music, TV. Reassurance. Relaxation techniques.
- Medications – include specific therapies that have worked previously, e.g., salbutamol.

Include dose and time interval for expected effect. Repeat doses if necessary.
- Oxygen if indicated.
- Who to call for help if above steps have failed.
- Ceiling of care or where documentation of this may be found.

Family or lay caregivers are integral to the success of a management plan for dyspnoea crisis. Family caregivers are deeply affected by a dyspnoea crisis which can cause feelings of anxiety, inadequacy, helplessness, and uncertainty. A qualitative interview of patients with lung cancer or COPD and their carers found that carers wished to know more about managing anxiety, panic, and breathlessness. More specifically, carers wish to know how to recognize panic and how to respond confidently in order to manage breathlessness. Carers acknowledged that their response was often unhelpful – e.g., asking the patient what they want during a time of crisis and that they themselves often felt anxious and panicked (Farquar et al. 2017). Mularski et al. suggest components for patient (and family/carer) education in dyspnoea crisis which include:

- Basic facts about triggers and causes
- Signs and symptoms that may indicate a crisis
- Measuring change in dyspnoea intensity and distress
- Breathing retraining
- Relaxation techniques
- Use of oxygen, ventilation, or fans
- Appropriate administration and dosing of medications

These facets of patient education should be delivered from diagnosis and reinforced at every encounter, not only with patients but also with those caregivers who are likely to be present at the time of a dyspnoea crisis.

One of the greatest challenges to healthcare currently is ensuring that such plans are visible and transferable across healthcare settings. Communication between patient, family/carers, and all healthcare professionals is key to successful implementation of an individualized dyspnoea crisis management plan and therefore control of a dyspnoea crisis. In some cases, it may be necessary to nominate a single family spokesperson to communicate with healthcare professionals. Many healthcare professionals are unfamiliar with the management of a dyspnoea crisis and will require targeted education within relevant local practice guidelines and continuing education programs (Mularski et al. 2013a).

8 Conclusion and Summary

Assessment of acute dyspnoea as well as management of specific conditions such as stridor, bronchospasm, and choking is essential knowledge for the palliative care practitioner.

Episodic breathlessness is a significant and distressing symptom for patients with advanced life-limiting illness, which at times may precipitate a dyspnoea crisis. Impeccable, holistic assessment of the patient presenting with an acute exacerbation of their dyspnoea is essential to reverse treatable causes. For those without an immediately reversible cause for their dyspnoea, or for whom investigation is inappropriate, management should focus on non-pharmacological and pharmacological approaches – which present unique challenges in this setting due to the short duration of episodic dyspnoea and lack of evidence in this area. Comprehensive management plans, including a stepwise approach to previously trialed interventions, should be individualized, shared, and reviewed on a regular basis. Carer engagement is key to successful implementation. Education and involvement of the interdisciplinary healthcare team across multiple settings is essential.

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Neutropenic Sepsis

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_81

Abstract

Febrile neutropenia is a common complication of cytotoxic therapies and can be potentially life threatening. Treatment for neutropenic fever has evolved with the advent of antibiotics with mortality rates falling as a consequence. Patterns of infection have changed from being predominantly related to gram-negative organisms to now being mostly caused by gram-positive organisms. However, in the majority of cases, no source is isolated.

Higher rates of febrile neutropenia are seen with cytotoxic treatments for hematological malignancies, compared to that for solid malignancies. Therapies to reduce the risk of febrile neutropenia should be considered in patients at high risk of prolonged (>7 days) and severe ($<1 \times 10^9$ cells/L) neutropenia and also in those who would poorly tolerate the complication. Risk factors for neutropenic fever include age >65, prior exposure to chemotherapy or radiation, persistent neutropenia, bone marrow involvement by tumor, recent surgery and/or open wounds, renal dysfunction, and liver dysfunction.

Management requires prompt commencement of antibiotics, careful investigations into a possible source, and supportive cares. Empiric antibiotics with an antipseudomonal cephalosporin or a carbopenem should be started early. Data around the synergism of aminoglycosides is unclear. Treatment should be modified dependent on the results of the investigations. In the setting of a persistent fever, the addition of vancomycin and/or an antifungal agent should be considered.

Patients should be well informed of this potential life-threatening complication. Mortality can vary from 1% in low-risk patients to 50% in those requiring ICU admission with septic shock.

1 Introduction

Febrile neutropenia is a potentially life-threatening complication of cytotoxic therapy in both oncology and hematology patients. Febrile neutropenia is defined as a temperature above 38.5 °C or consecutive temperatures above 38 degrees Celsius more than 1 h apart associated with a neutrophil count of less than 0.5×10^9 cells/L or one expected to fall below 0.5×10^9 cells/L (Table 1). The risk of febrile neutropenia is higher in patients receiving chemotherapy for hematological malignancies compared with those receiving treatment for solid organ cancers. In approximately 50% of cases, the cause of the fever is not found and

Table 1 Important definitions

	Definition
Febrile neutropenia	A temperature above 38.5 °C or consecutive temperatures above 38 °C more than 1 h apart associated with a neutrophil count of less than 0.5×10^9 cells/L or one expected to fall below 0.5×10^9 cells/L
Neutropenic sepsis	Severe sepsis in the context of febrile neutropenia
Severe sepsis	New evidence of organ dysfunction or decreased perfusion including lactic acidosis, oliguria (<0.5 mL/kg/hr), hypotension (<90 mmHg systolic blood pressure or a decrease of >40 mmHg), or delirium
Septic shock	A situation where severe sepsis and hypotension persist despite adequate fluid resuscitation and in the absence of other explanations for hypotension
Clinically unstable	The presence of severe sepsis or septic shock
Clinically stable	The absence of severe sepsis or septic shock
Complicated infection	One or more of the following: Persistent fever greater than 48 h despite treatment Evidence of secondary infection such as endocarditis, osteomyelitis, or abscess Development of a fungal infection Severe sepsis Septic shock Congestive heart failure, ECG changes, or arrhythmia Respiratory failure Renal failure Intensive care admission Bleeding requiring transfusion Allergic reaction
Uncomplicated infection	The absence of a complication as defined above

treatment is empiric. The prognosis for patients with neutropenic fever has improved with the advent of antibiotics. Prompt treatment with antibiotics and supportive care is critical. In this chapter, we will review the pathophysiology of neutropenic fever, causative organisms, treatment, and prognosis of febrile neutropenia.

2 History

Although previous studies had indicated a relationship between leukopenia and infection in patients with acute leukemia, it was not until 1966 that a *quantitative* relationship between leukocyte counts and infection was established (Bodey et al. 1966). Infection was the primary cause of death in these patients. Early efforts to treat infection were hampered by resistant organisms, with mortality from *Staphylococcus aureus* infections around 40%, predominantly due to high rates of penicillin resistance. This changed with the invention of methicillin with fatality falling to less than 5%, again by the 1960s (Bodey 1997). Over the last half century, patterns of infection associated with cancer treatments have continued to change.

A historic principle was that infection should not be treated until the causative organism had been identified. In 1971, this idea was challenged following the Schimpff et al. study, when it became recognized that empiric antibiotics should be used to treat patients with evidence of infection in leukemia (Bodey 1997). This principle was subsequently applied for all patients treated with myelosuppressive therapy presenting with this complication.

3 Pathophysiology

Chemotherapy-induced leukopenia can cause fever in the absence of infection, due to the release of cytokines such as interleukin-6 (IL-6) and tumor necrosis factor (TNF) (Bennett et al. 2013). However, fever in the context of chemotherapy-induced neutropenia is often the result of invasive infection and can be fatal. It is difficult to know the exact proportion of febrile neutropenia episodes resulting from invasive infection, as microbiological evidence of infection is found in less than 50% of cases of febrile neutropenia (Bucaneve et al. 2005).

Chemotherapy leads to impairment of the innate immune system in two ways. The first relates to impairment of the barrier function of the gut and to a lesser extent the skin. This is most commonly due to chemotherapeutic toxicity and mucositis allowing the transposition of bacteria into the bloodstream. In allogeneic hematopoietic stem cell transplant recipients, graft-versus-host disease (GVHD) may also affect this barrier function. In many cases, patients will also have long-term central venous catheters which can act as a route by which bacteria can bypass barriers and cause invasive infection. The second relates to chemotherapy-induced neutropenia. Neutrophils play a role in the non-specific phagocytic killing of bacteria and fungi as well as in the mediation of an inflammatory response, the absence of which allows infection to progress much faster.

3.1 Microbiology

Microbiological evidence of infection is found in less than 50% of cases of febrile neutropenia (Bucaneve et al. 2005). Bacteremia is found in only 20–30% of cases (Feld 2008). Over the last half century, patterns of infection have changed from a predominance of gram-negative organisms to now more commonly gram-positive organisms. One study found that the proportion of gram-negative and gram-positive organisms changed from 71% and 29%, respectively, in 1973–1975 to 33% and 67% in 1992–1994 (Klastersky 1998). This pattern has been less prominent in developing countries (Feld 2008). One possible explanation for this observation is the increasing use of prophylactic antibiotics and central venous catheters, particularly in developed nations. The use of prophylactic antibiotics can result in a reduced proportion of gram-negative to gram-positive bacteremia (from approximately 50% to 25%) (Feld 2008).

Patients with febrile neutropenia and gram-negative bacteremia have higher rates of mortality than those with gram-positive bacteremia (Feld 2008). Mortality in those with gram-negative bacteremia was found to be 18% in a population including both patients with hematological and solid organ malignancies treated in predominantly Western countries. This is compared with a mortality rate of 5% in those with gram-positive bacteremia from the same cohort. The most common gram-negative organisms included *E. coli*, *Klebsiella* species, and *P. aeruginosa*. The most common gram-positive organism was coagulase-negative staphylococci (in 50% of gram-positive bacteremia), followed by streptococcal species, and less commonly *S. aureus* and *Enterococcus*.

Fungal organisms are an important cause of mortality and morbidity in significantly immunosuppressed patients (Richardson 1998). The population primarily at risk are those patients with hematological malignancies undergoing hematopoietic stem cell transplant. The risk is increased in those with neutropenic periods longer than 7–10 days (Richardson 1998). In those receiving *allogeneic* transplants, the period of immunosuppression may be prolonged beyond the period of neutropenia, depending on the nature of the conditioning regimen and additionally on the use of immunosuppressives to reduce the risk of, or to treat, GVHD in the posttransplant period. The most common fungal organisms include *Aspergillus* and *Candida* species.

Candida are ubiquitous colonizers of mucosal surfaces, and breakdown of the skin and mucosa can lead to invasive infection (Freifeld et al. 2011). Azole prophylaxis has reduced their rates of invasive infection, but resistant forms of *Candida* such as *C. krusei* and *C. glabrata* are not uncommon and may be increasingly prevalent due to the use of prophylaxis (Freifeld et al. 2011). *Aspergillus* is an ubiquitous organism that is not usually pathogenic. Invasive aspergillosis is uncommon if neutropenia lasts less than 10 days, but beyond this time the incidence increases in proportion to the length of the neutropenic period (Gerson et al. 1984).

Finally, viral organisms can cause infections in the immunocompromised host. Herpes simplex virus (HSV) is common and can cause mucous membrane ulcers. Varicella zoster virus (VZV) is the cause of shingles, a vesicular skin rash typically in a dermatomal distribution. In those who are severely immunocompromised, VZV can present in a more widespread pattern. Both organisms can also cause encephalitis. These organisms typically become evident as a result of a deficiency in immune control, leading to reactivation of the latent virus. Other viral infections such as cytomegalovirus do not usually occur in the neutropenic period, but rather later as a result of other immunosuppressive agents used in the prevention of GVHD.

4 Incidence

It is difficult to estimate the true incidence of febrile neutropenia due to a number of factors, e.g., varying definitions of febrile neutropenia, the nature and extent of the underlying cancer, comorbidity in the studied population, the intensity of the chemotherapy, and the varying use of granulocyte colony-stimulating factor (G-CSF) prophylaxis. In addition, data often comes from trial patients who tend to be fitter and are treated with more rigorous adherence to regimen protocols.

As a general rule, chemotherapy for hematological malignancies is associated with a greater risk of febrile neutropenia than solid organ malignancies. Estimates range from a 10% to 40% risk of developing febrile neutropenia in those receiving chemotherapy for solid organ tumors to greater than 80% for those with hematological malignancies (Penack et al. 2014). The National Comprehensive Cancer Network (NCCN) guidelines provide a useful summary of approximate risks of febrile neutropenia with various chemotherapy regimens (NCCN 2017).

5 Prevention

A number of preventative strategies have been investigated to reduce the risk of febrile neutropenia. These include granulocyte colony-

stimulating factor and antimicrobials. Current practice can vary significantly between centers. Typically prophylactic antibiotics are only recommended in patients expected to have prolonged (>7 days) and profound (<0.1 x 10^9 cells/L) neutropenia (Freifeld et al. 2011; Flowers et al. 2013). In this section, different preventative strategies will be reviewed.

5.1 Granulocyte Colony-Stimulating Factor (G-CSF) Prophylaxis

International guidelines suggest that if the estimated risk of febrile neutropenia is greater than 20% with a given regimen, primary prophylaxis with G-CSF should be used (Bennett et al. 2013). In those with an intermediate risk of 10–20% prophylaxis should be considered if other risk factors are present (Table 2).

Guidelines also propose that secondary prophylaxis should be considered if the previous cycle was complicated by an episode of febrile neutropenia (NCCN 2017), particularly if neutropenia *alone* would otherwise require a chemotherapy dose reduction. The occurrence of non-hematological toxicities from chemotherapy may necessitate a dose reduction in any case. It is important to consider the intent of chemotherapy in this decision. A lower threshold for a dose reduction may be appropriate in those being treated with palliative intent, in contrast to those treated with adjuvant or curative intent where maintaining maximum dose intensity is of key importance.

Table 2 Risk factors for febrile neutropenia

Patient risk factors for febrile neutropenia
Age > 65
Prior exposure to chemotherapy or radiation
Persistent neutropenia
Bone marrow involvement by tumor
Recent surgery and/or open wounds
Renal dysfunction (CrCl <50mLs/min)
Liver dysfunction

Adapted from NCCN guidelines (NCCN 2017)

5.2 Antibiotic Prophylaxis

One strategy postulated to reduce the risk of febrile neutropenia and associated mortality is antibiotic prophylaxis. Balanced against this are fears of increasing rates of antibiotic resistance by the selection of resistant organisms.

Many studies have explored antibiotic prophylaxis, but only the recent Cochrane systematic review has shown a mortality benefit. However, these studies involved a selected group at high risk of prolonged neutropenia (>7 days) (Gafter-Gvili et al. 2012). Most studies included in this systematic review investigated patients undergoing hematopoietic stem cell transplantation or intensive treatment for acute leukemia. The number needed to treat to prevent one death in this group was 33, with a reduction in all-cause mortality from 7.9% to 4.2% (Gafter-Gvili et al. 2012). Only a few of the studies included investigated patients with lymphoma and solid organ cancers receiving chemotherapy (but still only those receiving regimens with a high risk of prolonged neutropenia). A smaller mortality benefit was seen in this group with a number needed to treat to prevent one death of 50 and a reduction in all-cause mortality from 3.1% to 1.4% (Gafter-Gvili et al. 2012). Based on these studies, quinolones are the preferred prophylactic antibiotics, but no significant difference has been shown compared to cotrimoxazole. In the population at risk of *Pneumocystis jirovecii*, cotrimoxazole is the preferred option.

Two large trials published in *The New England Journal of Medicine* in 2005 also serve to guide the use of prophylactic antibiotics, the first assessing a population at high risk of febrile neutropenia and the second a low-risk population.

The first trial randomized 760 patients with either hematological or solid organ tumors where neutropenia (<1 × 10^9 cells/L) was expected to last at least 7 days but excluded those receiving *allogeneic* transplantation (Bucaneve et al. 2005). Levofloxacin was given continuously from up to 3 days prior to the commencement of chemotherapy or infusion of stem cells until the resolution of neutropenia. Although no mortality benefit was seen, there were significantly less febrile

episodes (65% vs. 85%) and microbiologically documented infection (22% vs. 39%) in the levofloxacin group compared to placebo.

The second trial randomized 1565 patients with either lymphoma or solid organ tumors expected to have a neutrophil nadir of less than 0.5×10^9 cells/L with regimens not routinely given with G-CSF prophylaxis (Cullen et al. 2005). Levofloxacin was given for the 7 days of the expected neutropenic period. Although there were significantly less febrile episodes in the treated group (10.8% vs. 15.2%) and less hospitalizations (15.7% vs. 21.6%), there was no difference in severe infection defined as severe sepsis or death (1% vs. 2%).

Antibiotic resistance is difficult to assess and was not rigorously studied in these trials, although all groups acknowledged this as a potential issue. Multiple studies have been done in this area (Freifeld et al. 2011). For example, one hematology-oncology unit stopped fluoroquinolone prophylaxis in acute leukemia treatment for 6 months where it was previously routinely given. They showed that quinolone resistance in *E. coli* isolates reduced from >50% to 15% during this period, suggesting that antimicrobial resistance is an important consideration in the use of prophylactic antibiotics (Kern et al. 2005). In addition, there is thought to be a significantly increased risk of *Clostridium difficile*-associated diarrhea when using fluoroquinolones (Pépin et al. 2005).

Both the American Society of Clinical Oncology (ASCO) and the Infectious Disease Society of America (IDSA) guidelines recommend fluoroquinolone prophylaxis only for those expected to develop prolonged (>7 days) and profound ($<0.1 \times 10^9$ cells/L) neutropenia (Freifeld et al. 2011; Flowers et al. 2013).

5.2.1 Antifungal and Antiviral Prophylaxis

Antifungal and antiviral agents are only indicated in those at high risk of prolonged neutropenia, such as those receiving hematopoietic stem cell transplant and those with acute leukemia receiving intensive induction chemotherapy (Freifeld et al. 2011). ASCO practice guidelines recommend prophylactic use of antifungals in high-risk patient populations at risk of prolonged (>7 days) and profound ($<0.1 \times 10^9$ cells/L) neutropenia (Flowers et al. 2013).

6 Risk Assessment and Prognosis

There is a body of literature that seeks to stratify patients presenting with neutropenic fever into those at low or high risk of complication, for the purpose of identifying those who may be able to be treated with oral antibiotics or as an outpatient.

One such method which is recognized in international guidelines is the Multinational Association for Supportive Care in Cancer (MASCC) risk index (Table 3) (Klastersky et al. 2000). The derivation set included 756 patients, and independent factors predictive of complication were identified and weighted. Complications were defined as one or more of the following: hypotension, respiratory or renal failure, intensive care admission, confusion or altered mental status, congestive heart failure, bleeding requiring transfusion, ECG changes, arrhythmia, development of a fungal infection, or an allergic reaction.

In the initial validation cohort of 383 patients with febrile neutropenia, the index achieved a positive predictive value of 91% in identifying those who would not experience serious medical complications (Klastersky et al. 2000). The MASCC index was later validated in a prospective cohort including 80 episodes of febrile

Table 3 Multinational Association for Supportive Care in Cancer (MASCC) risk index

Prognostic factor	Score
Burden of illness (no or mild symptoms)	5
Burden of illness (moderate symptoms)	3
Burden of illness (severe symptoms)	0
No hypotension (systolic BP > 90 mmHg)	5
No chronic obstructive pulmonary disease	4
Solid tumor or lymphoma with no previous fungal infection	4
No dehydration	3
Outpatient (at onset of fever)	3
Age < 60 years	2

Scores ≥21 are at a low risk of complications. *MASCC Prognostic Index* (Klastersky et al. 2000)

neutropenia, all of whom received empiric intravenous antibiotics and inpatient management (Uys et al. 2004). It achieved a positive predictive value of 98.3%. Another study which utilized this index to identify low-risk cases, before management with initial oral antibiotics and a plan for early discharge (after at least 24 h), achieved a positive predictive value of 96.7% in identifying those who would not develop serious medical complication (Innes et al. 2008). The score's use has become widely accepted.

Alternative international guidelines specify characteristics of patients that place them in a group at high risk of complication in addition to those identified above (Freifeld et al. 2011; NCCN 2017). These recognize that low-risk patients are increasingly being managed with oral therapies or as outpatients after a period of observation. These include:

- Significant medical comorbidity or presence of clinical instability
- Hepatic (aminotransferases >5 times upper limit of normal) or renal insufficiency (CrCl <30 mL/min)
- Complex infection such as pneumonia or catheter-related infection
- Grade 3 or 4 mucositis
- Uncontrolled progressive cancer defined as a leukemic patient not in complete remission or any non-leukemic patient with evidence of disease progression after more than two courses of chemotherapy
- Alemtuzumab within the past 2 months
- Anticipated prolonged profound neutropenia ($< 0.1 \times 10^9$ cells/L expected to last >7 days)

6.1 Mortality from Febrile Neutropenia

The European Society of Medical Oncology (ESMO) guidelines suggest a mortality rate in febrile neutropenia of around 5% in those with solid tumors but as low as 1% in low-risk patients (de Naurois et al. 2010). Mortality rates may be as high as 11% in some hematological malignancies.

One population-based study assessed outcomes using a database of records from 115 university or community teaching hospitals across the USA between 1995 and 2000 (Kuderer et al. 2006). It included 41,779 patients hospitalized with febrile neutropenia. The overall inhospital mortality rate was 9.5%, 8.0% for solid tumors, and 14.3% for leukemia. The number of major comorbidities also significantly affected mortality rates. Those with no major comorbidities compared to one, and more than one major comorbidities had mortality rates of 2.6%, 10.3%, and >21.4%, respectively. Those with confirmed infection had higher mortality rates at 15.3% overall. The mortality rate was highest with invasive aspergillosis at 39.2%.

Using the MASCC prognostic index outlined above, in those with confirmed bacteremia, low-risk patients have a 3% mortality rate compared with up to 36% of those defined as particularly high risk (high risk in this instance was defined as a MASCC score of <15; high risk is normally defined as a score of <21 with low risk being a score of ≥21) (Feld 2008).

7 Management of Low-Risk Patients

A Cochrane systematic review has been conducted on the use of oral versus intravenous antibiotics for febrile neutropenia (Vidal et al. 2013). The typical oral regimen usually included a quinolone combined with ampicillin-clavulanic acid. All studies excluded those with severe sepsis or shock, most excluded those with acute leukemia, and about half excluded those with pneumonia, severe cellulitis, or intravascular infection. In this patient population (i.e., primarily patients with low-risk febrile neutropenia), there was no statistically significant difference in rates of treatment failure or mortality when treated with either oral or intravenous antibiotics.

Assuming, therefore, that oral antibiotics are a safe and effective alternative, further research has explored whether outpatient management of low-risk cases is feasible. There is some

evidence to suggest that early discharge, after a minimum of 24 h observation during which time the fever resolves and no complications have developed, is safe and also cost-effective (Innes and Marshall 2007).

Full outpatient management does not currently have evidence to support its routine practice. The MD Anderson Cancer Center developed an outpatient pathway with stringent follow-up and published outcomes on a series of 712 patients with low-risk febrile neutropenia for whom this was utilized (Elting et al. 2008). Approximately 20% of eligible patients were treated as inpatients for psychosocial reasons. Although 20% of outpatients subsequently required admission, all ultimately responded to antibiotics. There were no deaths, but there were serious medical complications in approximately 1% of both inpatients and outpatients. However, this data is not necessarily generalizable as outcomes would depend heavily on local protocols and systems. Randomized evidence is lacking in this area.

8 Management of High-Risk Patients

High-risk patients should be admitted and commenced empirically on broad-spectrum intravenous antibiotics as soon as possible, although preferably after at least two sets of blood cultures have been sent including one from any indwelling central venous catheter.

Time to administration of antibiotics has been shown to be important. Delayed time to antibiotics was associated with increased mortality in a population of patients with septic shock, with an absolute increase in inhospital mortality of 7.6% for every hour of delay following recognition of hypotension (Kumar et al. 2006). Data is not as strong in the febrile neutropenic population, but it is thought that the same principle applies. One Brazilian study, evaluating inpatients with hematological malignancies receiving chemotherapy, found that increased time to antibiotic treatment after the development of febrile neutropenia was associated with increased 28-day mortality (Rosa and Goldani 2014).

8.1 Supportive Care

The management of severe sepsis and septic shock has been extensively studied; however, there is less data specific to those with neutropenic sepsis. Similar principles have been applied including adequate fluid resuscitation and treatment of respiratory failure (Penack et al. 2014). It should be noted that steroid supplementation has not been consistently shown to be helpful, with the exception of those who have previously been on long-term steroids. The benefit in these patients is due to the risk of adrenal suppression and therefore an inadequate stress response. This group of patients were not included in the trials of glucocorticoids in septic shock, as steroid use is mandatory in this group (Sprung et al. 2008).

Other adjunctive therapies such as intravenous immunoglobulin and granulocyte transfusions do not have evidence to recommend their use (Penack et al. 2014).

The management of severe sepsis and septic shock is complex (Angus and van der Poll 2013). In those with septic shock (hypotension not responding to fluid resuscitation), or respiratory failure not responding to ward-based oxygen supplementation, or noninvasive positive pressure ventilation (if available), intensive care unit involvement is indicated for consideration of vasopressor therapy and/or invasive ventilation. Unfortunately, in patients requiring an admission to the intensive care unit for neutropenia and severe sepsis, or septic shock, mortality is high. One analysis of this population in a French teaching hospital found a mortality rate of around 50% (Legrand et al. 2012).

8.2 Antibiotic Choice

Antibiotic choice will be heavily influenced by local resistance patterns, but typical regimens include an antipseudomonal cephalosporin or a carbopenem.

A Cochrane systematic review has been conducted to determine whether adding an aminoglycoside to a beta-lactam antibiotic improves outcomes, when compared to a beta-

lactam antibiotic alone for empiric treatment of febrile neutropenic patients, primarily in a hematological population (Paul et al. 2013). Interestingly, the combination was not associated with a mortality benefit but was associated with a higher rate of nephrotoxicity and fungal superinfection. Theoretical benefits of the combination were not borne out in the data with no evidence of "synergism" improving patient outcomes. In addition, bacterial superinfection rates were similar with both monotherapy and the combination, suggesting that the combination did not reduce the development of resistant organisms. Limitations of the review largely stem from the contributing studies. The authors noted a paucity of data for some patient subgroups, such as those with microbiologically confirmed *Pseudomonas aeruginosa* and those with confirmed gram-negative bacteremia, making conclusions more difficult (Paul et al. 2013). It did not perform a subgroup analysis in those with severe sepsis or septic shock.

Most guidelines, therefore, suggest a broad spectrum antipseudomonal beta-lactam as first-line empiric therapy for febrile neutropenia (Fig. 1). However, due to the limitations in available evidence, some guidelines still suggest consideration of the addition of an aminoglycoside empirically in selected patients, such as those at a high risk of prolonged neutropenia (de Naurois et al. 2010), severe sepsis (Penack et al. 2014), septic shock (Penack et al. 2014), or radiologically confirmed pneumonia (Freifeld et al. 2011). In addition, an aminoglycoside may be added in unstable patients with complicated infections after confirmation of a gram-negative bacteremia (Freifeld et al. 2011; de Naurois et al. 2010). There is a lack of randomized data to support or refute this approach.

A regimen involving a beta-lactam with or without an aminoglycoside does not achieve good response rates for a number of gram-positive organisms. These primarily include less virulent organisms such as *Staphylococcus epidermidis* and corynebacteria. Therefore many guidelines recommend the commencement of vancomycin if fever fails to settle after 48 h. Introducing vancomycin at this stage rather than at presentation does not detrimentally impact mortality or complication rates (Paul et al. 2014). By using this approach, clinicians hope to minimize the rates of vancomycin-resistant organisms such as

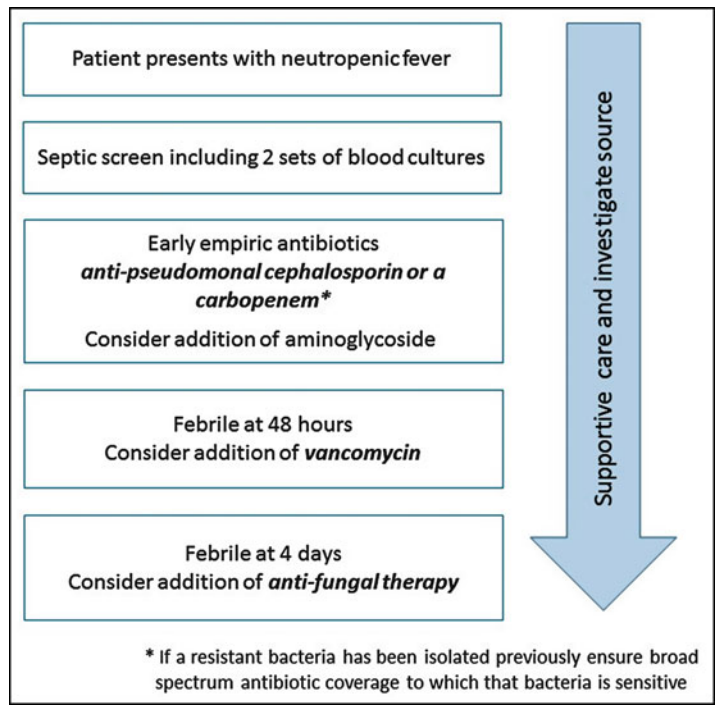

Fig. 1 Summary of empiric antimicrobial management for neutropenic fever

vancomycin-resistant enterococcus (VRE) which have emerged over the last decade or so. In centers with high rates of methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin might be appropriate as initial empiric therapy.

It remains uncertain whether the empirical use of vancomycin in all patients with persistent fevers of unknown origin is beneficial. One double-blind trial randomized 165 patients with persistent fever after 48–60 h on single agent piperacillin-tazobactam to additional vancomycin or placebo and found no significant difference in mortality or time to defervescence (Cometta et al. 2003). However, the power to detect a clinically significant difference was low. It should be noted that patients with septic shock, lung infiltrates, soft tissue or skin infection, catheter-related infection, microbiologically confirmed gram-negative infection, and microbiologically confirmed gram-positive infection resistant to piperacillin-tazobactam were excluded. In the absence of adequate evidence, delayed empiric vancomycin is a generally accepted practice.

Most guidelines suggest that patients who have previously had resistant bacteria isolated, causing either colonization or invasive infection, should receive a broad-spectrum antibiotic to which that bacteria is sensitive.

In addition, in those who have an evident focus of infection, or a high suspicion of this, targeted treatment should be commenced as summarized in Table 4. For example, in those with pneumonia, the addition of a macrolide antibiotic to cover for atypical infections is prudent.

Length of antibiotic course tends to depend on the organism and site of infection. Antibiotics are traditionally continued at least until the neutrophil count is increasing and above 0.5×10^9/L, although rationalization of antibiotics or a change to oral preparations may be considered before then, in stable patients with uncomplicated infection (Freifeld et al. 2011).

Table 4 Targeted treatment for cases with a focus of infection

Specific infection	Addition to empiric treatment
Pneumonia	Macrolide (to cover atypical organisms such as mycoplasma of legionella) Cotrimoxazole (if high suspicion of PJP pneumonia)
Diarrhea	Consider oral metronidazole (to cover *C. difficile*)
Intra-abdominal source	Metronidazole
Suspected meningitis (require lumbar puncture)	Amoxicillin or carbapenem (to cover *Listeria*)
Vesicular lesions	Acyclovir
Suspected invasive CMV	Ganciclovir
Viral encephalitis (require lumbar puncture)	High-dose acyclovir
Cellulitis	Consider addition of vancomycin

8.3 Role of Antifungal Agents

Rates of invasive fungal infection, particularly candida and aspergillosis, increase as the duration of neutropenia increases (Gerson et al. 1984). This is more relevant to the hematology setting. Therefore some guidelines suggest empiric antifungal therapy after 4–7 days of persistent fevers despite broad-spectrum antibiotics.

Traditionally amphotericin B, and more recently liposomal amphotericin B, which has less renal toxicity, has been used in this setting. However, even liposomal amphotericin B is associated with significant levels of renal dysfunction and hypokalemia, particularly when combined with aminoglycosides or calcineurin inhibitors (immunosuppressive agents used in allogeneic transplant patients). Alternatives include voriconazole, an azole which has activity against candida including the fluconazole-resistant C. *krusei* and *C. glabrata* as well as *Aspergillus*, and caspofungin, an echinocandin with a similar spectrum of activity to voriconazole (Freifeld et al. 2011).

Voriconazole is generally accepted as an alternative to liposomal amphotericin B in this setting, although it did not reach the defined threshold for non-inferiority in one randomized study (Walsh et al. 2002). A Cochrane review on the subject found some deficiencies in that study and concluded amphotericin B was significantly

more effective (Jørgensen et al. 2014). It should be remembered that azoles are not without side effects. Voriconazole can cause visual disturbance. In addition, immunosuppression is a suspected class effect of the azoles as evidenced by increased rates of bacteremia in azole-treated neutropenic patients, compared with placebo in a number of trials (Gøtzsche and Johansen 2014).

The empiric addition of antifungals in those with persistent febrile neutropenia has been questioned, as a result of data suggesting that while around 30% of febrile neutropenic patients would receive antifungals based on this approach, only about 4% will actually have fungal infection (Freifeld et al. 2011). Therefore, studies have compared outcomes using empiric antifungals, versus so-called preemptive antifungals whereby a combination of clinical, radiological, and biochemical information is used to then start early broad-spectrum antifungal treatment if indicated (Freifeld et al. 2011). Radiological evidence involves features suggesting fungal infection on CT of the chest. Biochemical evidence includes assays of either B-(1-3)-D glucan or galactomannin. Both suffer from poor sensitivity and specificity when assayed in blood, and therefore serial testing is generally utilized if at all. In bronchoalveolar lavage specimens, galactomannin is very specific and approximately 80% sensitive and may have more utility in this setting. Polymerase chain reaction (PCR) assays are also being developed.

In summary, small studies suggest that the "preemptive" approach (as opposed to empiric use) could reduce antifungal use without adversely affecting outcomes, but there is not enough evidence yet to make this standard practice (Freifeld et al. 2011). In high-risk populations, such as those receiving hematopoietic stem cell transplants (especially allogeneic stem cell transplants) or those receiving chemotherapy for acute leukemia, there is evidence that the use of liposomal amphotericin B, either prophylactically or empirically, decreases overall mortality when compared with preemptive treatment of fungal infection. This suggests empiric antifungal use is appropriate for these high-risk populations (Gøtzsche and Johansen 2014).

Treatment recommendations change little in those who develop a suspected fungal infection on antifungal prophylaxis, although there is little evidence in this setting (Freifeld et al. 2011). Typically an azole is avoided if one has been used as prophylaxis. Prophylaxis is used for very high-risk populations such as those with acute leukemia receiving intensive remission induction chemotherapy regimens or allogeneic stem cell transplant recipients. Agents commonly used include oral preparations of fluconazole and posaconazole. Both have limitations. Fluconazole has a narrow spectrum of activity covering primarily *Candida albicans*. Posaconazole has a very broad spectrum of activity but can suffer from poor absorption and therefore inadequate levels in the blood. As such, in the absence of clear pathogen and sensitivity information, a switch to intravenous therapy with either liposomal amphotericin B, caspofungin, or voriconazole is reasonable.

8.4 Role of Antiviral Agents

These agents are only indicated if there is microbiological or laboratory evidence of active disease (Freifeld et al. 2011). There is no role for empiric therapy. The exception to this guidance might be the empiric addition of a neuraminidase inhibitor such as oseltamivir, if a neutropenic patient presents with flu-like symptoms in the context of an influenza outbreak.

In neutropenic patients, the typical viruses are either herpes simplex virus or varicella zoster virus. Acyclovir is the treatment of choice, with the dose dependent on the site of disease.

8.5 Use of Hematopoietic Stimulating Factors

Granulocyte-macrophage colony-stimulating factor (GM-CSF) supports the survival and differentiation of multiple cells including neutrophils, eosinophils, basophils, monocytes, and dendritic cells while granulocyte colony-stimulating factor (G-CSF) primarily affects neutrophils. As well as increasing numbers of neutrophils in circulation, it also enhances their functionality (Bennett et al. 2013).

As previously described, prophylactic G-CSF is generally recommended in those considered to have a greater than 20% chance of febrile neutropenia when exposed to chemotherapy.

However, G-CSF or GM-CSF is not recommended to *treat* episodes of febrile neutropenia together with antibiotics. While there is statistically significant evidence that their use can shorten the duration of hospitalization, shorten the duration of fever, and hasten neutrophil recovery, a mortality benefit has not been demonstrated (Mhaskar et al. 2014). Despite this, many still advocate its use in some cases, due to a suspicion that there is a subgroup within the febrile neutropenic population who do benefit.

9 Specific Clinical Scenarios

Based on the results of the investigations and clinical setting, a potential source of the fever may be identified. It is important that treatment is directed to these specific clinical scenarios (de Naurois et al. 2010).

9.1 Lung Infiltrates

Diffuse lung infiltrates should raise suspicion of either *Pneumocystis jirovecii* infection or fungal infection with organisms such as *Aspergillus*.

Aspergillus in particular has distinctive features on CT, such as nodules with haloes or ground-glass change. Occasionally, it can also cause an interstitial pneumonia. It is resistant to fluconazole which is often used as antifungal prophylaxis in high-risk patients. Treatment therefore involves either voriconazole, liposomal amphotericin B, or caspofungin.

Pneumocystis jirovecii tends to occur in patients who have been on a prolonged course of corticosteroids, in those who are on immunosuppression for previous organ transplantation, or in those with previous exposure to purine analogues such as fludarabine or azathioprine. Clinically they present with a high respiratory rate and rapid desaturation with minimal exertion. Treatment is with cotrimoxazole. In those at risk, prophylactic cotrimoxazole is usually recommended.

9.2 Central Venous Catheter-Associated Infections

Central venous catheters are commonly used in oncology and hematology but also can be a potential source of infection. Bacteria and occasionally mycotic organisms can colonize the hub of a catheter and then multiply under the cover of a biofilm, which can protect them from host defense mechanisms before gaining entry into the circulation with infusions or physical movement of the catheter. There is little data specific to neutropenic patients with catheter-related infections and so general principles of management are applied. Estimates based primarily on ICU environments with a wide variety of patients suggest an incidence of infection of around 5 per 1000 catheter days (Wolf et al. 2008). Port-a-caths, used most commonly in those receiving outpatient chemotherapy for solid organ tumors, have lower rates of infection than this. A large pediatric series demonstrated a low rate of port-a-cath-related infections at 0.11 episodes per 1000 port-a-cath days (Hengartner et al. 2004).

Local infection, such as localized redness, induration, tenderness, and purulent discharge, does not always indicate the presence of systemic infection. Even deeper (more than 2 cm from the entry site) tunnel or pocket infections do not always result in systemic infection. While the gold standard for diagnosis of catheter-related infection relies on identifying the same organism (with identical antibiotic sensitivities) in both culture of the catheter tip and peripheral blood cultures, diagnosis prior to catheter removal can allow preservation of the catheter in some cases. One reliable method to diagnose catheter-related systemic infections with high sensitivity and specificity, *without catheter removal*, is the differential time to positivity (DTTP) (Blot et al. 1999). This is defined as blood cultures from the catheter becoming positive at least 2 h before peripheral cultures taken at the same time. In the absence of this finding, other clinical factors can suggest the

catheter as the source. These include local infection plus positive peripheral blood cultures; peripheral blood cultures growing an organism consistent with catheter-related infection; or the failure to identify another source, particularly in those with refractory fevers despite antibiotics (Wolf et al. 2008).

Organisms implicated in catheter-related infections tend to be commensal skin bacteria. By far the most common are the coagulase-negative staphylococci. Other common causes include the gram-positive organisms *Staphylococcus aureus*, corynebacteria, and enterococci. More rarely *Candida* species or gram-negative organisms, such as *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia*, and *Acinetobacter baumannii*, may be involved (Wolf et al. 2008).

Management depends on the organism identified, whether infections are uncomplicated or complicated (defined as persistent fever greater than 48 h or evidence of secondary infection such as endocarditis, abscess, or osteomyelitis) and whether the patient is clinically stable or unstable (defined as severe sepsis or septic shock) (Wolf et al. 2008). Antibiotic management is the same as that given above, although guidelines generally advocate the use of glycopeptides such as vancomycin in those highly suspected of having a catheter-related infection (de Naurois et al. 2010).

Another important consideration in management is whether catheters should be removed or preserved (Table 5). Catheter removal is associated with potential risk in patients with neutropenia, particularly those with associated thrombocytopenia. Additionally, many of these patients require a new central line to be placed for further treatment. *Staphylococcus aureus* infections generally require the immediate removal of the catheter as less than 20% of infections are resolved if the catheter remains in situ (Wolf et al. 2008). In addition, there are high rates of hematogenous spread of the organism, leading to invasive infections at other sites such as endocarditis or abscess. Candida infections are also resistant to treatment in the absence of catheter removal. However, one study identified the source of fungemia as the catheter in only 27% of cases, suggesting that a thorough search for another source is appropriate before removal of the catheter. Unstable patients or those with complicated infections should also have removal of the catheter. Local exit site infections can usually be managed with catheter preservation, but deeper tunnel or pocket infections require removal. Finally, in stable patients with fever of unknown origin and no microbiological evidence of catheter-related infection, catheter preservation is reasonable. This recommendation is based on a randomized study in non-neutropenic ICU patients demonstrating equivalent outcomes using either catheter removal or preservation (Wolf et al. 2008).

Table 5 Indications for catheter removal

Indications for catheter removal	Indications for trial of catheter preservation
Staphylococcus aureus infection Candidal infection (relative) Complicated infection (persistent fever or secondary infection) Unstable patients (severe sepsis or septic shock) Persistent fever despite antibiotics Recurrence of fever after antibiotic cessation Tunnel or pocket infections	Stable patient with uncomplicated infection by other organisms Stable patient with persistent fever of unknown origin Localized exit site infections *not* involving the tunnel or pocket

9.3 Diarrhea

Diarrhea in the context of chemotherapy can have multiple causes. Chemotherapeutic agents and particularly capecitabine, 5-fluorouracil, and irinotecan can cause grade 3 or 4 diarrhea (Common Terminology Criteria for Adverse Events (CTCAE) – grade 3 or above means hospitalization indicated) in patients at a rate of between 10% and 30% (Stein et al. 2010). Newer agents such as the immune checkpoint inhibitors and tyrosine kinase inhibitors can also cause enterocolitis. The management of enterocolitis may change depending on the cause, but this is outside the scope of this chapter. A key point is

that the normal barrier function of the gut will be impaired increasing the risk of bacterial translocation. As such, patients with febrile neutropenia and diarrhea should have an agent active against anaerobic bacteria such as metronidazole added to their empiric regimen (de Naurois et al. 2010).

Differential diagnoses to consider include the development of an infective gastroenteritis, *Clostridium difficile* and associated toxin-mediated diarrhea, or neutropenic enterocolitis (usually only in those receiving treatment for leukemia or stem cell transplant recipients). Therefore patients need investigation at least with a stool specimen and appropriate targeted treatment commenced as appropriate.

10 Conclusion

Febrile neutropenia is a common complication of cytotoxic therapies used to treat cancer and can be fatal. The patient should be well informed of this potentially serious complication and have a management plan in place should this occur. Therapies to reduce the risk of febrile neutropenia should be considered in patients at high risk, and also in those who would poorly tolerate the complication such as those with major comorbidities. Management requires the prompt commencement of antibiotics, careful investigation into a possible source, and supportive cares as appropriate.

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Seizures

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_75

Abstract

Seizures are a common occurrence in patients with a life-limiting illness. The assessment and management of seizures in the palliative patient require the interplay of many factors, including patient and treatment goals, counterbalanced with the need to maintain quality of life. Throughout this chapter, the reader is provided with current evidence regarding definitions, classification, assessment, and management of seizures. Antiepileptic medications are discussed in detail, with an emphasis on the administration routes, commonly used in the palliation population. Current concepts regarding status epilepticus are outlined, including pathophysiology and management. The chapter concludes with a comment on seizures, driving, and the palliative patient.

1 Introduction

Epilepsy and seizures are common neurological conditions and possibly among the few, true palliative emergencies. It has been estimated that up to 13% of patients with cancer will experience a seizure at some point of their illness (Grewal et al. 2008). The majority of these patients will have an underlying primary or secondary intracranial malignancy (Singh et al. 2007). Seizures can cause significant distress, to the patient and their family. Palliative patients with brain tumors, and their relatives, fear seizures at the end of life (Sizoo et al. 2014).

The management of a seizure, in the palliative patient with an advanced illness, requires the composite interplay of many different factors. Consideration needs to be given to the goals of care and the maintenance of quality of life. Reflection is provided throughout this chapter, on the need to consider these important factors in the assessment and management of the palliative patient presenting with a seizure.

Although the focus of this chapter is on seizures in the adult patient, the reader will be provided with additional references, where appropriate, for the pediatric population.

2 Definition and Etiology

In 2005, the International League Against Epilepsy (ILAE) provided a conceptual definition of seizures and epilepsy (Fisher et al. 2014). They defined an epileptic seizure as a "transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain" (Fisher et al. 2014). Epilepsy was defined as "a disorder of the brain characterised by an enduring predisposition to generate epileptic seizures, and by the neuro-biologic, cognitive, psychological, and social consequences of this condition" (Fisher et al. 2014). Additionally, the diagnosis of epilepsy required the occurrence of two unprovoked epileptic seizures occurring at least 24 h apart.

In 2014, the ILAE expanded the definition of epilepsy, by providing an operational (more practical than the previous conceptual one) definition of epilepsy, that better reflected the practice of expert epileptologists (Fisher et al. 2014). It had long been recognized that for some patients, the risk of subsequent seizures after the first unprovoked seizure, when due to an underlying enduring predisposition, was comparable to individuals who had two unprovoked seizures. It was formally recognized by the ILAE, in their new operational definition, that these individuals, with one unprovoked seizure and a probability

Table 1 ILAE operational (practical) definition of epilepsy

Epilepsy is defined by the presence of any one of the following conditions
1. At least two unprovoked seizures occurring at least 24 h apart
2. One unprovoked seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
3. Diagnosis of an epilepsy syndrome

of further seizures comparable to the general recurrence risk after two unprovoked seizures, should also be considered as having epilepsy. The current ILAE operational (practical) definition of epilepsy is summarized in Table 1. In this report, the ILAE definition of "unprovoked" "implies the absence of a temporary or reversible factor lowering the threshold and producing a seizure at that point in time" (Fisher et al. 2014). "Provoked" seizures are caused "by transient factor acting on an otherwise normal brain to temporarily lower the seizure threshold"(Fisher et al. 2014). Provoked seizures are not considered epilepsy. Table 2 outlines common list of such precipitating factors responsible for provoked seizures.

ILAE have provided recommendations in 2010, to enable the categorization of unprovoked seizures, based on underlying etiology (Berg et al. 2010). The previously used terms idiopathic, symptomatic, and cryptogenic were replaced by the terms "genetic," "structural/metabolic," and "unknown cause" to describe underlying causation. In the genetic category, the seizure(s) are the direct result of a known or presumed genetic defect(s) and are a core symptom of the condition. The structural, or metabolic group, includes various conditions associated with a significantly elevated risk of developing seizures. These structural or metabolic conditions may be congenital or acquired. The unknown category (previously cryptogenic) includes patients where the etiology is currently unknown. Seizures with unremarkable imaging and no chronicled genetic, metabolic, or immune etiology are included in this group.

The underlying etiology for epilepsy is undefined in more than half of cases. Table 3 outlines defined causes of epilepsy. The imprecise borders of the provoked and unprovoked seizure are recognized in that precipitating factors (Table 2) and may still be present in individuals with an underling enduring epileptogenic abnormality (Table 3). In the elderly, cerebrovascular disease, tumor, and degenerative etiologies predominate (Ropper et al. 2014). In children, congenital malformations are responsible for a significantly higher proportion of epilepsy (greater than 60% of seizures with a defined cause in the 0–14 age group), than in other age groups (Ropper et al. 2014).

Table 2 Causes of provoked seizures

Precipitating factors responsible for a temporary reduction in seizure threshold
Alcohol and drug withdrawal
Drug intoxication
Hyponatremia, hypernatremia
Hypomagnesemia
Hypocalcemia
Hypoglycemia
Non-ketotic hyperglycemia
Uremia
Hypoxia
Hyperthyroidism
Dialysis disequilibrium syndrome
Porphyria

Table 3 Epilepsy etiology

Epilepsy underlying etiology
1. Undefined
2. Head trauma
3. Stroke
4. Intracranial infection
5. Cerebral degeneration
6. Congenital brain malformations
7. Inborn errors of metabolism

3 Classification

The ILAE provided an opinion regarding the terminology and concepts with regard to seizure classification in 2010 (Table 4) (Berg et al. 2010). This new classification would allow an up-to-date arrangement, to better accommodate

Table 4 Classification of seizures

ILAE seizure classification 2010
Generalized seizures
Tonic-clonic
Absence
Typical
Atypical
Absence with special features
Myoclonic absence
Eyelid myoclonia
Myoclonic
Myoclonic
Myoclonic atonic
Myoclonic tonic
Clonic
Tonic
Atonic
Focal seizures
Unknown
Epileptic spasms

changes in neuroimaging, molecular biology, and genomic technologies. The principle subdivision of seizures, as currently defined by the ILAE, is by mode of onset into "generalized," "focal" (previously partial), and "unknown." Generalized seizures derive from some point within the brain and rapidly engage bilaterally distributed networks. Hence, for these seizures, the clinical and electroencephalographic (EEG) findings reflect bilateral hemispheric involvement at seizure onset. Focal seizures emanate from networks limited to a single hemisphere. Where the mode of onset is unknown as to whether generalized or focal, the seizure is classified as unknown. Important changes to the 1981 classification include seizures in neonates no longer being considered as a separate entity, a new group for spasms (epileptic spasms), and the elimination of the previously used terms simple and complex partial as well as secondary generalization. Instead of the terms simple or complex partial seizures, the use of clinical descriptors to delineate focal seizures is recommended. This can include statements reflecting states of consciousness/awareness, dyscognitive features, localization, and ictal progression.

Table 5 Seizure history

Relevant details for seizure history
Associated features
Health at seizure onset
Precipitating events other than illness – examples include sleep deprivation, stress (physical and emotional), and alcohol
Symptoms during seizure
Aura
Pre-ictal symptoms
Motor features during seizure
Conscious state during seizure
Symptoms following seizure
Amnesia
Confusion
Transient focal weakness (Todd's paralysis)
Tongue biting

4 Assessment

The initial assessment should take place after the emergency stabilization of the patient. This should include history, examination, and investigations to firstly exclude other significant disorders that may be differentials to the diagnosis of epilepsy and secondly to determine causation. The need to exclude other diagnoses is especially important in the elderly who may present with a first seizure-like event. The increased prevalence of cardiac and neurological differentials in this population is important to consider. The history should include a thorough review of the medical, past medical, and family history, not only from the patient but also from relevant witnesses. Table 5 outlines important relevant areas that need exploration in the history. The physical examination is often unremarkable but is necessary to evaluate the presence of lateralizing signs.

In a review paper, Krumholz et al. (2007) explored the utility of various imaging, electrophysiological, and laboratory tests in the evaluation of the first seizure in adults. With respect to the electrophysiological studies, they recommended that the EEG should be considered for all adults presenting with an apparent unprovoked first seizure. Its utility is because of its yield (29% of EEGs in the above context

demonstrating significant abnormalities) and for defining the risk of seizure recurrence. With respect to neuroimaging, the authors have recommended either computed tomography (CT) or magnetic resonance imaging (MRI) as a core requirement for evaluation of the adult with a first seizure. The yield of imaging in the unprovoked first seizure in an adult was 10%. In the same population, Krumholz et al. (2007) found no evidence to support or refute a routine recommendation for the testing of blood glucose, blood counts, or electrolytes. The authors have suggested that such testing should be guided on an individual basis, according to the findings of the history and examination. The authors reached similar conclusions for lumbar puncture and routine toxicology. It is important to note here that Krumholz et al. (2007) excluded individuals who had "provoked seizures" (as earlier defined), in their analysis. Practitioners need to assess for "precipitating factors," as applicable for each individual concerned (Table 2), as part of their assessment of the adult who presents with a seizure. For the assessment of seizures in the pediatric population, the reader is encouraged to examine the review paper by Hirtz et al. (2000).

The above discussion provides an evidence-based framework for the assessment of seizures. In the context of a palliative patient faced with a life-limiting diagnosis, the health practitioner is faced with the need for possible compromise. The practitioner needs to carefully determine the treatment and patient goals. The benefits of a detailed history, examination, and additional investigations need to be balanced with the burden of undertaking these assessments. The variability of circumstances, and the paucity of research in this area, limits the ability to make generalizable or explicit recommendations for the assessment of seizures in palliative patients.

5 Overview of Management

The management goals for the patient with a life-limiting diagnosis that presents with a first seizure need to include the following: control of seizures, minimization of treatment adverse effects, and maintenance of quality of life.

For the palliative patient, who presents with a provoked seizure (Table 2), there is a need to treat the underlying precipitating factor that has caused a temporary reduction in the seizure threshold. The failure to manage the relevant precipitating factor may predispose the patient to continuing or further seizures. However, the need to undertake this treatment will, by necessity, be guided by the shared treatment goals agreed upon by the patient and their clinician. As an example, the assessment and reversal of underlying electrolyte abnormalities may be entirely appropriate for a patient with good pre-seizure quality of life, in the early stages of a life-limiting illness. Alternatively, in some circumstances, the underlying abnormalities are a reflection of advanced stage illness. In these circumstances, the assessment and management of provoking factors may be inappropriate. In the latter, the availability of advanced care directives and substitute decision-maker(s) can assist health practitioners in their decision-making.

For the palliative patient presenting with an unprovoked seizure, the role for antiepileptic medications needs consideration, in addition to discussions regarding shared treatment goals. The risk of seizure recurrence plays an important additional role in the decision to commence an antiepileptic drug (AED). Krumholz et al. (2015) have identified certain clinical factors associated with a heightened risk of seizure recurrence. These include an underlying brain lesion or insult, an EEG with epileptiform abnormalities, significant brain imaging abnormality, and nocturnal seizures. These patients may have up to twice the risk of seizure recurrence, when compared to patients with no defined underlying cause (Krumholz et al. 2015). Krumholz et al. (2015) additionally noted that the following features were not associated with recurrence after an unprovoked first seizure: age, sex, family history, type of seizure, and status epilepticus as presentation. The authors of this review also revealed that immediate AED therapy, when compared with no treatment, is likely to reduce the 2-year absolute risk of seizure recurrence by about 35%. The above conclusions from the review by Krumholz

et al. (2015) should be considered alongside the new operational definition of epilepsy (see Table 1), to guide the health practitioner in decision-making. For an excellent review on the management of the pediatric patient with a first unprovoked seizure, the reader is encouraged to consult the paper by Hirtz et al. (2003).

The decision to treat a patient who presents with their first unprovoked seizure with an AED, or to defer treatment, will need consideration of the impact on quality of life. A large randomized trial in the UK examined this question of quality of life in patients with unprovoked seizures with respect to two treatment groups: immediate AED treatment vs deferred treatment (Jacoby et al. 2007). The authors found no significant differences in quality of life outcomes between these two treatment groups at 2 years. This included areas such as general health, cognitive function, psychological well-being, and social functioning. Their findings suggest a balance of impacts on quality of life, between taking AEDs and continuing of further seizures. The authors, however, add that the only area where there was a clear disadvantage with regard to quality of life was in the deferred treatment group, with respect to driving (Jacoby et al. 2007). Therefore, in the palliative patient, with a reasonable prognosis and for whom driving is still a valuable and important task, the balance may favor early AED treatment.

When deemed appropriate, guidelines recommend the use of a single AED (i.e., as monotherapy) (Glauser et al. 2013). Despite the rapid increase in the number of AEDs, no single agent has been deemed superior to another for all seizure types (Glauser et al. 2013). Treatment with an AED, hence, needs to be individualized to the patient. Therefore, in consideration of an agent, the palliative care practitioner needs to review the following: the effectiveness of the AED for the seizure type concerned, the potential adverse effect profile of the AED, the drug interaction profile of the AED, the patient age, and the presence of comorbidities.

In a recent review, Glauser et al. (2013) examined the evidence for various AEDs as monotherapy in relation to specific seizure types (see Table 4 for seizure types). For adults with focal seizures, levetiracetam, zonisamide, carbamazepine, and phenytoin, all have class A (established as effective) evidence, supporting their use for monotherapy. For the elderly (65 years and older), with focal seizures, gabapentin and lamotrigine, both have class A evidence, supporting their use. There is a lack of adequate trials examining AED monotherapy in both children and adults with generalized seizures (Glauser et al. 2013). Glauser et al. (2013) conclude that the following AED should be considered as first-line but have only class C (possibly effective) evidence backing their use in adults with generalized onset tonic-clonic seizures: carbamazepine, lamotrigine, oxcarbazepine, phenobarbital, phenytoin, topiramate, and valproate.

6 The Antiepileptic Drugs

Although structurally and functionally distinct, all the AEDs act by the inhibition of rapidly firing neurons, with the resultant effect on symptoms originating from this excessive neuronal action, in any component of the nervous system (Twycross et al. 2014). The mode of action of the AEDs commonly used in palliative care, as well as other AEDs that the palliative care health practitioner may frequently encounter, is detailed in Table 6. First-generation AEDs include carbamazepine, phenobarbital, phenytoin, and valproate. The other AEDs, discussed below, belong to the second generation (i.e., coming into use after the first-generation agents). The present section will discuss dosing (as monotherapy) and current evidence relating to subcutaneous route of administration in relation to specific AEDs. It is important to note that none of the AEDs discussed were developed to be used subcutaneously, and hence much of their use in palliative care is "off-label" (Leppik and Patel 2015). Health practitioners using these AEDs subcutaneously need to follow appropriate local guidelines with regard to "off-label" use of pharmaceuticals and inform the patient of this fact. The dose recommendations detailed below are as they apply to an adult. For recommendations regarding the pediatric population, the reader is

Table 6 Mode of action of antiepileptic drugs

Drug	Na+ channel blocker[a]	K+ channel activator[a]	Ca+ channel blocker[b] (N, P, Q type)	SV2A binding[c]	NMDA antagonist[d]	GABA receptor[e]	GABA metabolism[e]
Benzodiazepine						++	
Carbamazepine	++						
Gabapentin		+	++				
Lamotrigine	++		++				
Lacosamide	++						
Levetiracetam				++			
Oxcarbazepine	++	+					
Phenobarbital						++	
Phenytoin	++						
Pregabalin			++				
Topiramate	++					++	
Valproate	+				+		+
Zonisamide	++		++				

Adapted from Twycross et al. (2014)
++ = predominant mode of action, + = non-predominant mode of action
[a]Membrane stabilization action through blocking of sodium channels and/or opening potassium channels
[b]Ca channel blockade in pre-synaptic neurons reduces neurotransmitter release
[c]*SV2a* synaptic vesicle protein 2A. Binding to SV2A reduces neurotransmitter release from vesicles in the pre-synaptic neurons
[d]*NMDA* N-methyl-D-aspartate. Antagonism of the NMDA receptors in the post synaptic neurons alters neurotransmitter effect
[e]*GABA* Gamma aminobutyric acid. Action through augmented GABA receptor activation or altered GABA reuptake and breakdown

encouraged to review a local reference source for that population (e.g., the *Australian Medicines Handbook*, in Australia). The doses recommended will need appropriate adjustment for comorbid conditions and drug-drug interactions. The subsequent section will examine the adverse effects, drug interactions, and the impact of comorbid conditions on the AEDs.

6.1 Levetiracetam

The starting dose for this medication is 250–500 mg twice daily, with the therapeutic daily dose required being between 750 and 3000 mg (maximum recommended daily dose) (Twycross et al. 2014). Oral and parenteral doses are equivalent for levetiracetam (Twycross et al. 2014). Although not licensed for subcutaneous administration, the evidence for the use of levetiracetam through this route relies on case series (Remi et al. 2014; Wells et al. 2016; Murray-Brown and Stewart 2016). The PO:IV:SC ratio for levetiracetam is 1:1:1. Remi et al. (2014) undertook a retrospective chart review of 20 palliative patients who were commenced on continuous subcutaneous infusion of levetiracetam, due to the inability to swallow medications orally. The authors combined this AED with at least one other commonly used palliative care medication in 19 of the cases. These medications included midazolam, morphine, hyoscine butylbromide, hydromorphone, levomepromazine, metoclopramide, dexamethasone, and glycopyrrolate. Levetiracetam, through this route, was effective (80% of the patients had no further seizures) and well tolerated. The authors concluded that levetiracetam is an ideal AED for subcutaneous administration, in a palliative care patient who is unable to swallow, and where there is a need to avoid the adverse effects and drug interactions of the other AEDs that are commonly administered in such instances (phenytoin, valproate, phenobarbital, and benzodiazepines) (Remi et al. 2014).

The diluent that has been suggested for the infusion is water for injection or sodium chloride 0.9% (normal-saline) (Twycross et al. 2014).

6.2 Valproate

The starting dose for this medication is 200 mg twice daily, with the therapeutic daily dose required being between 1000 and 2500 mg (maximum recommended daily dose) (Twycross et al. 2014). The IV route is an alternative when the oral route cannot be used and is given as a continuous or intermittent infusion (Twycross et al. 2014). Although not licensed for the subcutaneous route, the *Palliative Care Formulary* (PCF) has outlined the use of this drug in a continuous subcutaneous infusion at a PO: SC dose ratio of 1:1, with water for injection as a diluent, resulting in seizure benefit and minimal infusion site reactions (Twycross et al. 2014). A recent case series of seven patients (personal communication) has demonstrated the safety and efficacy of sodium valproate, when administered subcutaneously, for seizure prophylaxis, at the end of life (O'Connor 2016).

6.3 Phenobarbital

The adverse effect (cognitive, behavioral, and sedation) profile of this drug limits its utilization as an AED even among those with a life-limiting diagnosis (Twycross et al. 2014). The exception is in the context of status epilepticus. When used as a maintenance antiepileptic, in the palliative patient who is unable to swallow, it should be second-line to valproate, levetiracetam, and midazolam (Twycross et al. 2014). Because of the irritant nature of parenteral phenobarbital, the loading dose (100 mg) should be given IV and only then followed by a continuous subcutaneous infusion (Twycross et al. 2014). The maximum daily dose via continuous subcutaneous infusion, for this indication (maintenance AED), is 400 mg over 24 h, although substantial higher doses have been used in the context of status epilepticus and terminal agitation (Twycross et al. 2014). With substantially higher doses, the volumes required to achieve the dilution recommended by the PCF are substantial (80 ml for a 24 h infusion dose of 1600 mg).

In the context of its irritant nature when administered subcutaneously, and the unlicensed nature of this route of administration, a recent study examined the injection site tolerability of phenobarbital (Hosgood et al. 2016). In this retrospective review that included 69 patients and 774 distinct subcutaneous injections, local reactions (maximum Grade 1 only) were seen in only 0.3% of injections. The patients in this study were being treated with this agent for refractory palliative symptoms and not exclusively as an AED; however, some patients received up to 35 injections. Importantly, in this study all doses were administered at a concentration of 65 mg/ml, with maximum volumes used for individual injections and continuous subcutaneous infusion rates, being 2 ml and 3 ml/h, respectively (i.e., at greater concentrations than that recommended by the PCF).

6.4 Benzodiazepines

Although benzodiazepines are the first-line treatment for the management of acute seizures (including status epilepticus), the development of tolerance and adverse effects (especially sedation) generally precludes their chronic use as an AED (Twycross et al. 2014). In this setting, their use is restricted to seizures refractory to other measures. The PCF recommends clonazepam in chronic treatment, 500 mcg to 1 mg as a nighttime dose to a maximum daily dose of usually no more than 4 mg (Twycross et al. 2014). In the end-of-life setting with loss of oral intake, midazolam is recommended at starting doses of 20–30 mg over 24 h as a continuous subcutaneous infusion for seizure prevention (Twycross et al. 2014). Alternatively, if the practitioner prefers to maintain the patient on the same benzodiazepine, clonazepam can be administered via continuous subcutaneous infusion with non-PVC tubing or as a single or twice daily subcutaneous dose. The use of PVC tubing results in adsorption of clonazepam onto

syringe driver tubing with loss of medication. Schneider et al. (2006) demonstrated that with PVC tubing, at 2 and 4 mg of clonazepam administered over 24 h, the loss was 50% and 25%, respectively. This additionally suggests that clonazepam loss is concentration dependent. However, the loss was not dependent on the co-administered medication or diluent. Dickman and Schneider (2016) commented that although the clinical significance of this effect is undetermined, the use of non-PVC tubing is recommended.

6.5 Phenytoin

The initial dose recommended for this AED is 4–5 mg/kg daily in one to two divided doses, with the usual therapeutic daily dose recommended lying between 200 and 500 mg (Pharmaceutical Society of Australia 2014). There is a dearth of evidence examining the role of phenytoin in the palliative care population. In a recent study, Wallace et al. (2012) reviewed AED use in patients with high-grade central nervous system tumors; the authors demonstrated that phenytoin was the most commonly utilized AED. They criticized the inconsistent nature of seizure management, with the lack of expert neurologist involvement in AED selection. No studies have detailed the use of phenytoin sodium via the subcutaneous route.

6.6 Lacosamide

The initial dosing recommendation for lacosamide is 50 mg twice daily, increased gradually to the typical therapeutic daily dose of 200 mg (maximum daily dose is 400 mg) (Pharmaceutical Society of Australia 2014). Lacosamide is well tolerated, has low risk for drug interactions, and is available in a parenteral formulation. There is limited case report evidence for effectiveness of this agent through the subcutaneous route. As an adjunct to subcutaneous levetiracetam, Remi et al. (2016) used a PO:SC dose ratio of 1:1, undiluted solution, with an infusion rate of 20 mg/min. They did not mix the AED with any other drugs and reported no significant adverse effects. Remi et al. (2016) concluded, albeit based on single case experience, that lacosamide was an appropriate option for use as an AED via the subcutaneous route, in circumstances when the oral or intravenous routes were unavailable or inappropriate for palliative patients.

7 Antiepileptic Drugs Only Available Through the Oral Route

7.1 Carbamazepine

The *Australian Medicines Handbook* recommends a starting dose of 100 mg twice daily, with the therapeutic daily dose required for seizure control ranging from 400 to 2 g (maximum recommended daily dose) (Pharmaceutical Society of Australia 2014).

7.2 Gabapentin

The initial starting dose for gabapentin is 300 mg at bedtime, with the dose increased as tolerated to the therapeutic daily dose range of 1800–3600 mg (maximum total daily dose) (Pharmaceutical Society of Australia 2014).

7.3 Pregabalin

The initial starting dose for pregabalin is 75 mg twice daily, with the dose increased to the therapeutic daily dose range of 300–600 mg (maximum total daily dose) (Pharmaceutical Society of Australia 2014).

7.4 Oxcarbazepine

The initial starting dose for oxcarbazepine is 150 mg twice daily, with the dose increased to the therapeutic daily dose range of 900–2400 mg

(maximum total daily dose) (Pharmaceutical Society of Australia 2014).

7.5 Lamotrigine

The initial starting dose for lamotrigine is 25 mg daily, with the dose increased to the therapeutic daily dose range between 100 and 400 mg (maximum daily dose is 700 mg) (Pharmaceutical Society of Australia 2014).

7.6 Zonisamide

The initial starting dose for zonisamide is 100 mg daily, with the dose increased to the therapeutic daily dose range between 200 and 600 mg (maximum daily dose is 600 mg) (Pharmaceutical Society of Australia 2014).

7.7 Topiramate

The initial starting dose for topiramate is 25 mg daily, with the dose increased to the therapeutic daily dose range between 75 and 200 mg (maximum daily dose is 500 mg) (Pharmaceutical Society of Australia 2014).

8 Adverse Effects of the Antiepileptic Drugs

All AEDs can produce adverse effects, and the side effect profiles play a significant role in individualized AED selection (Cramer et al. 2010; Perucca and Meador 2005; Perucca and Gilliam 2012). The frequency of AED adverse effects is dependent on the mode of assessment. Spontaneous patient reporting when compared to the systematic use of a checklist has been demonstrated to result in significant underreporting of adverse effects (Perucca and Gilliam 2012). The evidence from studies that have used screening methods and checklists suggests that adverse effects to AEDs are very common (65–90%) (Perucca and Gilliam 2012). Tolerability is best achieved by slow introduction and gradual titration to achieve the ideal balance between bearable side effects and seizure control (Cramer et al. 2010).

Perucca and Gilliam (2012) have recommended a classification of AED adverse effects into five groups.

Type A – related to the known mode of action of the AED, typically acute, and dose related.

Central nervous system (CNS) effects are shared by all the AEDs and include somnolence, dizziness, fatigue, ataxia, and cognitive impairment. Cognitive effects include impairment in attention, executive function, intelligence, language skills and memory. Perucca and Meador (2005) have outlined the impact of cognitive impairment on quality of life and work. CNS adverse effects are more pronounced in first-generation AEDs and with topiramate (Cramer et al. 2010).

Based on a large meta-analysis in 2008, the US Food and Drug Administration (FDA) issued a warning for suicidal ideation risk with all AEDs (Perucca and Gilliam 2012). In 2013, the ILAE released an expert consensus statement that raised concerns with regard to the meta-analysis underpinning the FDA decision (Mula et al. 2013). They concluded that suicidality in epilepsy was multifactorial (complex interplay of biological, constitutional, and psychosocial variables) and the benefits of seizure prevention will often exceed the potential risk of AED-induced suicidal ideation. Nevertheless, the ILAE recommended the screening of patients prior to AED commencement for underlying mood disorders (Mula et al. 2013). With reference to the AEDs discussed previously, phenobarbital, topiramate, and zonisamide have been associated with depressed mood. Levetiracetam and lamotrigine have been associated with irritability, hostility, and emotional lability (Mula et al. 2013).

Type B – not related to the known mode of action of the AED, related to individual vulnerability, and not usually dose related.

Severe mucocutaneous reactions, which are potentially fatal, have been associated with the AEDs (Perucca and Gilliam 2012). These include Stevens-Johnson syndrome, drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis. Mortality rates associated with these conditions range from 10% to 40% (Yang et al. 2011). The most common associated AEDs are carbamazepine, phenytoin, phenobarbital, and lamotrigine (Yang et al. 2011). A genetic predisposition for severe mucocutaneous reactions has been suggested, through a study involving a Han Chinese population, by the presence of the HLA-B*1502 haplotype in 100% of patients with carbamazepine-induced Stevens-Johnson syndrome (Yang et al. 2011).

Other important Type B (idiosyncratic) reactions include aplastic anemia (carbamazepine, phenytoin, valproate, zonisamide), agranulocytosis (carbamazepine, phenytoin, valproate, zonisamide, lacosamide), prolonged PR interval-heart block (lacosamide), pancreatitis (carbamazepine, valproate), and hepatotoxicity (carbamazepine, phenytoin, valproate) (Perucca and Meador 2005).

Type C – longer term, related to cumulative exposure.

Type C adverse effects include changes in weight (Perucca and Gilliam 2012). This may be a gain (valproate, gabapentin, pregabalin) or loss (topiramate, zonisamide) of weight associated with AED use. Other important Type C reactions can include endocrine disturbances, gingival hyperplasia, hair loss, osteoporosis, hirsutism, kidney stones, visual field loss, and vitamin deficiencies (Perucca and Meador 2005).

Type C reactions may have decreased relevance in the patient facing a life-limiting diagnosis.

Type D – teratogenic and carcinogenic effects.

The use of certain AEDs (particularly first-generation agents) in the first trimester of pregnancy has been associated with an elevated risk of congenital malformations (Perucca and Gilliam 2012). The evidence for safety of second-generation agents is lacking due to sparse exposure data. The evidence from animal models suggests carcinogenic risk with the first-generation AED phenobarbital and phenytoin (Perucca and Meador 2005).

As with category C adverse effects, the palliative care health practitioner needs to make an individualized selection of the appropriate AED – Type D adverse effects may have limited relevance to the vast majority of palliative patients.

Type E – adverse drug interactions.

The most important pharmacokinetic drug interactions associated with the AEDs are related to metabolism. Carbamazepine, phenytoin, and phenobarbital are potent inducers of different isoforms of cytochrome P450 hepatic enzymes (Patsalos et al. 2002). The consequence of this is a reduced serum concentration of a wide range of co-administered medications (potentially including antibiotics and antineoplastics). Valproate is a potent inhibitor of cytochrome P450 enzymes; its co-administration may increase the serum concentrations of other medications and hence their potential for toxicity (Patsalos et al. 2002). Lamotrigine, levetiracetam, gabapentin, and pregabalin do not inhibit or induce enzymes involved in drug metabolism (Patsalos et al. 2002). Another important pharmacokinetic interaction relates to protein binding. The addition of a highly protein-bound drug will displace other protein-bound drugs, thereby increasing their free fraction and potential for toxicity. This is accentuated in the low-protein states seen in many patients with life-limiting illnesses. Gabapentin, pregabalin, topiramate, lamotrigine, and levetiracetam are not significantly protein bound and have lower risk for this pharmacokinetic interaction (Patsalos et al. 2002).

With regard to the adverse effects of the AEDs in the pediatric population, the reader is directed to excellent reviews by Perucca and Gilliam (2012) and Rosati et al. (2015).

9 Comorbid Medical Conditions

The palliative care patient population is likely to suffer from significant comorbid medical issues. Hepatic and renal impairment can act as precipitating factors in seizure causation, and their presence needs consideration in AED selection and dose determinations (Lacerda et al. 2006).

In the setting of renal impairment, the dose of the following drugs (from the list in Table 6) needs reduction (the degree is dependent on creatinine clearance): gabapentin, pregabalin, zonisamide, lacosamide, and levetiracetam (Lacerda et al. 2006). During hemodialysis, water-soluble and low protein-bound AEDs (from the list in Table 6, this includes gabapentin, pregabalin, topiramate, levetiracetam, lacosamide, and phenobarbital) are likely to be removed and require supplemental dosing following dialysis (Lacerda et al. 2006).

In hepatic impairment, there is a need to avoid valproate, which has the potential of causing further hepatotoxicity (Perucca and Gilliam 2012). Additionally, caution is required in the use of AEDs that are highly protein bound (includes the following from Table 6 – carbamazepine, valproate, phenytoin, and clonazepam) or that are predominantly metabolized by the liver (includes the following from Table 6 – carbamazepine, valproate, phenytoin, phenobarbital, oxcarbazepine, clonazepam, and lamotrigine) (Lacerda et al. 2006). Lacerda et al. (2006) have recommended the following AEDs in the setting of hepatic impairment: pregabalin, gabapentin, levetiracetam, or topiramate.

10 Special Populations

10.1 Poststroke Seizures

Strokes are the most commonly defined cause of seizures and account for 30% of newly diagnosed seizures in the elderly (Camilo and Goldstein 2004). A large, prospective, multicenter, cohort study carried out by Bladin et al. (2000) identified that seizures occurred in 8.9% of patients after a hemispheric stroke. This proportion of patients with seizures poststroke was higher for individuals who sustained a hemorrhagic stroke (10.6%) when compared with patients who sustained an ischemic (8.6%) stroke. Cortical location of insult was a risk factor for seizures (in both hemorrhagic and ischemic strokes). Seizures associated with both types of strokes were predominantly "partial" (note old classification) and usually occurred within 24 h post event. Recurrent seizures only occurred in 2.5% of the stroke patients in this study. The risks for recurrent seizures were higher for patients with later onset (more than 2 weeks post stroke) seizures. After adjusting for other variables, only late-onset ischemic (not hemorrhagic) strokes were associated with recurrent seizures. Camilo and Goldstein (2004) outlined the underlying pathophysiology in early seizure poststroke, as resulting from "cellular biochemical dysfunction leading to electrically irritable tissue," and in late seizure poststroke, as "gliosis . . .[with] the development of a meningocerebral cicatrix."

A recent Cochrane review failed to show any benefits for AEDs for the primary or secondary prevention of seizures after stroke (Sykes et al. 2014). However, this review only included one trial, which utilized valproate, in primary prevention after hemorrhagic stroke. Sykes et al. (2014) concluded that despite the paucity of evidence with regard to this issue, recurrent unprovoked poststroke seizures probably warrant treatment. Given the typical focal onset of these seizures, Silverman et al. (2002) have suggested the use of agents typically utilized for seizures of this classification (levetiracetam, phenytoin, carbamazepine, zonisamide) in monotherapy. In selecting an AED, the palliative health practitioner additionally needs to consider the following issues, which are likely to be accentuated in this age group: adverse effects, interactions, and comorbid conditions.

10.2 Primary and Metastatic Brain Tumors

Seizures are a common problem in patients with brain tumors (Avila and Graber 2010). They may

represent the initial manifestation (in up to 50%) or as a later complication (van Breemen et al. 2007). The palliative care health practitioner needs to be aware of precipitating factors (see Table 2), even in the brain tumor population, as they may be responsible for a reversible reduction in the seizure threshold. These precipitating factors have a higher prevalence in this population, resulting from the impact of metabolic encephalopathies (organ dysfunction, electrolyte abnormalities), chemotherapy, radiotherapy, other drugs, and opportunistic infections (van Breemen et al. 2007). Important factors that influence the risk for seizure in a patient with a brain tumor include the tumor type, grade, and location (Avila and Graber 2010). Low-grade primary tumors are more epileptogenic (low-grade astrocytoma 75% risk, high-grade astrocytoma 30–50% risk) (Rossetti and Stupp 2010). While Avila and Graber (2010) outlined that this may relate to the greater time to allow the formation of aberrant pathways, van Breemen et al. (2007) added that the longer survival in these patients might account for the higher frequency of seizures. Seizures are, in general, less common in patients with metastatic brain tumors, when compared to those with primary brain tumors, with the exception being melanomas (Oberndorfer et al. 2002). Primary and secondary brain tumors in the cortex (especially temporal, frontal, and parietal) are more epileptogenic, in comparison to tumors in other locations (Avila and Graber 2010).

The patient with a primary or secondary brain tumor that has a seizure should be classified as having epilepsy (see ILAE definition in Table 1), because of the significant risk of further unprovoked seizures, resulting from the persistent structural abnormality. In this context, treatment with an AED is justified to prevent recurrent seizures and the resultant impact on functional and emotional well-being (Avila and Graber 2010; van Breemen et al. 2007; Rossetti and Stupp 2010). Published evidence does not point to any single AED with superior efficacy in patients with primary or secondary brain tumors (Schiff et al. 2015). Previous reviews on this subject have recommended the use of a second-generation agent (lower impact on hepatic enzymes) in monotherapy, as they offer the best balance between effectiveness and toxicity (Rossetti and Stupp 2010; Schiff et al. 2015). Rossetti and Stupp (2010) suggested a choice between levetiracetam, gabapentin, pregabalin, and lamotrigine, while Schiff et al. (2015) recommended lacosamide, as an additional option. Rossetti et al. (2014) have recently completed a small, open-label randomized controlled trial (RCT), comparing the safety and efficacy of levetiracetam to pregabalin, in patients with primary brain tumors and at least one seizure. They concluded that both drugs were effective (65% seizure-free in levetiracetam group and 75% seizure-free in pregabalin group) and well tolerated. It is important that the palliative care health practitioner additionally considers the role of tumor-directed therapies (surgery, radiotherapy, and systemic therapy), for patients with primary and secondary brain tumors. Systemic therapy may include the use of steroids, such as dexamethasone for reduction of peritumoral edema (van Breemen et al. 2007). In the appropriately selected patients, these therapeutic options may ameliorate seizure activity (Avila and Graber 2010).

Previous reviews including one by the Cochrane collaboration have failed to demonstrate any benefit for AEDs in primary seizure prophylaxis for the patient with a primary or secondary brain tumor (Tremont-Lukats et al. 2008). The Cochrane review found no evidence for benefit but a greater risk for adverse events. However, they were clear that these conclusions were only applicable to the first-generation agents: phenytoin, phenobarbital, and valproate. A more recent review suggested a favorable role for levetiracetam for seizure prevention in brain tumor patients (Nasr et al. 2016). The authors included 21 studies including 3 RCTs. However, two of the RCTs were for patients post craniotomy, and the other was the Rossetti et al. (2014) RCT, which included patients who already had at least one seizure. Certainly the tolerability and reduced risk for drug interactions make the second-generation AEDs more suitable for primary seizure prophylaxis; however in the absence of more robust evidence, there can be no clear endorsement of this recommendation.

For the patient commenced on an AED, Rossetti and Stupp (2010) have recommended they remain on AED treatment as long as the underlying structural abnormality is present. For patients who have had successful operative clearance, the cessation of AEDs needs careful assessment, with consideration of the risk of local tumor recurrence (especially gliomas) and seizure return. Others have counseled long-term continuation of treatment, because of the impaired life expectancy, and quality-of-life concerns with seizure recurrence (including loss of driving) (van Breemen et al. 2007).

10.3 Preventing Seizures at the End of Life

Seizures at the end of life are not an uncommon occurrence in the palliative population and are an important consideration in patients with brain tumors. In one large retrospective study involving high-grade glioma patients, 36.9% of the patients had a seizure in the last 4 weeks of life (Pace et al. 2013). In the last week of life, when patients are less likely to have the ability to swallow oral AEDs, the proportion of high-grade glioma patients who had a seizure, in the retrospective cohort of Sizoo et al. (2014) was 29%. Therefore, proper control of seizures even at the end of life is warranted, and furthermore their occurrence has been associated with a non-peaceful death (Bausewein et al. 2003). An important determination in this context is the role of the AED in the end of life. A discussion regarding the appropriateness and timing of AED cessation needs to occur at an early stage, allowing patient participation and preferably included in an advanced care directive. At the very least, the nomination of a substitute decision-maker at early stage of illness may help ensure that the patient's wishes are followed where appropriate at the end of life. Where possible, if the patient was commenced on the AED for an unprovoked seizure, and especially if there is an underlying persistent structural abnormality, the patient should continue these medications while they can swallow (Krouwer et al. 2000). When the ability to swallow is lost, and the patient/family or treating palliative health practitioner believes continuing seizure prevention is important, alternative routes of administration need to be sought. There is insufficient data regarding the preferred drug or route in this situation (Pace et al. 2013). Pace et al. (2013) espouse the use of intramuscular phenobarbital, or intravenous levetiracetam, for seizure prevention at the end of life. Krouwer et al. (2000) have outlined options for the rectal route (parenteral solution of phenobarbital and oral carbamazepine solution) for seizure prevention in the context of patients at the end of life. Koekkoek et al. (2016) used the buccal route (clonazepam) to administer prophylactic antiseizure treatment. Finally, the author has earlier discussed the subcutaneous route (not licensed) for various AEDs. The treatment of the acute seizure and status epilepticus will be discussed in the following sections.

11 Status Epilepticus

The definition of status epilepticus has seen many revisions over the past few decades. In particular this has been related to the duration of continuous seizure activity. Lowenstein and Alldredge (1998), in a review paper, outline initial definitions that do not define a length of time, to later ones that specified 30 min of continuous seizure activity, as status epilepticus. The derivation for 30 min was from animal models that suggested that neuronal injury is likely in continuous seizure activity beyond this point (Trinka et al. 2015). Lowenstein and Alldredge (1998) suggested the need for a more "operational definition," as the need for treatment is imperative well before this period of time has elapsed. They suggested a definition for generalized convulsive status epilepticus of "either continuous seizures lasting at least 5 minutes or two or more discrete seizures between which there is incomplete recovery of consciousness" (p. 970). Chen and Wasterlain (2006) provided statistical argument for the 5 min threshold, documenting that this was 18–20 standard deviations away from the duration of generalized convulsive seizures (the isolated seizure).

In 2015, the ILAE proposed a broad definition that would encompass all types of status

epilepticus (tonic-clonic, focal with impaired consciousness, absence) (Trinka et al. 2015). They defined status epilepticus as:

> A condition resulting either from the failure of mechanisms responsible for seizure termination or from the initiation of mechanisms which lead to abnormally prolonged seizures (after time point t1). It is a condition that can have long-term consequences (after time point t2), including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures. (p. 1517)

The definition for t1 would guide clinicians as to the timing of when a seizure needs to be considered as status epilepticus. For tonic-clonic seizures, the ILAE has suggested this be set at 5 min (focal with impaired consciousness and absence set at 10 min). The definition for t2 would guide clinicians as to the time beyond which neurological sequela may be expected. For tonic-clonic status epilepticus, this has been set at 30 min (focal with impaired consciousness at greater than 60 min and undefined for absence).

Lowenstein and Alldredge (1998) have outlined that the fundamental pathophysiology involved in status epilepticus as a "failure of mechanisms that normally abort an isolated seizure" (p. 971). They delineate this as the result of the confluence of persistent, excitatory, and ineffective inhibitory mechanisms. Chen and Wasterlain (2006) have further detailed this interplay between loss of inhibition and promotion of excitation, in their hypothesis of "receptor trafficking." In the transition from isolated seizure to status epilepticus, they document animal models demonstrating a reduction in GABA (gamma aminobutyric acid) receptors (resultant loss of inhibition) and increased AMPA (α-amino-3-hydroxyl-5-methyl-4-isoxazole-propionate) and NMDA (N-methyl-d-aspartate) receptors (increased excitation), per synapse. Understanding of these mechanisms assists in elucidating the loss of potency of GABAergic drugs as status epilepticus becomes established (pharmacoresistance) and the potential for NMDA blocker effectiveness even in prolonged status (Chen and Wasterlain 2006). With persistent status epilepticus, there are, additionally, a depletion of inhibitory and increase in pro-convulsant neuropeptides in the hippocampus (Chen and Wasterlain 2006).

Chen et al. (Trinka et al. 2015) have suggested that the neuronal injury and death in status epilepticus is the result from "excessive neuronal firing, through excitotoxic mechanisms" (p. 249). The evidence for neuronal death in status is derived from the finding of elevated levels of markers of nerve cell death in the serum, and the demonstration on imaging of cerebral edema and atrophy, in patients post status (Trinka et al. 2015). Furthermore, Chen et al. (Trinka et al. 2015) elaborate that postmortem findings of reduced neuronal density in the hippocampi of patients deceased from status epilepticus are also consistent with the evidence for nerve cell death associated with status. Status epilepticus is therefore a neurological emergency.

Brophy et al. (2012) have outlined that the 30-day mortality for convulsive status epilepticus ranges from 19% to 27%, while that for non-convulsive status epilepticus approaches 65%. These outcomes are likely to be poorer if status epilepticus occurs in association with an advanced life-limiting condition (Droney and Hall 2008). In such group of patients, status epilepticus may be the terminal event. In the survivors of an episode of status epilepticus, there is additional morbidity related to neurological or cognitive sequelae (up to 16%) and decline in functional status (up to 26%) (Brophy et al. 2012).

Factors associated with poorer outcomes in convulsive status epilepticus include underlying cause, advanced age, presence of comorbidities, duration of seizure, impaired conscious state at presentation, and the presence of focal neurological features at seizure onset (Brophy et al. 2012). It is the underlying etiology, however, that has the greatest importance as an outcome predictor for status epilepticus (Rosetti et al. 2006; Scholtes et al. 1994). As outlined by Rosetti et al. (2006), in patients with potentially fatal underlying conditions, it is the etiology "rather . . . [than] status epilepticus per se . . . [that] is the major determinant of outcome." Finally, Brophy et al. (2012) have outlined the role of both insufficient therapy or lack of adherence to treatment protocols as being associated with poorer outcomes. In a

prospective study, Aranda et al. (2010) demonstrated that the key factor in predicting convulsive status epilepticus termination (with resultant reduced refractory status, length of stay, and complications) was adherence to protocol.

Factors associated with poorer outcome, in nonconvulsive status epilepticus, include underlying etiology and duration of seizures. Delayed diagnosis of nonconvulsive status epilepticus (more likely than convulsive status epilepticus, owing to lack of motor activity) is additionally an important factor in the poorer outcome associated with nonconvulsive, when compared to convulsive status epilepticus (Young et al. 1996). Young et al. (1996) have suggested that nonconvulsive status epilepticus is "often unsuspected in patients with comorbid conditions such as cancer or organ failure" (p. 89). In their cohort of intensive care patients, with continuous EEG monitoring, they outline a better outcome with respect to mortality for those patients whose seizures were identified within 30 min of onset (36%), when compared to those whose diagnosis was delayed by more than 24 h (75%) (Young et al. 1996). Lorenzl et al. (2008) have recommended the need for the palliative health practitioner to be aware of the possibility of nonconvulsive status epilepticus in the patient with an acute change in mental status or behavior. Important examination findings suggestive of this condition include mild myoclonic jerks of the facial muscles and epileptic nystagmus (Lorenzl et al. 2010). Given the common occurrence of myoclonic jerks in the patient with an advanced illness (opioid toxicity, metabolic derangement), the detection of nonconvulsive status epilepticus requires an acute awareness of this disorder and a thorough neurological assessment of the patient with a sudden altered conscious state or behavioral change.

The etiology of status epilepticus has classically been defined as acute symptomatic, remote symptomatic, and idiopathic (DeLorenzo et al. 1996). DeLorenzo et al. (1996) outlined that status epilepticus with an acute symptomatic etiology develops within 7 days of the onset of an acute event, while remote symptomatic status epilepticus has no acute trigger but instead has a remote history of central nervous system insult. With idiopathic etiologies, there is no acute or remote cause that can be identified as being responsible for the status epilepticus (DeLorenzo et al. 1996). Table 7 summarizes the common etiologies underlying status epilepticus. In practice, the underlying etiology for any individual patient may have a combination of acute and remote factors, for example, a previous insult with a superimposed acute trigger.

In their retrospective review of 204 status epilepticus events, DeLorenzo et al. (1996) identified that almost 50% of adult status epilepticus had a cerebrovascular disease (acute and remote) etiology. Additionally, they identified anoxia and hypoxia acute symptomatic etiologies, as having the highest mortality (71% and 53%, respectively). Cerebrovascular disease similarly was responsible for a significant proportion of acute and remote symptomatic status epilepticus in the 172 cases examined by Coeytaux et al. (2000). Acute symptomatic status, occurring in the context of anoxia/hypoxia and especially in older patients, is associated with the highest mortality (Lowenstein and Alldredge 1998).

12 Treatment of the Acute Seizure and Status Epilepticus

The treatment of the acute seizure in the patient with a life-limiting diagnosis needs to be guided by the goals of care, stage of illness, and prognosis. The management of the acute seizure in this setting needs therefore be considered in the context of the patient's clinical situation. For many patients a seizure event may be anticipated because of the pathophysiology and natural history of the underlying life-limiting condition. For these patients a preemptive discussion with the patient and family can delineate appropriate treatments that may be offered within the context of the patient's goals, stage of illness, and overall prognosis. However, anxiety in the patient and family may occur with such discussions, and it is important that these discussions occur judiciously. The outcome of such discussions should be recorded in advanced care directives.

Table 7 Etiology underlying status epilepticus (Brophy et al. 2012; DeLorenzo et al. 1996)

Status epilepticus etiology	
Acute symptomatic	
Anoxia	Acute deprival of oxygen to the central nervous system from prolonged cardiorespiratory arrest
Hypoxia	Respiratory insufficiency
Cerebrovascular disease	Includes occlusion, embolism, and infarct
Hemorrhage	Includes intracerebral and subarachnoid
Tumor	Primary and secondary
Sepsis	Systemic febrile illness
Central nervous system infection	Includes bacterial, viral, fungal, and other causes
Metabolic disturbances	Includes electrolyte abnormalities, hypoglycemia, hyponatremia, hypocalcemia, hypomagnesemia, hepatic encephalopathy, and uremia
Sub-therapeutic anticonvulsant medications	Includes non-compliance with medications
Drug toxicity	Includes overdose (drugs lowering seizure threshold) and intoxication
Drug withdrawal	Includes opioids, benzodiazepines, and alcohol
Head trauma	Includes closed head injuries
Autoimmune	Includes multiple sclerosis and anti-NMDA receptor encephalitis
Remote symptomatic	
Prior central nervous system insult	Includes cerebrovascular accidents, central nervous system infections, congenital pathologies (malformations, hydrocephalus, genetic diseases), trauma, hemorrhage, or tumor
Idiopathic	

Adapted from Brophy et al. (Chen and Wasterlain 2006) and DeLorenzo et al. (Lorenzl et al. 2010)

In the treatment of the acute seizure, the palliative health practitioner needs to consider the presence of precipitating factors (Table 2) and the appropriateness of investigation and treatment of these triggers. Importantly, the vast majority of seizures cease spontaneously within 2 min from onset, usually obviating the need of medications for seizure termination (Chen and Wasterlain 2006). However, as seizure time elapses, there is not only increased neuronal injury but also progressive development of pharmacoresistance to the commonly used anticonvulsants (Chen and Wasterlain 2006). Therefore, in the patient who has active treatment goals and an excellent prognosis, aggressive treatment needs to be commenced early as "time is brain" (Chen and Wasterlain 2006).

The Neurocritical Care Society has provided excellent consensus-based guidelines for the management of status epilepticus, which has been summarized in Table 8 (Brophy et al. 2012). The guidelines as per Table 8 are pertinent for the patient for whom intensive care unit (ICU), intubation, ventilation, and cardiopulmonary resuscitation are still considered appropriate. It is important to note that the notion of "time is brain" is reflected in the timing of interventions as outlined in Table 8, and therefore, the health practitioner needs to consider that any acute seizure may progress to status epilepticus. For additional pediatric guidelines, the reader is encouraged to review the manuscripts by Glauser et al. (2016) and Sofou et al. (2009).

Portions of the Neurocritical Care Society guidelines may have applicability for the palliative patient with less aggressive goals of treatment and care. While intubation, vasopressor support, and refractory status epilepticus require ICU level of care, the other components of care can be provided at the ward level in most tertiary hospitals. Furthermore, for others much of the guideline recommendations may be inappropriate if the prognosis is poor or if the patient is at the end of life.

Table 8 Status epilepticus treatment outline (convulsive and nonconvulsive)

Critical care treatment	Timing – minutes post onset
1. Noninvasive airway protection +O2	0–2
2. Intubation – if step (1) compromised	0–10
3. Vital signs	0–2
4. Vasopressor support of BP if required	5–15
5. Finger stick blood glucose	0–2
6. IV access	0–5
Emergent initial AED[a]	
Fluids	
Thiamine/dextrose	
7. Urgent SE control therapy[b]	5–10
8. Neurological examination	5–10
9. Lab tests[c]	5
10. Refractory SE therapy[d]	20–60

02 oxygen therapy, *BP* blood pressure, *IV* intravenous, *AED* antiepileptic drug, *SE* status epilepticus
[a]Emergent initial AED therapy: benzodiazepine – lorazepam IV is preferred. If not available, diazepam, clonazepam, or midazolam IV is secondary options
[b]Urgent SE control therapy: phenytoin, valproate, or levetiracetam as IV bolus dosing
[c]Lab tests: diagnostic studies should be tailored to the individual patient
[d]Refractory SE (RSE) therapy: midazolam, propofol, or pentobarbital continuous IV infusion, this will necessitate ICU support, assisted ventilation, and continuous EEG monitoring (determines cessation of RSE)
[e]Adapted from Brophy et al. (2012)

The PCF recommends lorazepam intravenously as first-line agents for acute seizure (Twycross et al. 2014). For the treatment of an acute seizure, there is a need to use a route that allows for the shortest time for that AED to reach maximum plasma concentration. Droney et al. (Droney and Hall 2008) urged for consideration of the intravenous route, even in the palliative patient, as the suffering from continuing or repetitive seizure activity needs to be weighed against the distress of obtaining intravenous access. In circumstances when an intravenous route is not possible, a recent review concluded that midazolam given intramuscularly and diazepam given per rectally have characteristics that allow rapid absorption and efficacy (Leppik and Patel 2015). In a review of pediatric status epilepticus, Brigo et al. (2015) demonstrated that buccal midazolam was more effective than rectal diazepam in seizure control (also more socially acceptable). The authors do caution that the generalizability of these findings is limited to the pediatric population. Kalviainen (2015) reported on a review of adult and pediatric studies examining the use of intranasal therapies for seizures and concluded that intranasal midazolam was more effective than rectal diazepam. These studies help provide the palliative care health practitioner with options for use in the abortion of seizures, for both the community and inpatient setting.

For prolonged seizures, the PCF demonstrates a preference for intravenous phenobarbital in preference to phenytoin, because of its more likely availability in palliative care units (Twycross et al. 2014). In the context of an end-of-life setting, the subcutaneous route may be used to treat seizures. The *Therapeutic Guidelines Palliative Care* outlines the use of clonazepam or midazolam bolus doses for the acute seizure, with phenobarbital as second-line agent (Palliative Care Expert Group 2010). Continuous subcutaneous infusions, with phenobarbital, midazolam, or clonazepam, may be considered to maintain seizure control (Palliative Care Expert Group 2010). In certain patients, where it is important to avoid the adverse effects of sedation (associated with phenobarbital, midazolam, and clonazepam), valproate, levetiracetam, and lacosamide may be considered for seizure prevention (Remi et al. 2014, 2016). However, it is important to note that in Remi et al. (2014) levetiracetam was administered with midazolam in 75% of their patients (i.e., not in monotherapy), and similarly, in Remi et al. (2016) lacosamide was not administered as the sole AED (administered with levetiracetam and midazolam). Valproate, being a potent inhibitor of cytochrome P450 hepatic enzymes, has risk of drug interactions and toxicity. Table 9 details the drugs commonly used in seizure management, including for status epilepticus. The reader is reminded that the use of AEDs via some of the routes detailed is "off-label" and based on limited evidence supporting efficacy and safety.

Table 9 Acute seizure and status epilepticus: agents commonly used, route[a], and dosing

Medication	Dose
Lorazepam	IV: 4 mg may repeat in 5–10 min
Diazepam	IV: 10 mg may repeat in 10–15 min
	Rectal solution: 10–20 mg may repeat in 10–15 min
Midazolam	IV/IM/SC[b]: 10 mg (acute seizure-bolus dose)
	Buccal/intranasal: 10 mg (parenteral soln) may repeat in 10–15 min
	IV (RSE)[c]: 0.2 mg/kg then 0.05–2 mg/kg/h CI
	CSCI[b]: 30–60 mg/24 h
Clonazepam	IV/SC[b]: 1 mg (acute seizure-bolus dose)
	CSCI[b, d]: 2–10 mg/24 h
Phenytoin	IV[e]: 20 mg/kg
Valproate	IV[e]: 20–40 mg/kg
	CSCI[b]: 400–1800 mg/24 h
Levetiracetam	IV[e]: 1000–3000 mg
	CSCI[3]: 1000–4000 mg/24 h
Lacosamide	CSCI[b]: 100–400 mg/24 h
Propofol	IV (RSE)[c]: 1–2 mg/kg then 30–200 mcg/kg/min CI
Pentobarbital	IV (RSE)[c]: 5–15 mg/kg then 0.5–5 mg/kg/h CI
Phenobarbital	IV/IM[b]: 100 mg
	CSCI[b]: 600–2400 mg/24 h

Adapted from Brophy et al. (2012), Twycross et al. (2014), Remi et al. (2014, 2016), Droney et al. (Droney and Hall 2008), Wells et al. (2016), and the Pharmaceutical Society of Australia (2014)
RSE refractory status epilepticus, *CI* continuous infusion, *CSCI* continuous subcutaneous infusion
[a]Where possible the IV route is always preferable, the subcutaneous route may be acceptable in the end-of-life setting
[b]These are options for seizure control in the palliative patient at the end of life
[c]Note these are instructions for RSE in the patient ventilated and managed in ICU (see Table 8)
[d]Non-pvc tube recommended
[e]Doses are for Table 8 status epilepticus IV bolus therapy

13 Seizures, Driving, and the Palliative Patient

Most countries have driving licensing authorities (DLAs), who are charged with the responsibility of deciding on an individual's safety to drive a motor vehicle. The relevant DLAs rely on appropriate health professional input in their decision-making process. As a result, there is often an interplay between patient, DLA, and health professional, which can create complex ethical and legal issues for the health practitioner. The health professional may find themselves entangled, between the importance of patient autonomy, confidentiality, and preservation of the doctor-patient relationship on one side and an obligation to public safety on the other. Furthermore, the failure to report the "at-risk" driver, who subsequently causes injury or death, additionally exposes the health practitioner to potential civil or criminal liability.

Previous research suggests inconsistent reporting to DLAs of the patient at increased risk of seizure, or with a history of seizures, from an underlying brain tumor. One such study was a large survey of neurosurgeons and oncologists, treating patients with brain tumors (primary and secondary), in the United States (Thomas et al. 2011). Over a quarter of the respondents acknowledged that they did not discuss any driving restrictions with their patients, and a similar proportion were unaware of their state regulations with respect to the need to inform DLAs of medically unfit drivers. A Canadian study found that only 57% of brain tumor patients with seizures were reported to the DLA, despite this being clearly mandated by the Canadian Medical Association (Louie et al. 2013). In an Irish study by Wallace

et al. (Pharmaceutical Society of Australia 2014) of the medical records of patients with high-grade primary brain tumors, it was revealed that instructions with regard to driving were not documented in any of the 27 cases examined.

In circumstances where their patient continues to drive, the palliative care practitioner has a responsibility to discuss fitness to drive with their patients. Patients with advanced life-limiting illness are likely to be exposed to many factors that risk impairing their neurocognitive capabilities. Palliative health practitioners need to familiarize themselves with the standards and regulations that are applicable to their region of practice. In general, all patients with a seizure need a period of restricted driving, the duration of which is as regulated by their relevant national standards. As national standards define periods of restriction based on seizure history, a difficulty arises in the management of the patient who has not had a seizure but who has a brain tumor (and hence risk of seizure and progressive or sudden deficits). Every patient in this circumstance who is considering continuing to drive needs a thorough neurocognitive assessment to determine fitness for this task. In such circumstances, the assistance of allied health practitioners (occupational therapist) and other specialists (neurologists) may be necessary. An excellent algorithm (produced by the Cancer Institute NSW) is available, which helps illuminate the assessment of the brain tumor patient, with regard to fitness to drive (McDonald 2011; Cancer Institute NSW 2016).

14 Summary

It is important to recognize that there is no "standard" palliative patient. Therefore, the palliative care health practitioner is faced with the task of adapting the information provided here to their individual patient. The goals of care, stage of disease, and prognosis, all help guide the health practitioner, in determining how best to utilize the recommendations provided in this chapter, for their specific patient.

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Tumor Lysis Syndrome

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Contents

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Abstract

Tumor lysis syndrome refers to the laboratory and clinical results of rapid breakdown of high volumes of malignant cells. Significant electrolyte disturbances, particularly hyperkalemia, hypocalcemia, and hyperphosphatemia, in

R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_76

tandem with severe hyperuricemia, are disease hallmarks. The most significant clinical sequelae of these disturbances include life-threatening cardiac arrhythmias, sudden death, seizures, and renal failure due to precipitation of uric acid or calcium phosphate in the renal tubules.

With the advent of more potent targeted and biological therapies, tumor lysis syndrome is being encountered in diverse oncology patient settings, with increasing incidence, and in diseases previously not considered high risk. Failure to identify and apply preventative strategies to at-risk patients may result in life-threatening complications and premature death. Once established, tumor lysis syndrome is a medical emergency that requires acute intervention but is inherently reversible with appropriate supportive measures.

In the palliative care setting, cancer patients remain at risk of tumor lysis syndrome, and clinicians should be aware of its potential at all times, particularly as its onset may be iatrogenic. Clear communication between clinicians and patients is critical in order to ensure that appropriate interventions are delivered in a timely fashion while considering a patient's wishes delimiting ceilings of care.

This chapter provides an overview of the etiology, symptomatology, and standardized definitions of tumor lysis syndrome. We also discuss prevention, management, and special considerations in the palliative care setting.

1 Introduction

Tumor lysis syndrome (TLS) represents a medical emergency due to the potentially severe clinical sequelae of electrolyte disturbances resulting from rapid tumor cell breakdown. Following the first descriptions of renal complications of cancer by Frei in 1963 (Frei et al. 1963), the full clinical spectrum of TLS has now been defined, and guidelines for prevention and management are well annotated. Disease states such as acute leukemia or Burkitt lymphoma, hallmarked by a high tumor burden and rapid cell turnover (Swerdlow et al. 2008), exemplify the classical scenario in which a high TLS risk is usually cognizant to the treating clinician. However, the increasing deployment of more potent biological and targeted therapies has resulted in an increased potential for TLS and a broadening of the diseases considered at risk. This includes ambulatory patients being with diseases considered incurable by conventional therapies and thus being treated with "palliative intent."

While the complications of TLS can usually be successfully navigated, appropriate treatment may be both intensive and invasive, albeit for a short period of time until the underlying tumor breakdown subsides. In the palliative care setting, this may present a difficult clinical management scenario as acute interventions (e.g., hemofiltration or dialysis) may contradict advanced care directives in a patient where the presence of TLS may indicate that the underlying malignancy is actually susceptible to therapeutic intervention. Thus, short-term intensive management of the reversible complications of TLS may be warranted in the context of underlying cancer control and longer-term alleviation of symptomatology for the patient.

This chapter provides a contemporary overview of TLS with the aim of updating the knowledge of health providers and alerting them to the potential for TLS in patients with cancer. Special attention is given to the palliative setting, where awareness of the risk of TLS allows effective preventative strategies, and early recognition and intervention may alleviate morbidity. Indeed, TLS may be a "biomarker" of a tumor's responsiveness to therapeutic intervention, and with appropriate management this inherently reversible complication may herald improvements in both symptomatology and prognosis.

2 Etiology

Historically, TLS was usually associated with the administration of conventional cytotoxic therapy. However, spontaneous TLS is also observed in untreated patients with highly proliferative tumors, such as acute leukemia, Burkitt lymphoma, and small-cell lung carcinoma (Cohen et al. 1980; Kalemkerian et al. 1997; Agha-Razii et al. 2000;

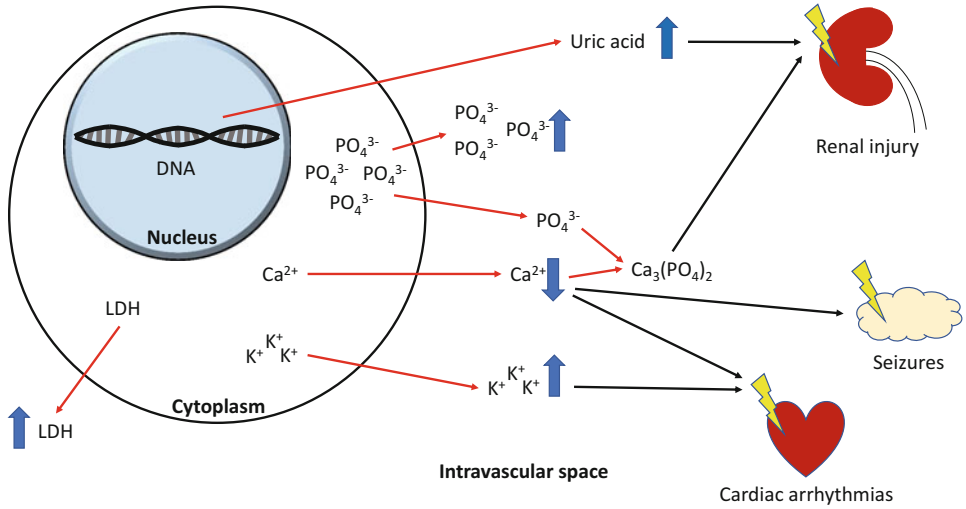

Fig. 1 Schematic overview of the etiology, key serum electrolyte aberrations, and resultant toxicities of tumor lysis syndrome. *DNA* deoxyribonucleic acid, *LDH* lactate dehydrogenase, PO_4^{3-} phosphate, Ca^{2+} calcium, $Ca_3(PO_4)_2$ tricalcium phosphate (representative of calcium phosphate family), and K^+ potassium. Red arrows denote shift of electrolytes; blue arrows denote laboratory assessable aberrations resulting from tumor lysis syndrome; black arrows denote severe clinical sequelae of tumor lysis syndrome

Riccio et al. 2006; Kanchustambham et al. 2017). Indeed TLS may be precipitated in chemo-refractory lymphoid malignancy simply by the addition of corticosteroids, which are frequently employed for symptom control in palliative care. Hallmarks of TLS are also observed in the absence of symptomatic end-organ dysfunction, the so called laboratory TLS. With the recent introduction of novel biological (noncytotoxic) therapies, both clinical and laboratory features of TLS may be observed in unanticipated disease contexts – particularly where conventional therapies did not usually result in rapid tumor destruction. These factors have led to a broadening in the use of the term to encompass any situation of laboratory or clinical TLS (as described below) attributable to active malignancy in the presence or absence of therapy.

3 Pathophysiology

TLS results from the rapid release of intracellular components from cancer cells into the extracellular and intravascular spaces. This rapid metabolic and electrolyte shift leads to the classical pattern of hyperuricemia, hyperphosphatemia, hypocalcemia, and hyperkalemia with resultant features of acute renal failure (Fig. 1).

3.1 Hyperuricemia

Breakdown of deoxyribonucleic acid (DNA) strands leads to the release of purine nucleotides, which may be even more abundant in tumor cells due to chromosomal aneuploidy. These nucleotides are initially catabolized to hypoxanthine, and then the enzyme, xanthine oxidase, sequentially catalyzes the generation of uric acid via a xanthine intermediary (Fig. 2). Uric acid is renally excreted though poorly soluble in urine, particularly at acid pH where it exists as urate (Klinenberg et al. 1965; Goldfinger et al. 1965). Uric acid precipitation is one of the mechanisms by which the metabolic derangement of TLS leads to acute renal dysfunction. Other mammalian species possess the enzyme, urate oxidase, which converts uric acid to the more soluble allantoin (Fig. 2). However, an evolutionary conserved nonsense mutation has led to absence of this enzyme in *Homo sapiens* and several other non-human primates (Yeldandi et al. 1991).

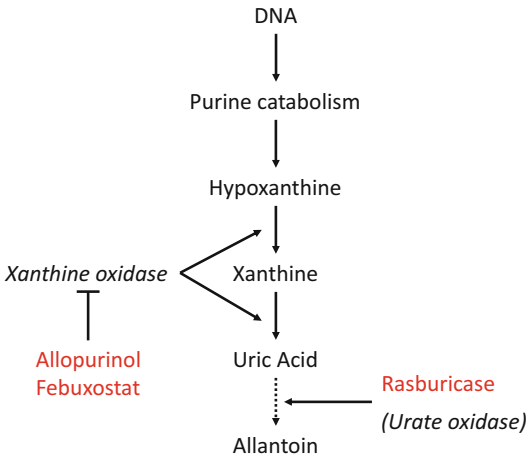

Fig. 2 Pathway leading to purine catabolism and uric acid generation. Italic font denotes enzymes with brackets indicating site of action of urate oxidase which is absent in humans. Red text denotes uricosuric agents and their sites of activity. (Modified with permission from Cairo and Bishop 2004).

3.2 Hyperphosphatemia

Intact cells contain a rich supply of organic and inorganic phosphate, which is a substrate for critical cellular functions including intracellular signaling and synthesis of DNA and phospholipid (Bergwitz and Jüppner 2011). Furthermore, malignant cells have been reported to contain significantly greater intracellular phosphate when compared to nonmalignant cells (Frei et al. 1963). Upon rapid release of intracellular phosphate, renal excretion increases and tubular resorption reduces until saturation occurs. This excess excretion of phosphate may also precipitate in the renal tubules as calcium phosphate, to further exacerbate renal dysfunction associated with TLS. Indeed, since introduction of allopurinol use to reduce uric acid formation (discussed later), nephrocalcinosis has become a more prevalent cause of renal dysfunction complicating TLS than precipitation of uric acid. The development of hyperphosphatemia (serum phosphate $\geq$1.45 mmol/L in adults or $\geq$2.1 mmol/L in children; Table 1) is typically indirectly symptomatic through induction of hypocalcemia (Cairo and Bishop 2004).

3.3 Hypocalcemia

Following the release of intracellular phosphate, calcium phosphate deposition in the renal tubules and other tissues leads to hypocalcemia. Symptomatic hypocalcemia may take the form of neuromuscular irritation with muscle weakness and cramping, tetany, paresthesia, and occasionally bronchospasm or dysphagia relating to smooth muscle spasm.

3.4 Hyperkalemia

The abrupt release of intracellular potassium can cause potentially fatal hyperkalemia, representing the most significant acute and life-threatening complication of TLS. Mild to moderate hyperkalemia is asymptomatic, so clinicians and nursing staff must be aware of this possibility in order to implement appropriate treatments. Hyperkalemia may induce arrhythmias, including loss of consciousness or cardiac arrest due to ventricular tachycardia (VT) or ventricular fibrillation (VF) as the first clinically evident sign. As such, many guidelines advocate the use of frequent electrocardiographic (ECG) monitoring to detect the development of arrhythmias including the classical sinusoidal tracing of the QRS complex through to frank VT/VF.

4 Diagnosis

The earliest formal classification of TLS was described by Hande and Garrow (1993). Almost a decade later, Cairo and Bishop provided an updated classification system which remains the standard to this day (Cairo and Bishop 2004). The Cairo-Bishop classification provides definitions of laboratory TLS (LTLS) and clinical TLS (CTLS), as shown in Tables 1 and 2.

4.1 Cairo-Bishop Classification

The Cairo-Bishop LTLS classification addresses aberrant biochemical results occurring within a

Table 1 Laboratory tumor lysis syndrome Cairo-Bishop definition (modified with permission from Cairo and Bishop 2004). The definition requires two or more of the listed criteria be met within the period from 3 days prior to 7 days post initiation of therapy. The definition assumes the use of hyperhydration and hypouricemic agent as preventative measures

Cairo-Bishop definition: laboratory tumor lysis syndrome	
Electrolyte	Criterion
Uric acid	≥476 μmol/L or ≥25% increase from baseline
Potassium	≥6.0 mmol/L or ≥25% increase from baseline
Phosphate	≥1.45 mmol/L (adult) or ≥2.1 mmol/L (pediatric) or ≥25% increase from baseline
Calcium	≤1.75 mmol/L or ≥25% decrease from baseline

L liter

Table 2 Clinical tumor lysis syndrome Cairo-Bishop definition (Modified with permission from Cairo and Bishop 2004). The definition requires the presence of one or more of the listed criteria and the presence of laboratory tumor lysis syndrome as per Table 1

Cairo-Bishop definition: clinical tumor lysis syndrome
Criterion
Creatinine ≥1.5 × laboratory ULN[ab] (age >12 or age adjusted)
Cardiac arrhythmia or sudden death[a]
Seizure[a]

[a]Definition requires the clinical criterion that is not otherwise attributable to another therapy such as nephrotoxic agent

[b]Definition does not specify guidance for interpretation of preexisting renal dysfunction due to comorbid illness or nephrotoxic agent. *ULN* laboratory upper limit of normal

window from 2 days prior to 7 days post-therapy (Cairo and Bishop 2004). It requires two or more derangements of serum uric acid, phosphate, calcium, and potassium according to predefined laboratory limits or 25% derangement from baseline in the expected direction for TLS (Table 1). Furthermore, this algorithm assumes the application of preventative measures such as adequate hydration and hypouricemic agent administration.

The Cairo-Bishop classification also provides criteria for clinical stigmata of TLS. This requires the patient meets the criteria for LTLS and also demonstrates one or more clinical sequelae including renal dysfunction (according to creatinine measurement), cardiac arrhythmia, sudden death, or seizure (Table 2). The definition concedes that intercurrent nephrotoxic therapies may contribute to renal dysfunction and allows for this to negate that criterion. Notably however, the criteria do not include reference to preexisting renal dysfunction due to comorbid illness. In such a situation, the clinician would not attribute such derangement to CTLS unless a significant worsening of the renal function were to occur. No arbitrary criteria have been included in the Cairo-Bishop classification to provide guidance as to what level of creatinine or glomerular filtration rate derangement is required in the setting of preexisting renal dysfunction for CTLS to be defined.

In order to quantitatively grade TLS, Cairo-Bishop also provides a grading classification beyond the qualitative assessment. This quantitative grading (Table 3) assesses the relative severity of the CTLS signs and renal dysfunction and provides a grading from 0 to V, whereby 0 is the absence of LTLS and CTLS and V is death attributable to TLS. This differs from the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) where the only applicable grades for TLS are 3 (present), 4 (life threatening with urgent intervention indicated), and 5 (death), as shown in Table 4 (National Cancer Institute 2009).

5 Risk Factors

Historically, at-risk diseases for TLS were those characterized by a high rate of proliferation and sensitivity to cytoreductive therapy. Aggressive hematological malignancies (e.g., acute leukemias and aggressive lymphomas) have previously been considered highest risk. However, with the identification of oncogenic dependencies of other malignancies and the advent of potent targeted therapies against these, other conditions previously considered low risk have had to be reclassified due to frequent observation of TLS at initiation of therapy.

Table 3 Severity grading classification of tumor lysis syndrome (Modified with permission from Cairo and Bishop 2004)

Cairo-Bishop definition: grading classification						
	0	I	II	III	IV	V
LTLS	Absent	Present	Present	Present	Present	Present
Creatinine[a, b]	≤1.5 × ULN	1.5 × ULN	1.5–3 × ULN	>3–6 × ULN	>6 × ULN	Death[c]
Cardiac arrhythmia[a]	Absent	No intervention required	Non-urgent medical intervention required	Symptomatic and incompletely controlled or requiring device	Life-threatening (symptomatic arrhythmia)	Death[c]
Seizure[a]	Absent	–	One brief seizure, seizure controlled by anticonvulsant or infrequent focal motor seizures not interfering with ADL	Complex seizure, poorly controlled seizure, breakthrough seizures despite intervention	Prolonged, repetitive, or difficult to control seizures such as status epilepticus and intractable epilepsy	Death[c]

[a]Definition requires the clinical criterion that is not otherwise attributable to another therapy such as nephrotoxic agent
[b]Definition does not specify guidance for interpretation of preexisting renal dysfunction due to comorbid illness or nephrotoxic agent
[c]Death is attributable to tumor lysis syndrome. *LTLS* laboratory tumor lysis syndrome, *ULN* laboratory upper limit of normal, *ADL* activities of daily living

Table 4 National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) grading classification for tumor lysis syndrome (National Cancer Institute 2009)

NCI-CTCAE: grading classification for tumor lysis syndrome	
Grade	Description
1	–
2	–
3	Present
4	Life-threatening consequences, urgent intervention indicated
5	Death

5.1 Disease-Based Risk Stratification

In order to assist clinicians to identify patients at high risk for developing TLS, evidence-based guidelines have been published and subsequently updated (Coiffier et al. 2008; Cairo et al. 2010). These contemporary guidelines were based upon the disease type, tumor burden, therapeutic intervention, anticipated response to therapy, and the patient's baseline renal function. From these parameters, patients are stratified into three risk groups. High risk are those where the incidence of TLS exceeds 5%, intermediate risk are those where the incidence is 1–5%, and low risk captures the group with an incidence less than 1%. The stratification of risk in these guidelines is predominantly based on disease biology and stage (Table 5) (Cairo et al. 2010).

However, as discussed below, this risk stratification model requires amendment in the context of novel agents and chemo-immunotherapy combinations in diseases not previously considered high risk. In particular, low-grade leukemias and lymphomas such as chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma are an area of recognized hazard. Therefore, where emerging therapies have been recurrently linked to TLS, CLL patients with lymph node diameter ≥10 cm or 5–10 cm with peripheral blood lymphocytosis $\geq 25 \times 10^9$/L are now considered high risk (Goede et al. 2014).

Table 5 Evidence-based and disease-based risk stratification for TLS. *AML* acute myeloid leukemia, *WBC* white blood cell count, *ALL* acute lymphoblastic leukemia, *LDH* lactate dehydrogenase, *ULN* upper limit of normal for the laboratory, *CLL* chronic lymphocytic leukemia (Adapted with permission from Cairo et al. 2010)

Disease-based risk stratification
High-risk disease states (TLS >5%)
Burkitt leukemia/lymphoma
AML with WBC $\geq 100 \times 10^9$/L
ALL with WBC $\geq 100 \times 10^9$/L or LDH $\geq$ two times the ULN
Lymphoblastic lymphoma with advanced stage or LDH $\geq$ two times the ULN
Adult T-cell lymphoma, diffuse large B-cell lymphoma, peripheral T-cell
Lymphoma, transformed indolent lymphoma, and blastoid variant mantle cell lymphoma with
Adult: LDH > ULN and disease bulk
Pediatric: Ann Arbor stage III/IV and LDH $\geq$ two times the ULN
Intermediate-risk disease with baseline renal dysfunction or baseline LTLS parameters indicating TLS prior to initiation of therapy
Intermediate-risk disease states (TLS incidence 1–5%)
CLL treated with targeted or biological therapies
AML with WBC 25–100×10^9/L or $<25 \times 10^9$/L with LDH $\geq$ two times the ULN
ALL with WBC $<100 \times 10^9$/L and LDH < two times the ULN
Lymphoblastic lymphoma with early stage and LDH < two times the ULN
Pediatric patients with anaplastic large-cell lymphoma
Adult T-cell lymphoma, diffuse large B-cell lymphoma, peripheral T-cell lymphoma, transformed indolent lymphoma, and blastoid variant mantle cell lymphoma
Adult: LDH >ULN and non-bulk disease
Pediatric: Ann Arbor stage III/IV and LDH < two times the ULN
Otherwise low-risk lymphoma and leukemia with renal impairment
Solid tumors: neuroblastoma, small-cell lung cancer, and germ cell tumors
Low-risk disease states (TLS incidence <1%)
Solid tumors not listed in "intermediate-risk group" above
Multiple myeloma and associated plasma cell dyscrasias
Chronic myeloid leukemia
Hodgkin lymphoma
Indolent B-cell lymphomas including marginal zone lymphoma, follicular lymphoma, mucosa-associated lymphoid tissue, non-blastoid variant mantle cell lymphoma, and cutaneous T-cell lymphoma

5.2 Therapy-Related TLS Risk

The risk of TLS is not restricted to the disease type but also contingent of the treatment that is being delivered. The 2010 risk guidelines specifically addressed this for the first time by adapting the algorithm addressing CLL (Cairo et al. 2010). Here, CLL treated only with alkylating agents is classified as low risk, whereas treatment with biological or targeted therapies is classified as intermediate risk. Howard et al. recently performed a systematic contemporary review of TLS in hematological malignancies in the era of targeted and novel therapies and such ongoing updates are periodically required in order to maintain vigilance with risk stratification guiding TLS prevention (Howard et al. 2016).

5.2.1 Radiotherapy

Radiotherapy is frequently used due to its efficacy in symptom control of malignancy. Due to its direct DNA-damaging effects, purine catabolism rapidly ensues, and this may occur on a large scale in the setting of disease bulk. There have been a number of publications describing TLS attributable to radiotherapy, in both settings of

hematological or solid organ cancer (Fleming et al. 1991; Schifter et al. 1999; Rostom et al. 2000; Yamazaki et al. 2004).

5.2.2 Chemotherapy

The highest-risk diseases for development of TLS include acute leukemia and Burkitt lymphoma (Cairo et al. 2010). These diseases share the properties of rapidly proliferative disease and often high tumor burden in the bone marrow or lymphoid compartments (in the case of acute lymphoblastic leukemia and Burkitt lymphoma). The mainstay of therapy for these diseases remains chemotherapy, incorporating the use of corticosteroids for lymphoid malignancies. Hence, clinicians have gained their greatest insight into the identification, prevention, and management of TLS through experience with cytotoxic chemotherapies and their use in these high-risk diseases.

5.2.3 Venetoclax

Venetoclax is a small molecule that directly antagonizes antiapoptotic cellular proteins to induce cell death. It has demonstrated unprecedented single-agent activity in CLL and mantle cell non-Hodgkin lymphoma. This includes patients with very poor-prognosis disease who would otherwise be managed with palliative intent. Indeed, the median progression-free survival of 18–24 months from early-phase venetoclax studies (Roberts et al. 2016) of heavily pre-treated individuals (median three prior lines of therapy) is comparable to historical age-matched cohorts treated with immunochemotherapy at first progression after just one prior line of fludarabine-containing regimen (Tam et al. 2014). Presently a number of phase II studies combining venetoclax with both conventional and novel agents further augment its capacity to induce rapid tumor lysis. Unfortunately, a failure to recognize this risk in the early stages of drug development led to TLS-related fatalities (Roberts et al. 2016). During the initial safety component of the phase I clinical trial in patients with relapsed and refractory CLL, an 18% incidence of TLS was reported, including one death (Roberts et al. 2016). This prompted an amendment requiring a dose-escalation schedule to be initiated and for frequent monitoring for LTLS. While the product information states that low-risk patients (lymph nodes <5 cm and blood lymphocyte count $<25 \times 10^9$/L) may have therapy initiated at home with 1.5–2 L oral hydration required, in practice many clinicians favor venetoclax initiation in an inpatient setting to assist timely diagnosis of TLS and acute intervention. Despite identification of this risk, two other early-phase clinical trials of venetoclax in CLL have each also reported one fatality attributable to TLS (Howard et al. 2016).

5.2.4 Cyclin-Dependent Kinase Inhibitors

Cyclin-dependent kinases (CDKs) regulate cell growth and proliferation and play a critical role in oncogenic transcription. For these reasons, a number of CDK inhibitors are in clinical development for both solid and liquid tumor indications. The risk of TLS is associated with drugs targeting transcriptional CDKs, rather than predominantly cell-cycle active drugs such as palbociclib, which was recently approved as a treatment for breast cancer. In particular, flavopiridol and dinaciclib, which rapidly reduce the cellular transcription of key antiapoptotic proteins, have been associated with high incidences of TLS when used either alone or in combination, although no associated deaths were reported (Flynn et al. 2015; Zeidner et al. 2015; Gregory et al. 2015).

5.2.5 Monoclonal Antibody Therapy

Therapeutic antibodies binding to antigens predominantly expressed on tumor cell populations also have the capacity to induce rapid cell death. The anti-CD20 antibody rituximab is widely used in B-cell malignancies and may induce TLS, particularly when used in combination with nucleoside analogues (Keating et al. 2005). Rituximab is an example of a "type 1" antibody with antineoplastic effects predominantly mediated by complement fixation and engagement of antibody-dependent cell cytotoxicity. More recently "type 2" antibodies such as obinutuzumab have been developed which demonstrate a different binding mode to target cells conveying a greater capacity

to directly induce cell death (Mossner et al. 2010). The CLL11 clinical trial assessed the efficacy of obinutuzumab plus chlorambucil versus rituximab plus chlorambucil versus chlorambucil monotherapy in patients with previously untreated CLL (Goede et al. 2014). The incidence of TLS in the obinutuzumab arm was 4% as compared to less than 1% with chlorambucil monotherapy. This again highlights that the disease-related risk of TLS is much higher for CLL in the era of potent targeted therapies.

5.2.6 Other Agents

A recent systematic review (Howard et al. 2016) also identified several cases of TLS attributable to other biological agents in the form of ibrutinib or lenalidomide for CLL (Wendtner et al. 2012), carfilzomib for multiple myeloma (Berenson et al. 2014), panobinostat for acute leukemia (Kalff et al. 2008), and the drug-antibody conjugate, brentuximab vedotin, for anaplastic large cell lymphoma (Pro et al. 2012). TLS is also being increasingly described with biological therapies in solid organ malignancies (Saylor and Reid 2007; Huang and Yang 2009). The rapidity with which new classes of novel and biological agents are being introduced to the clinic makes it increasingly difficult to predict at-risk patients. A paradox of the palliative care setting is that patients considered to be in the terminal phases of their illness "without conventional treatment options" are often the exact population exposed to such drugs as part of clinical trials.

6 Prevention

Despite the inherent dangers and potentially fulminant onset of TLS, in practice it is readily managed so long as it is anticipated, simple preventive measures are put in place, and the patient is closely monitored. Timely intervention typically ensures that patients can safely negotiate the period of TLS, following which sufficient tumor is debulked and the risk of clinical sequelae soon abates. The reader is reminded that the information discussed in this chapter is not to be used in lieu of institutional guidelines when dealing with potentially life-threatening emergencies associated with this syndrome.

6.1 Monitoring

Although spontaneous TLS is well recognized in association with specific and rare disease entities, the vast majority of TLS cases occur immediately following the initiation of or re-exposure to an active therapeutic in a high-disease-burden setting. Patients identified as having a low risk of TLS may be safely managed in the outpatient setting, particularly where ambulatory laboratory testing and clinical monitoring are available. However, our practice is to admit all patients with high-risk features or those with intermediate risk in the context of comorbidities for initial inpatient management. This is particularly relevant for those patients with low baseline organ reserve (e.g., renal impairment) or an impaired capacity to maintain oral hydration due to active malignancy or on going toxicities from prior therapies.

6.1.1 Blood Sampling

A number of laboratory measurements can be readily performed to diagnose and monitor TLS. For high-risk patients, blood sampling immediately pretreatment then every 4–6 h for 48 h is adequate to allow early detection of LTLS. In addition to monitoring serum electrolytes, renal function, and uric acid levels (Fig. 1), lactate dehydrogenase (LDH) is a useful biomarker as this represents an intracellular enzyme present in malignant and normal cells of hematopoietic origin and a number of other tissues, which is released on cell lysis. For hematopoietic malignancies in leukemic phase, assessment of the peripheral blood cell counts provides another indication of tumor cell volume and response to therapy, which may correlate with risk for TLS development. It is critical that blood sampling for serum uric acid after rasburicase treatment (discussed below) be transported on ice and processed within 4 h to avoid ex vivo urate catabolism. In this context, delayed sample processing may provide a falsely reassuring

low serum uric acid level to the treating clinician (Jones et al. 2015).

6.1.2 Clinical Review

The development of electrolyte disturbances such as hyperkalemia and hypocalcemia may be relatively asymptomatic, but their effects on cardiac conduction are readily measurable through ECG monitoring. If there is any suspicion for development of these electrolyte aberrations clinically or through laboratory evaluation, an ECG should be promptly performed and treatment initiated without delay. Evidence-based guidelines recommend continuous monitoring with cardiac telemetry if the serum potassium reaches $\geq$6.0 mmol/L (Jones et al. 2015). ECG signs of hyperkalemia include peaking of the T-waves and widening of the QRS complex through to VT or VF (Cairo and Bishop 2004).

Clinical review of the patient may also allow for detection of symptomatic hypocalcemia, as painful muscle cramping or tetany will be reported by the patient and readily assessed by clinical examination. Furthermore, clinical review will identify the rarer clinical manifestations of hypocalcemia such as bronchospasm/wheeze through auscultation, pulse oximetry, and changes of the respiratory rate.

While acute renal dysfunction may manifest clinically as uremia, associated symptoms, e.g., pruritus, are usually only evident with the development of chronic renal impairment. Careful clinical monitoring of volume status is required, particularly in patients receiving hyper-hydration as a means to mitigate renal damage. The concurrent management problem of acute electrolyte disturbances and aggressive hydration requirements is particularly difficult in patients with comorbidities that exacerbate volume overload, such as left ventricular failure or liver disease. Given the inherent reversibility of TLS as a complication, consideration of aggressive supportive measures remains appropriate in patients being treated with palliative intent. Specific considerations include the placement of a central venous catheter (for fluid and electrolyte replacement), indwelling urinary catheter insertion (to accurately quantify urine output), and transfer to a high-dependency or critical care environment.

6.2 Fluid Management

To prevent acute renal dysfunction due to TLS, the patient should be adequately hydrated to promote excretion of uric acid, potassium, and phosphate. Concurrent nephrotoxic agents such as nonsteroidal anti-inflammatory drugs ought to be withheld where possible. Intravenous hyperhydration (3 L/m^2 of body surface area per day inclusive of oral intake in adults) without potassium supplementation must be initiated prior to therapy (Cairo and Bishop 2004; Hochberg and Cairo 2008; Jones et al. 2015). Hartmann's solution is not favored due to its potassium content. The target urinary output is $\geq$100 mL/m^2/h (or $\geq$3 mL/kg/h for pediatric patients weighing less than 10 kg) (Coiffier et al. 2008). To maintain urinary output and further assist excretion of potassium and phosphate, diuresis is often assisted by a loop diuretic such as frusemide, with avoidance of potassium-sparing diuretics such as spironolactone. If required, diuresis may be further augmented by the administration of 0.5 mg/kg mannitol. Urinary alkalinization has previously been considered important as it promotes the solubilization and excretion of uric acid. However, alkaline conditions render hypoxanthine and xanthine less soluble and may precipitate xanthine crystals in the urinary tract to cause acute renal impairment. As such, urinary alkalinization is no longer recommended for the prevention or treatment of TLS (Jones et al. 2015).

6.3 Hypouricemic Agents

6.3.1 Allopurinol

Hypouricemic agents provide the mainstay of medical prevention of TLS. Allopurinol inhibits xanthine oxidase and leads to a reduced production of uric acid (Fig. 2). Its use is recommended for all patients at high or intermediate risk of TLS. As allopurinol prevents production but does not assist excretion of uric acid, it should be initiated

up to 7 days prior to initiation of therapy in order to reduce baseline serum uric acid effectively and should be continued for at least 7 days post-therapy. The recommended adult dose is 200–400 mg/m^2/day in one to three divided oral doses, though often a flat dose of 300 mg daily (or 100 mg daily in moderate-severe renal impairment) is used. Intravenous allopurinol may be used at the same doses in situations where oral intake or retention of medications is not feasible (Smalley et al. 2000). In situations where hyperuricemia develops despite the 300 mg daily dose, the dose should be further increased and rasburicase considered (Jones et al. 2015). The recommended dose of allopurinol for children is 300–450 mg/m^2/day with a daily total up to 400 mg in three divided doses or 3.3 mg/kg three times daily for infants weighing less than 10 kg (Jones et al. 2015).

Hypersensitivity reactions are rare but may be severe, including Stevens-Johnson syndrome. As allopurinol also interferes with the metabolism of purine analogues, 6-mercaptopurine and azathioprine should be withheld or significantly dose reduced when commencing allopurinol. In the event of contraindication, hypersensitivity, or intolerance of allopurinol, the non-purine selective inhibitor of xanthine oxidase, febuxostat, may be considered as an alternative; however, clinical experience in TLS is limited.

6.3.2 Rasburicase

In the case of high-risk situations for development of TLS, the pharmacological urate oxidase, rasburicase, should be administered instead of allopurinol. Such situations include Burkitt lymphoma and acute leukemia according to tumor bulk and (WBC) blood cell count, patients with renal impairment and intermediate-risk diseases as shown in Table 5, and high-risk patients with CLL (lymph node $\geq$10 cm or 5–10 cm with lymphocytosis $\geq 25 \times 10^9$/L) starting treatments such as venetoclax (Cairo et al. 2010; Howard et al. 2016). Rasburicase is administered by the intravenous route, and the recommended dose is 0.2 mg/kg/day as a 30 min infusion for adults or children, though in practice many hematologists use the flat dose of 3 mg for adult patients and this is considered acceptable according to published guidelines (Jones et al. 2015). Repeated dosing for a total of 3–7 days should be considered pending the serum uric acid measurements following administration of therapy.

Rasburicase converts poorly soluble uric acid to the more soluble allantoin, which is readily renally excreted (Fig. 2). As rasburicase promotes removal of uric acid, it should be used instead of allopurinol when the patient already has baseline elevation in serum uric acid pretreatment ($\geq$0.45 mmol/L) or when manifestations of TLS are apparent despite allopurinol use (Jones et al. 2015). The use of rasburicase is contraindicated for patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency due to the risk of acute hemolytic anemia and methemoglobinemia. As such, preemptive testing for G6PD deficiency is recommended and is usually readily performed in the diagnostic pathology laboratory.

The relative efficacy of allopurinol versus rasburicase for at-risk adult patients with hematological malignancies has been assessed in a phase III clinical trial comparing allopurinol versus allopurinol plus rasburicase versus rasburicase alone (Cortes et al. 2010). This trial found a statistically significant improvement in rates of normalization of serum uric acid in the group treated with rasburicase, and a trend toward improvement in the combination arm, when each were compared to allopurinol monotherapy. The time to normalization of serum uric acid was also significantly shorter for the rasburicase-containing arms, with a median time of 4 h compared with 27 h for those treated with allopurinol monotherapy. These changes led to a significant reduction in incidence of LTLS with rasburicase (21%) and a trend toward significant reduction for the combination arm (27%) when compared with allopurinol alone (41%). However, there was no benefit in terms of reduction in incidence of CTLS with the addition or rasburicase (3% for each of the rasburicase arms and 4% for allopurinol monotherapy). It must be noted that this study was not restricted to high-risk populations, and therefore caution must be used in extrapolating conclusions to specific risk groups.

6.3.3 Pre-phase Treatment

In some situations, debulking of tumor with other therapies such as "pre-phase corticosteroids" for

lymphoid malignancies should be considered to prevent or minimize TLS severity. Such an approach has typically been utilized for elderly, frail patients with aggressive lymphoma as a means to reduce their overall disease burden and improve their performance status in order to allow delivery of definitive therapy (Pfreundschuh 2004; Chaganti et al. 2016). Specific guidance regarding emerging TLS inducing therapies (e.g., venetoclax and obinutuzumab) borne out of early clinical trial experience is likely to be agent specific.

7 Treatment

7.1 Hyperkalemia Management

The most dangerous acute complication of TLS is development of hyperkalemia. Hyperkalemia represents a medical emergency due to risk of potentially fatal cardiac arrhythmias, and prompt diagnosis and intervention are required. Many centers have institutional guidelines for the management of hyperkalemia, and these should be initiated without delay. The principles of hyperkalemia management are briefly discussed here, but the reader is advised to familiarize themselves with their own institutional guidelines for patient management.

Criteria as to what level of hyperkalemia grades as mild, moderate, or severe vary in their definition. One example used lists mild hyperkalemia as $<$6.0 mmol/L, moderate as 6.0–6.4 mmol/L, and severe as $\geq$6.5 mmol/L. Evidence-based guidelines provided by the British Committee for Standards in Haematology (BCSH) recommend that hyperkalemia $\geq$6.0 mmol/L or $\geq$25% increase from baseline should prompt continuous cardiac monitoring (Jones et al. 2015). At levels $\geq$7.0 mmol/L dialysis is indicated and indeed may also be at lower levels according to clinical assessment and local guidelines.

Hemodialysis represents the most rapid and effective method for correction of electrolyte abnormalities associated with severe TLS. As a temporizing measure, interventions to redistribute intravascular hyperkalemia to the intracellular space may be beneficial, including inhaled or intravenous salbutamol and the use of intravenous insulin and dextrose. Enteric calcium resonium (polystyrene sulfonate) is also commonly used for management of non-TLS hyperkalemia, though as the time to onset is prolonged it is of little to no benefit for acute TLS. Furthermore, in the setting of abundant intravascular phosphate, enteric or parenteral calcium should be kept to an absolute minimum in order to minimize calcium phosphate formation. Similarly, many centers include early use of intravenous calcium gluconate for prevention of cardiac arrhythmias in the setting of hyperkalemia. The benefit of this intervention must again be weighed against the risk of calcium phosphate development in the setting of TLS.

7.2 Hypocalcemia Management

Due to the risk of calcium phosphate formation described above, asymptomatic hypocalcemia should not prompt replacement. Should corrected serum calcium levels reach $\leq$1.75 mmol/L or fall 25% or more from baseline levels, the BCSH again recommend cardiac monitoring be initiated (Jones et al. 2015). Symptomatic hypocalcemia should be corrected with intravenous calcium gluconate as per institutional dosing instructions, though only for the purposes of abrogating symptoms and not with the intent of correcting the serum calcium to within the normal biochemical range.

7.3 Hyperphosphatemia Management

Asymptomatic hyperphosphatemia is not an indication for treatment. Previous guidelines have included use of phosphate binders, but the oral forms of these are delayed in their onset of action, and due to issues of poor tolerability, they are not recommended according to current guidelines (Jones et al. 2015). The most effective treatment for correction of symptomatic hyperphosphatemia is through hemodialysis.

7.4 Renal Replacement Therapy

Renal replacement therapy represents the single most definitive and rapid treatment through which to correct the biochemical aberrations caused by TLS. If any clinical concern exists or the trend is toward dangerous parameters with TLS, urgent arrangements for renal replacement therapy should be made. Indications for hemodialysis in TLS are non-responsive fluid overload, hyperuricemia, hyperkalemia, hypocalcemia, or hyperphosphatemia (Jones et al. 2015).

Hemodialysis is the form of renal replacement therapy recommended for TLS as it can be rapidly facilitated and provides the fastest correction of electrolyte abnormalities. Furthermore, hemodialysis allows for rapid removal of fluid for those patients already developing oliguric/anuric renal failure with signs of fluid overload. In terms of the optimal modality of renal replacement therapy, there are no reported trials that have assessed the efficacy of intermittent hemodialysis versus continuous hemofiltration. The decision of the intensivist and renal physician regarding preferred dialysis modality is typically contingent upon the hemodynamic stability of the patient and the need for continuous cardiac monitoring. Dialysis should be continued until correction of renal function, urine output, and severe electrolyte abnormalities occurs (Jones et al. 2015). Peritoneal dialysis is not indicated as the time to correction of electrolyte abnormalities is protracted. Furthermore, fluid is less readily removed in the setting of overload when compared with hemodialysis. Finally, a significant proportion of high-risk patients (ALL and Burkitt/high-grade lymphoma) may have intra-abdominal malignancy or hepatosplenomegaly, limiting the safety and utility of peritoneal dialysis.

While hemodialysis is clearly the gold standard treatment of emergencies associated with TLS, it is invasive and costly and requires extensive resources to implement. In the palliative setting, early or preemptive discussion with the patient is important in order to determine whether they wish hemodialysis to be performed if indicated. Open communication is key in this situation, as some staff may empirically consider the palliative patient to be inappropriate for renal replacement therapy. However, case-by-case discussion is warranted as hemodialysis for TLS is often limited in duration and indicative of responsive disease, which may improve the patient's overall symptomatology and prognosis.

7.5 Implications for Further Therapy

The onset of TLS indicates a potential for subsequent TLS episodes with retreatment, where tumor bulk in any compartment (i.e., solid organ, bone marrow, or blood) persists or recurs in the treatment-free interval. This phenomenon was highlighted by a recent study of the CDK inhibitor, dinaciclib, in relapsed and refractory acute leukemia (37). Here, dinaciclib was dosed every 3 weeks, including administration to patients with highly proliferative disease. Initial objective responses, as evidenced by a reduction in WBC count and LTLS, were unfortunately only transient, and LTLS recurred with subsequent doses in tandem with rebound of the underlying leukemia (Gojo et al. 2013). However, the onset of TLS is not an absolute contraindication to continuing or re-challenge with the precipitating agent, as the initial tumor debulking heralded by TLS is often protective against future episodes.

8 Conclusions

Tumor lysis syndrome represents a medical emergency that ought to be readily prevented and managed. With the advent of more potent biological and targeted cancer therapies, TLS is now observed more frequently and in diseases which were previously considered low or intermediate risk. These agents are often administered to frail, older, or otherwise comorbid patients in diverse healthcare settings, including patients being managed with palliative intent. While prevention and

management usually allow resolution of TLS, it is appreciated that some patients will have documented directives precluding some of the interventions listed within this chapter. It is important to distinguish, for example, short-term hemodialysis support for TLS from long-term dialysis in irreversible chronic renal failure. This highlights the need for open and transparent communication between clinicians and patients as to the potential for development of TLS with initiation of a new therapy and the potential complications thereof. As TLS is readily managed, its development in the palliative setting should not necessarily be seen as a terminal event and indeed may herald significant tumor debulking and potential improvement in symptomatology.

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Suicide and Attempted Suicide

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_84

Abstract

To provide a broader perspective on suicide, this chapter has drawn on knowledge from the areas of suicide risk assessment in general psychiatry and consultation liaison psychiatry. Epidemiology of suicide and contextual factors are mentioned briefly to set the scene. A framework to assess and manage the suicidal patient is described in some detail, to assist the palliative care clinician. This is followed by a description of the key issues involved in the care of a psychiatric patient within the palliative care context. The latter part of the chapter elaborates on the experiences of those bereaved after a suicide. The impact of suicide on clinicians is explored, as well as strategies to manage the distress that can ensue. The chapter ends with a discussion of the unspoken issue of physician suicide. Terms such as mental illness, psychiatric illness, and psychiatric disorder will be used interchangeably. Specific aspects of management of underlying psychiatric disorders are detailed in the Chap. 85, "Distinguishing and Managing Severe Psychological and Psychiatric Distress" (authored by Ms. Jane Fletcher and Dr. Di Clifton). Acute non-suicidal self-harm (previously termed para-suicide), chronic suicidal ideation, chronic self-harm, and suicide in special populations, e.g., adolescents, have been excluded from the chapter. Requests for a hastened death, physician-assisted suicide, and euthanasia have been detailed in the chapter 90, "Request for Assisted Suicide" (authored by Dr. Diamond, Dr. Khurana, and Prof Quill).

1 Introduction

The following points are of relevance to the palliative care clinician:

- Acute suicidal ideation is an emergency.
- The rates of suicide are higher in the medically unwell and in those with cancer.
- The palliative care physician has knowledge of the biological contributors to suicidal ideation (e.g., intractable pain) and biological mitigating factors (e.g., medical management of pain).
- The palliative care team may need to take the lead in the assessment and management when a patient refuses to engage with the mental health service or if an immediate referral to the mental health clinician is not feasible.
- Desire for hastened death statements may reflect underlying suicidal thoughts.
- A positive therapeutic relationship is associated with lower rates of suicidal ideation and may reduce future episodes.
- Knowledge of risk factors is key, and the palliative care clinician is an integral part of the global challenge to reduce suicide.

2 Definitions

- Suicidal ideation is defined as thinking about, considering, or planning suicide.
- A suicide attempt is defined as a nonfatal, self-directed, potentially injurious behavior with an intent to die as a result of the behavior.
- Suicide is defined as a death caused by self-directed injurious behavior with an intent to

die as a result of the behavior (Centers for Disease Control and Prevention 2016). Suicidal thoughts range from mild and transient to severe and persistent. The suicidal behavior may be impulsive, ambivalent, planned, or recurrent.

3 Background

Neither attempted suicide nor suicide is a diagnosis, and there is no known precise cause. They are both complex behaviors resulting from the interaction between an individual and the environment. Suicide is reported in three main populations: the general population, those with a mental illness, and the medically unwell (including those with cancer). There are some common risk factors and some that are specific to the palliative care population. Given the relative paucity of research in this area, this chapter draws on knowledge from the areas of suicide risk assessment in the general psychiatric practice, consultation liaison psychiatry, and palliative care setting. Suicidal ideation and behaviors are assessed on a spectrum from mild and transient to severe and persistent. Suicidal behavior is multi-determined, and mental illness, including depression and demoralization in the palliative care population, is risk factor for suicide. The chapter aims to provide a framework for clinicians who wish to perform a suicide risk assessment. It is anticipated that palliative care clinicians will refine their risk assessment skills and embed them into routine practice.

4 Epidemiology and Contextual Issues

Suicidal thoughts and behaviors are common in the general population. From a survey in 2013, 4% of the American population reported having suicidal thoughts in the preceding year, 1.1% had made plans to attempt suicide, and 0.6% had attempted suicide (Results from the 2013 2014a). It is difficult to determine true prevalence rates for attempted suicide because the available data relies on self-reporting, not all suicide attempts require medical intervention, and reporting practices vary. Suicide is also underreported but remains a leading cause of death worldwide (World Health Organisation 2012). Unless the person had expressed suicidal intent or left a suicide note, the coroner may not make a finding of suicide, and it is likely that many open and indeterminate findings represent deaths by suicide. Given the reporting constraints, true suicide figures are likely to be higher than the observed figures. In 2012, suicide accounted for an annual global suicide rate of 11.4 deaths per 100,000 population (males were twice as likely to suicide than females). More than 800,000 lives were lost through suicide that year, i.e., one suicide death every 40 seconds.

The rates of suicide vary greatly from one country to another, e.g., suicide rates in the USA were less than half the rates observed in Southeast Asia (World Health Organisation 2012). Inconsistency in suicide data collection methodology makes it difficult to draw any firm conclusions about the reasons for considerable regional variation. However, it is hypothesized that there exists a base rate of suicide worldwide (attributed to medical and psychiatric disorders) and the variation is attributed to local sociocultural, economic, and political factors (Goldney 2015). This finding has substantial implications for suicide prevention, in that sociocultural interventions may be necessary to reduce and prevent suicide.

A process described as a psychological autopsy has examined the association between suicide and mental illness. The process involves making retrospective assessments through speaking to informants, and gathering medical records of people who have completed suicide, to identify indicators of mental illness. There are studies reporting that 90% of those who completed suicide had a psychiatric disorder or substance use disorder (Cavanagh et al. 2003).

The rates of psychiatric disorders in the cancer population are reported to be higher than the general population. Half the proportion of patients with an advanced cancer meet the

threshold for a psychiatric diagnosis, and 40% of patients in oncological, hematological, and palliative care settings had some form of a mood disorder (Mitchell et al. 2011). The most common diagnoses include adjustment disorder and major depression (Miovic and Block 2007). Serious mental illness is seen in 10–20% of cancer patients, with only half accessing mental health services (Kadan-Lottick et al. 2005). Palliative care frontline clinicians are well placed to identify psychiatric comorbidity and ensure access to care. It is generally accepted that suicide is twice as common in the cancer population (Misono et al. 2008).

People with a serious mental illness, such as schizophrenia, bipolar disorder, and personality disorder are almost twice as likely to die prematurely (between 10 and 20 years earlier than those without a mental illness) as a result of medical conditions including diabetes and heart disease (Kisely et al. 2005). Interestingly, persons with a serious mental illness have a lower incidence of cancer than the general population (male cancer incidence rate ratio = 0.86 and female cancer incidence rate ratio = 0.92) (Kisely et al. 2013). Patients with schizophrenia have lower rates of prostate and colorectal cancer (Tabarés-Seisdedos et al. 2011), in which genetic and immune mechanisms are implicated. Furthermore, despite high rates of tobacco smoking, patients with schizophrenia have a lower lung cancer incidence. However, the overall cancer-related mortality is higher in persons with a mental illness, for the following reasons: they are less likely to participate in screening measures, e.g., women with a serious mental illness are half as likely to have screening mammography than the general population (Mitchell et al. 2014); they are more likely to present late with metastases; and they are less likely to have specialist interventions like chemotherapy, radiotherapy, and surgical treatment (Kisely et al. 2015).

In summary, patients with a serious mental illness have higher rates of premature death, lower cancer incidence but higher cancer-related mortality, and increased rates of suicide.

5 Ethics and Related Issues

Suicide is confronting for the physician. Firstly, in the pursuit of relief from suffering, there needs to be a shared view on the path to wellness. It is this shared view that forms the basis of the therapeutic relationship; however suicide is a departure from this shared view. Secondly, the value of life as an end in itself is a fundamental value held by clinicians, but it is a value that is difficult to articulate. The clinician knows that life has value, but the suicide of a patient confronts this deeply held view. Despite our best efforts in healthcare, we have been unable to eliminate suicide, which in turn challenges our belief system around the value of life. Subsequently, we become aware that the drive to preserve life may succumb to a drive to end life. The clinician has to revisit personal attitudes and beliefs about suicide that inevitably evoke strong personal feelings that may impact on the care of the suicidal patient. When clinicians care for a suicidal patient, they are uncomfortably reminded of the fact that they too are at risk of suicide, and suicide rates are higher among physicians than the general population.

Clinicians may avoid asking about suicide, and their own fears can hinder their engagement with the suicidal patient. The language used to elicit suicidal ideation is vital. The question "You haven't had suicidal thoughts, have you?" is very different from "Have you ever felt that life had no meaning, or that you couldn't go on with life?" The former puts pressure on the patient to respond in the negative, and the latter is more likely to set the scene for a dialogue. Our patients ask us to prognosticate and expect us to respond to a question like "Doctor, how long do I have?" Managing this type of question requires experience and skill because the answer to this question will impact on the patient. The physician has to walk the fine line of responding to the patient's query with integrity while communicating a broader sense of hope, even when the prognosis is poor or uncertain. The refusal of lifesaving medical treatment raises questions of capacity to refuse such treatments, and this is particularly so in those with a known or suspected psychiatric disorder, especially depression.

A discourse on the relationship between various religions and suicide is beyond the scope of this chapter; however, religion has long been viewed as a protective factor against suicide. O'Reilly and Rosato (2015) examined the relationship between religion and suicide in one million residents of Northern Ireland, where 40% were Roman Catholic, 40% were Protestant, 7% were Conservative Christians, and only 13% did not identify with any religion. If church attendance is protective, then the rates of suicide should be lowest in Catholics and greatest in those with no religious affiliation; and if religiosity is important, then suicide rates should be lowest in conservatives and highest in those without religious affiliation. Younger Roman Catholics had higher suicide rates, but as a whole Roman Catholics, Protestants, and those who had no religious affiliation had similar suicide rates. Conservative Christians had a lower suicide rate, possibly attributable to lower alcohol consumption rather than church attendance or religiosity (O'Reilly and Rosato 2015). These findings challenge common societal perceptions; however, church attendance is a poor measure of religiosity. It remains unclear whether religiosity (religious salience) is associated with lower suicide rates.

In summary, in assessing the suicidal patient, the clinician needs to not only know what to ask but also how to ask exploratory questions. The clinician's preconceptions, values, and fears will impinge on the therapeutic relationship.

6 Risk Factors

There are some common risk factors observed in the general, psychiatric, nonmalignant palliative care, and cancer populations, e.g., male gender, single status, depression, hopelessness, etc. However, there are also some specific risk factors observed in the cancer population. The risk factors vary in their strength of association and temporal correlation with the suicide attempt.

6.1 Family History of Mental Illness and Family History of a Suicide Death

From family, twin, and adoption studies, it has been established that psychiatric illnesses and suicides cluster within families. It is plausible that suicides cluster within families because psychiatric illnesses cluster within families; however, there is evidence to suggest that the genetics of suicide may be independent of the genetics of psychiatric illness. Qin et al. (2002) examined suicide risk in relation to family history of completed suicide and psychiatric disorders (Qin et al. 2002). For a patient without a family history of suicide but with a family history of a psychiatric admission, the adjusted odds ratio (OR) for suicide was 1.31; and for a patient with a family history of a suicide but without a family history of a psychiatric admission, the adjusted odds ratio (OR) for suicide was 2.58. When the patient had both a family history of a psychiatric admission and a family history of suicide, the adjusted OR for suicide was 2.68. Genetic factors account for almost 50% of the variance in the familial transmission of suicide risk (Statham et al. 1998).

In summary, suicidal behavior runs in families, and half the vulnerability is attributed to genetics. A positive family history of suicide and a family history of psychiatric disorder "significantly and independently" increase suicide risk.

6.2 Past History of a Self-Harm or Suicide Attempt

After an episode of self-harm, the risk of suicide increases incrementally over the subsequent 15 years, especially in men and with increasing age at the time of self-harm (Hawton et al. 2003). Similarly, a past suicide attempt is a strong risk factor for future suicide, and the risk remains high for several decades (Suominen et al. 2004). Only 50% of suicide attempters receive intervention, which is typically only for a few weeks (Hunt et al. 2009).

In summary, it is clinically relevant to ask about past history of an attempted suicide and brief after-care does not address the high long-term suicide risk.

6.3 Substance Use and Comorbidity with Psychiatric Disorder as Risk Factors

In the general population, adults with a substance abuse or dependence diagnosis in the past year were more likely to have serious suicidal thoughts, to make suicidal plans, and to attempt suicide (Results from the 2013 2014b). There was substantial comorbidity between substance abuse disorders and mental disorders, and having one disorder more than doubled the risk of having the other. The OR for a suicide attempt seemed to follow a gradient (lowest in nonusers, followed by those with substance use history, followed by those with a substance abuse disorder, and highest in those with a substance dependence disorder). This gradient was particularly evident in alcohol users. The OR for alcohol nonusers was 1.0, for alcohol use (without abuse/dependence) was approximately 2.0, alcohol abuse (without dependence) was approximately 3.0, and for those with alcohol dependence was approximately 6.0, even after controlling for comorbid mental illness (Borges et al. 2000). The association between substance use and suicide revealed much higher odds ratios when mental illness was not controlled, suggesting that mental illness plus substance abuse may have cumulative effects on suicidal behavior. Substance use disorders are more prevalent in cancer, e.g., alcohol abuse and dependence are more prevalent in head and neck tumors (further details are in ▶ Chap. 85, "Distinguishing and Managing Severe Psychological and Psychiatric Distress").

6.4 Psychiatric Disorder

As stated in the chapter entitled ▶ Chap. 85, "Distinguishing and Managing Severe Psychological and Psychiatric Distress" the rates of psychological distress and psychiatric disorder are significantly elevated in the cancer population. The comorbidity confers greater vulnerability to suicide. Bipolar disorder, schizophrenia, substance use disorder, and borderline personality disorder have substantially higher rates of suicide (five- to tenfold) compared to the general population (Chesney et al. 2014). Depressive disorders confer the greatest suicide risk (20-fold risk) (Harris and Barraclough 1997). Therefore, an accurate psychiatric diagnosis and prompt treatment are central to suicide prevention.

In summary, substance use disorder and mental disorders are two independent risk factors for suicide. The risk of suicide is greatest with a substance dependence disorder and comorbid psychiatric disorder. This is of particular relevance because substance use disorders and psychiatric disorder are more prevalent in the cancer population.

6.5 Developmental Adversity

The experience of emotional neglect and abuse (physical, emotional, and sexual) is a risk factor for mental illness generally and suicide in particular, but not everyone with this history will develop a mental illness or attempt suicide. It is hypothesized that early adversity may induce long-term epigenetic changes in gene expression, resulting in an upregulation of the hypothalamo-pituitary-adrenal axis and an increased stress response. Adversity may also impact on the genes involved in the downregulation of brain-derived neurotrophic factor (BDNF), which is central to neurogenesis and neuronal plasticity. Neglect and abuse also impact on the psychological development of the individual and are associated with low self-esteem, a risk factor for suicide. There are observable problem-solving deficits in those with a remote history of abuse in the context of adverse life events, and they are more likely to experience hopelessness, thus increasing suicide risk.

6.6 History of Medical Illness

Certain medical illnesses are more likely to be associated with mental illnesses and therefore suicide. There are studies suggesting an independent

link between medical illness and suicide (even after controlling for mental illness) (Goodwin et al. 2003; Druss and Pincus 2000). Neurosurgical disorders increase suicide rates by 20-fold, renal disease confers a 14-fold increase, epilepsy confers a 5-fold increase, and malignant disease doubles the risk of suicide (Harris and Barraclough 1997; McGirr et al. 2008).

6.7 Cancer-Specific Suicide Risk Variables

The shared risk factors observed in the general population and in patients with a mental illness may also be observed in the cancer patient, such as male gender, age greater than 65, and social isolation. However, there are some cancer-specific risk factors. Depression is more common in the cancer population, and there are neurobiological causes to support this finding. Cancer activates a persistent humoral immune response leading to an upregulation of inflammatory cytokines such as IL-6 (Spoletini et al. 2011). Immune dysregulation and cytokines are associated with onset and progression of cancer and depression. Patients are more likely to attempt suicide within 1 year of a cancer diagnosis. Advanced stage at diagnosis, locally advanced cancer, and metastatic disease are also at risk. While the total number of deaths from suicide in cancer patients is relatively small in comparison to cancer-related deaths, suicide rates are higher in the cancer population in comparison to the general population (by a factor of 1.5–2.0) (Vyssoki et al. 2015). Certain cancer sites are particularly associated with suicide such as lung, biliary-pancreatic, head and neck, and CNS tumors. The risk of suicide was greater in those who underwent high-morbidity surgery. While surgery may offer renewed hope, there are postoperative outcomes that can increase suicidal behavior, e.g., physical disability, loss of bodily function, loss of autonomy, existential distress, poor pain control, and the use of disinhibiting drugs (e.g., opiates). Other risk factors include a past history of self-harm or suicide attempt and poor social support especially in advanced cancer (Chochinov et al. 1998). Patients with advanced disease are more likely to have a high symptom burden, functional impairment, pain, and depression. The perception of poor pain control, and associated hopelessness, was a more significant risk factor for attempted suicide than the intensity of pain (Passik et al. 2007).

In summary, certain types of cancer, a new diagnosis, and advanced cancers pose a greater risk of suicide. Suicide deaths in the cancer population constitute a small proportion of all-cause deaths; however, the rates of suicide are twice as high.

Palliative care patients not uncommonly express a desire for hastened death. Such statements may reflect an underlying request for physician-assisted suicide, euthanasia, and a communication of suicidal thoughts. Depression and hopelessness are two independent factors that contribute to a desire for hastened death. Depressed patients were four times more likely to have a high desire for hastened death than the non-depressed palliative care inpatients. Hopelessness is more strongly associated with suicidal behavior (and desire for hastened death) than depression in the terminally ill. Hopelessness is a pessimistic cognitive style rather than the patient's knowledge of a hopeless prognosis. It is the patient's appraisal of their situation that leads them to feel hopeless, and it may have little to do with the reality of their prognosis. Patients who had neither depression nor hopelessness were unlikely to desire a hastened death. Lack of social support and physical functioning also contributed to a desire for hastened death (Breitbart et al. 2000). These findings fundamentally change how we as a society should conceptualize the desire for a hastened death in a palliative care context, in that such a desire should not be dismissed as an understandable response to a cancer diagnosis.

In summary, the expressed desire for hastened death may represent underlying depression, hopelessness, and suicidal ideas.

6.8 Mediating Mental States that Increase the Desire to Die

Palliative care patients not uncommonly express a desire for hastened death. Such statements may reflect an underlying request for physician-assisted suicide, euthanasia, and a communication

of suicidal thoughts. Depression and hopelessness are two independent factors that contribute to a desire for hastened death (Breitbart et al. 2000). Depressed patients were four times more likely to have a high desire for hastened death than the nondepressed palliative care inpatients. Hopelessness is more strongly associated with suicidal behavior (and desire for hastened death) than depression in the terminally ill. Hopelessness is a pessimistic cognitive style rather than the patient's knowledge of a hopeless prognosis. It is the patient's appraisal of their situation that leads them to feel hopeless, and it may have little to do with the reality of their prognosis. Patients who had neither depression nor hopelessness were unlikely to desire a hastened death. Lack of social support and physical functioning also contributed to a desire for hastened death (Breitbart et al. 2000). These findings fundamentally change how we as a society should conceptualize the desire for a hastened death in a palliative care context, in that such a desire should not be dismissed as an understandable response to a cancer diagnosis.

The key mental states that directly mediate an increase in suicidal thoughts are 1) a sense of the pointlessness or meaninglessness of life, 2) hopelessness or helplessness, 3) worthlessness, 4) loss of control, and 5) shame (Kissane 2014; Robinson et al. 2017). The intensity of these mental states is moderated by inadequate physical and mental symptom control, poor social support, increasing loss of pleasure (anhedonia) and growing frailty. On the other hand, religious beliefs, close relationships and improved quality of life prove protective. Demoralization is a clinical syndrome that captures much of the phenomenology present in these mediators of the desire to hasten death. Demoralization is a mental state of lowered morale and poor coping, which is characterized by feelings of hopelessness, helplessness, loss of meaning and purpose in life, and feeling trapped or stuck in a predicament. Demoralisation then interferes with a person's appreciation of the value of life and may adversely impact on medical treatment decision-making processes and treatment choices. This is a common clinical syndrome, with a prevalence of 13–18 percent of patients in palliative care and predictors include single status, female gender, physical symptom burden, reduced social support and the presence of severe psychiatric disorders (Robinson et al. 2015). Studies in cancer have shown that loss of meaning and demoralization contribute a 3-fold greater risk of developing suicidal thoughts than depressive symptoms (Fang et al. 2014; Robinson et al. 2017; Vehling et al. 2017). In summary, suicidal ideation may represent underlying hopelessness, demoralization and depression.

7 Management of the Suicidal Patient

7.1 Understanding the Suicidal Cancer Patient

Religious, sociological, and philosophical conceptualizations predate medical perspectives on suicide. It was only in the nineteenth century that the physician Esquirol viewed suicide as a medical problem (Berrios 1996). Psychiatry and psychoanalysts have since dominated the medical arena in the conceptualization of suicide. Freud (1856–1939) conceptualized mental life in terms of sexual and aggressive drives, at a time in history when the expression of aggression and sexuality was taboo. Freud understood suicide to be a consequence of aggressive drives turned inward (homicidal impulses are converted into suicidal impulses). Over the last decade, neurobiological research has led to a better understanding of the genetics of suicidal behaviors and biomarkers that indicate a predisposition to suicidal behavior. Juxtaposed with this emerging evidence, there are fundamental gaps in our understanding of suicide. For instance, suicidal behaviors are also observed in the absence of psychiatric disorders, and suicide is not a common outcome in those who have psychiatric disorders and cancer.

Contemporary models for suicide are based on a "stress-diathesis model" and are essentially biopsychosocial in approach (Turecki 2016) (Fig. 1). The model suggests that suicidal behavior is a consequence of the interaction between various risk factors (Turecki and Brent 2016). As we endeavor to move toward understanding

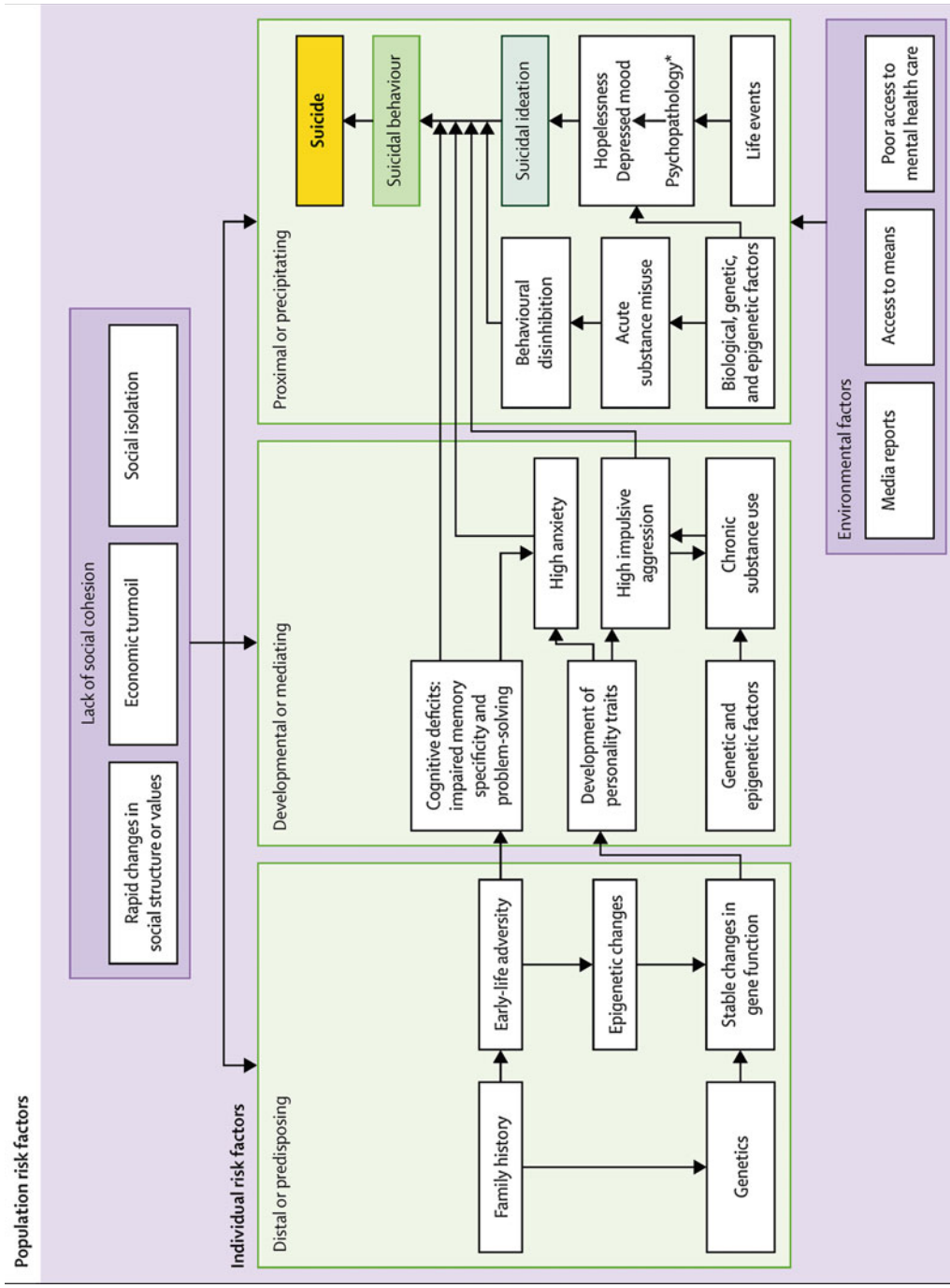

Fig. 1 Model for suicide risk. (Reprinted with permission from Turecki G, Suicide and suicidal behaviour. The Lancet 2016; 387:page 1229, Elsevier 2016)

the plight of our suicidal patient, we undertake a process of integrating information about interconnected factors; the process is described as a formulation (refer to Table 1). The formulation aims to answer a fundamental question: "Why does this patient suffer these problems, in this way, at this point of time?" (Selzer and Ellen 2014).

7.2 Approach to the Assessment of the Suicidal Patient

Most palliative care patients are assessed by a range of clinicians (medical, nursing, and allied health) at the point of entry to the service. The multidisciplinary approach can provide different perspectives and a deeper understanding of the whole patient through integrating the available information. Nurses are often the frontline staff responding to the concerns of family members, provide hands-on care, and respond to the emotional needs of the patient. Patients may open up when being nursed at vulnerable times or during intimate care. Junior medical staff should take a meticulous medical history enquiring about pre-existing medical illness, onset, duration, progression and associated treatments, and relevant negatives in the history and examination to provide the necessary details required in the biological column in the Table 1. A respectful and curious clinician can elicit the psychological factors. The social circumstances and how they have changed over time are often known to the team social worker. Social workers routinely ask about the family context and adjustment to illness, as well as provide counseling. Pastoral care service may explore the personal meaning attached to life and enquire about the spiritual and existential aspects of the patient's experience.

The multidisciplinary team should integrate the data obtained by various clinicians, from different sources, to provide a succinct formulation of the presenting problem for the patient and their family. Suicidal ideation is no different, and all members of the team should be vigilant for signs that suggest the patient may be suicidal. Breitbart provides sample questions that can be used to assess suicidal risk (refer to Table 2). Clear communication between team members, including clear documentation, well-defined roles, and mutual respect for one another, are prerequisites for a well-functioning multidisciplinary team and, as a consequence, effectively manage the suicidal patient.

The suicidal patient may be identified as at risk at the point of entry to the service or early in the admission. Early identification allows the clinicians time to prepare an approach to the patient. At other times, the patient may not be identified as at risk, and the patient may voice suicidal thoughts after a significant incident, e.g., after disclosure of a poor prognosis. Staff will intuitively check on the emotional state of the patient who has received bad news. Clinicians will need to be attentive to any verbal or nonverbal communication from the patient and be willing to explore further. For instance, the patient may say, "What's the point, I can't do it anymore!" which would need to be explored by the clinician to elicit suicidal ideation. The patient's refusal to shower or refusal to eat a meal may present the nurse with an opportunity to engage the patient in a discussion of their emotional state. A well-timed question such as "Are you are too tired to shower today?" can provide a point of engagement.

After a preliminary assessment conducted by the frontline staff, a decision may be made to perform a more detailed examination of the patient. The assessment should ideally be conducted by the clinician who is:

- able to understand the nature of the underlying medical condition and its impact on the brain and mind.
- curious about patient's psychological experience of cancer.
- willing to engage with the distressed, indifferent, uncooperative, or guarded patient.
- aware of their own fears and attitudes toward the suicidal patient. The clinician may experience anxiety, anger, denial, and helplessness or may view suicide as understandable or even justifiable.

There are at least three good reasons for the palliative care clinician to participate in the task of risk assessment:

Table 1 Formulation of suicide risk

	Biological factors	Psychological factors	Social/cultural/ spiritual factors
Predisposing factors confer vulnerability to suicide			
Predisposing factors	Male and increasing age (>65 years) **Family history of suicidal behavior and psychiatric disorder**[a,c] **Psychiatric disorder**[a,c] **Prior suicide attempts**[a,c] **Substance use disorder**[a,c] **Chronic medical illness**[c], especially brain disease/injury[b], delirium[a] Impulsivity – genetic contribution[c] Neuropsychological vulnerabilities; poor problem-solving skills; **Cancer-related variables**[a] (within 1 year of diagnosis, advanced stage, locally advanced or metastatic disease of the lung and pancreas and cancer-related pain and fatigue), treatments of cancer and drug interactions, e.g., role of steroids in mood disorders	Childhood maltreatment and developmental adversity[c] Modeling (knowing someone who attempted suicide) **Hopelessness**[a,b] as a cognitive style (rather than a hopeless prognosis) **Helplessness**[a] **Depression**[a] Low self-esteem Loss[c] (in relationships, employment, and leisure activities)	Single status Unemployment **Social isolation**[a,c] Homelessness or unstable housing Migration and displacement (indigenous people) Cultural and religious beliefs Local epidemics of suicide[c] Barriers to access to healthcare services, stigma, and barriers to receiving care[c]
Precipitating factors temporally correlate with the onset of suicidal ideation			
Precipitating factors	Identify a change in the trajectory of cancer that correlates with the onset of suicidal ideation, e.g., disease progression and increasing pain or fatigue Change in the trajectory of psychiatric illness, e.g., new onset/ relapse of depression Delirium Change in medications/treatments (e.g., radiotherapy to the brain or thyroid, steroids) and new drug interactions Drug dependence (withdrawal) or intoxication Nonadherence to interventions	Identify a change in experience of cancer. **Trigger points**: at initial diagnosis, initiation of curative treatment, side effects or intolerance of treatment, refusal or withdrawal of treatment, disease progression, relapse and recurrence, transition to palliative care where the focus may change from curative treatment to quality of life issues, and confronting issues of death and dying and survivorship Explore the following domains (**five Ds of cancer**): death, dependence, disfigurement, disruption in relationships, and disability Current suicidal ideation, plan, or intent [a]**Hopelessness and feeling a burden** **Demoralization** [a]**Loss of meaning** [a]**Loss of dignity and worthlessness** Depressive cognitions, e.g., "I am worthless"	Change to single status Recent unemployment Recent homelessness **Social isolation**[a,c] Financial strain Legal issues Child custody issues Cultural and religious issues Access to lethal means[c] (e.g., guns) Disasters Discrimination (LGBT) issues

(*continued*)

Table 1 (continued)

	Biological factors	Psychological factors	Social/cultural/ spiritual factors
Perpetuating factors are the persistent or ongoing risk factors that are known to increase risk			
Perpetuating factors	Ongoing biological factors (as listed above) that may contribute to persistent suicidal thoughts	Ongoing psychological factors (as listed above)	Ongoing social factors (as listed above)
Protective factors are often an absence of risk factors listed above			
Protective factors	*Absence* of psychiatric disorder[c] or substance use disorder[c] *Effective treatment of above risk factors*, e.g., effective treatment of pain	*Absence of above risk factors* Extroversion and optimism[b] Ability to identify their psychological experience (psychological mindedness) Problem-solving skills and conflict resolution skills[b,c] Motivation to improve their situation and willingness to seek help Strong reasons for living[b] Deeper sense of meaning and purpose	*Absence of above risk factors* Social connectedness[c] and family cohesion Stable employment and housing Responsibility for children[b] Positive therapeutic relationship[c] Access to mental healthcare[c]

Information extracted from the following sources: Alici et al. (2016) indicated with a, (Turecki and Brent 2016) indicated with b, and (Violence Prevention 2016) indicated with c

Table 2 Assessing suicidal thoughts, plan and intent

Assessing suicidal thoughts	
Suicidal ideation	Many patients have passing thoughts of suicide, such as "if my pain was bad enough, I might. . .." Have you had thoughts like that? Have you found yourself thinking that you do not want to live or that you would be better off dead? Have you stopped or wanted to stop caring for yourself?
Suicide plan	Have you thought about how you would end your life? Do you plan to hurt yourself?
Suicide intent	Do you intend to hurt yourself? What would you do? Do you think you would carry out these plans?

Reprinted with permission from Olden M, Pessin H, Lichtenthal W, and Breitbart W. Suicide and desire for hastened death in the terminally ill. In Chochinov HM and Breitbart W, editors. Handbook of psychiatry in palliative medicine. New York. Oxford University Press; 2012. p. 107

1. Data suggests that 45% of those who complete suicide see a physician in the month before their suicide and may not volunteer suicidal ideation unless specifically asked (Luoma et al. 2002).
2. Talking about suicide does not increase suicidal thoughts in the person who is being assessed (Law et al. 2015).
3. A strong therapeutic relationship with the treating oncologist is associated with lower rates of suicidal ideation and may reduce future suicidal ideation (Trevino et al. 2014).

The assessment of the suicidal patient may begin with the request from a team member or a family member, in which case begin with step 1. At other times, the patient will disclose suicidal thoughts during a routine consultation that will require further exploration: begin with step 3. A structured approach to the assessment of the suicidal patient is suggested.

Step 1: Speak to the "team" before assessing the patient.

- A team member, or a member of the family, may initiate the request for an assessment. Enquire about the event that has triggered the need for further assessment and be specific about the enquiry: "Has the patient said or

done something to suggest that the patient is suicidal; have they made a suicide attempt?"

- Enquire about the patient's past history including that gathered by the other members of the team:
  - Past psychiatric history, the specific prescribed treatment, and last known mental state examination, including a cognitive assessment.
  - Past suicide attempts.
  - Be aware of the nature and impact of the medical condition, pain, and the results of blood tests and imaging.
  - Drug and alcohol history – intoxication/dependence/withdrawal.
  - Family history of psychiatric illness, suicide, and substance use.
  - Current medications (medical and psychiatric).
  - Social history – next of kin details; is there an advance care directive?
  - Premorbid values and goals and attitudes toward treatment.

Step 2: Thinking time.

- Ask yourself "Why might the patient be suicidal at this time (consider the biopsychosocial vulnerabilities/predisposing factors listed in Table 1) and what has changed for the patient of late (precipitating or perpetuating factors)?"
- Consider differential diagnoses before examining the patient (e.g., dementia, delirium, depressive disorder, or other).
- What are the gaps in your knowledge of the patient and who can help fill in the gaps? Often collateral history from informants helps.
- Consider consulting a senior colleague or a psychiatrist before seeing the patient as this may help in planning an approach to the assessment, particularly if the assessment is likely to occur in the patient's home. It is important to be aware of the local legislation that pertains to the treatment of those with a mental illness.

Step 3. Speak to and examine the patient.

- Introduce yourself to the patient and explain your role in the team; it is important to be explicit with the patient about the purpose of the review, e.g., "I am here because your nurse mentioned that you were feeling hopeless about your situation and had been thinking that life was not worth living. If it is okay with you, I am here to understand what you are going through and then to suggest a way forward." Inform the patient of the limitations of the right to confidentiality and that you may need to consult the duty psychiatrist. Take a confident but curious stance. Respect and empathy go a long way in managing the patient's distress as they tell their story. Interview in a quiet space and be clear about the time available to address this issue.
- Obtain a full psychiatric history:
  - Ask about the current cancer and the impact on the person.
  - Ask about the current psychiatric symptoms to exclude a major mental illness (such as dementia, delirium, depression) and current suicidal thoughts and plans and ask about access to firearms.
  - Ask about the current psychiatric and physical health medication history and elicit information regarding any recent medication changes.
  - Ask about the current drug and alcohol use to elicit a change in the pattern of drug use, intoxication, and withdrawal states.
  - Ask about the current social context and stressors. Asking the patient: "How do you understand the factors that led you to feel suicidal?" is a reasonable question. Enquiry about the meaning of the suicidal thoughts for the patient is helpful. Suicidal comments may represent a mere communication of their suffering, a wish to be relieved of intolerable suffering, a fear of a painful death, a wish to be reunited with a deceased person, or a statement to reassert their autonomy on life and death. In the context of a cancer diagnosis, loss and threat emerge as recurring themes. Understand that for the patient, there is a threat to their physical and psychological integrity as a result of the cancer diagnosis and a loss of previous good health and loss of future possibilities. The nature and quality of

relationships also change as a consequence of ill health. The spouse may become the carer. Patients may be physically debilitated and may be more dependent on others for basic activities of daily living, and this may be intolerable for them.

- Identify risk factors conferring vulnerability to suicide. Ask the patient about prior adverse life events and challenges and how the person coped with the challenge. Ask about how the person maintains a sense of dignity, and a deeper sense of meaning.
- Ask about past psychiatric history with specific treatment details and previous suicide attempts. For example, the patient may have had a past history of depression with previous suicide attempts that required electroconvulsive therapy (ECT) and psychiatric medications to achieve remission.
- A general physical examination is usually documented in the records at the point of entry to the service; however, focus on biological factors known to precipitate suicidal ideation. If the patient has attempted suicide, a targeted physical examination will be necessary, for instance, examination after a laceration or an overdose.
- Mental state examination (MSE):

  A typical mental state examination includes an assessment of cognition (to exclude delirium or dementia), appearance and behavior, speech, mood, affect, thought stream, form, and content. Specific and detailed inquiry into suicidal ideation, intent, and plan is important. It is also important to exclude psychotic symptoms, to assess insight and the patient's capacity to make medical and psychiatric treatment decisions.

  The following features suggest high acute suicide risk: agitation, disturbance in the affect (which is the emotional tone during the interview). Elicit despondency, despair, suicidal preoccupation with intent or plan, and access to lethal means. Perception of being a burden on others and feelings of hopelessness are potent risk factors. Command auditory hallucinations and nihilistic delusions also increase suicide risk. Insight and judgment also need to be assessed because they influence management. Ask the patient: "What is the medical condition you suffer from? How does it affect you? What are your treatment options? What is your understanding of your prognosis? Help me understand how suicide is the best option for you at the moment?"

Step 4: Construct a "formulation" to understand the patient and guide management.

The focus is on the patient and their unique circumstances and not on a collection of risk factors. The assessment needs to be contextualized in the formulation wherein risk factors are juxtaposed with protective factors. The formulation requires a process of integration and prioritization of the information obtained by the team which in turn informs management (Simon 2009).

In formulating a case, the first task is to identify the **predisposing factors** (refer to Table 1), which are remotely implicated in the presentation of the person. The information is elicited during the process of history taking, examination, investigations, and information obtained from collateral sources, often at the point of entry into the service. These factors are historical, such as family history of mental illness. For instance, when a patient reports that a parent suffered a mental illness, the clinician may speculate that the patient has a genetic vulnerability to mental illness (and possibly suicide). It would also be important to consider the impact of parental mental illness on the nature and quality of the parenting, parent-child relationship, and the patient's personality development. It would be reasonable to ask the patient: "How did your father's mental illness impact on the way he raised you and your relationship with him?" If the patient reports that a parent committed suicide, the clinician may speculate that the family history of suicide suggests genetic loading for mental illness and suicide. Suicide is a powerful behavioral incentive for others to suicide, a process described as modeling, and family members who attempt suicide provide powerful

maladaptive messages to the living about the challenges of life and how to overcome them. The patient is more likely to attempt suicide within 1 year of a cancer diagnosis, especially in the context of a locally advanced pancreatic cancer or if the patient has had a high-morbidity surgical procedure, often with substantial psychological consequences. The social (cultural and spiritual) predisposing factors are often elicited by the social worker and pastoral care worker on the team.

The next task is to identify the **precipitating factors**. Reflect on "Why is this person suicidal now?" and temporally correlate onset of suicidal ideation with changes in the patient's biopsychosocial situation. For instance, if the patient says that (s)he began contemplating suicide 1 month ago, the clinician should search for a change in the patient's context that corresponds to that timeframe. Note however, that there can be a time lag between a change in the situation and the onset of suicidal ideation. Gene-environment interaction may explain the apparent time lag.

There are key *trigger points* in the illness trajectory that may cause substantial emotional distress. These trigger points correspond to the time when the patient first notices a symptom, the time of a new diagnosis, initiation of curative treatment, side effects or intolerance of treatment, refusal or withdrawal of treatment, relapse and recurrence, survival, advancing disease, transition to palliative care, and dying. As the patient transitions from one stage to another, the clinician should explore the psychological experience of a change in their circumstances and explore the **five Ds of cancer** (Hodgkiss and Mascarenhas 2012):

- **D**eath anxiety and fear of what dying entails (e.g., "With all that has happened to you lately, have you been thinking about death?")
- **D**ependence on others, which may be distressing (e.g., "How has your situation impacted on your capacity for independence?")
- **D**isfigurement as a result of the cancer or treatments (e.g., "How has the cancer and the treatment impacted on how you see yourself?")
- **D**isruption in relationships and changed dynamics (e.g., "How has the cancer changed the quality of your relationship with. . .?")
- **D**isability associated with the cancer (e.g., "How has the cancer changed what you can do for yourself or what you would like to do for yourself?")

The loss of **D**ignity, **D**emoralisation and **D**epression may also lead the person to contemplate suicide. Dignity is defined as the state of being worthy of honor or respect. There are three factors that impact upon the sense of dignity. Firstly, the cancer may cause distressing symptoms and may impact upon the person's level of independence and therefore their dignity. These are the illness-related concerns. Secondly, the person may maintain a sense of dignity through adhering to a set of personal values and attributes such as hopefulness, wish to maintain autonomy, or by doing things to preserve their dignity, termed dignity-conserving repertoire. Lastly, the dynamics within key relationships may either bolster or undermine the patient's sense of dignity, termed social dignity inventory.

Then aim to identify the **perpetuating factors**. Here the clinician aims to identify persistent or ongoing biopsychosocial risk factors that are known to increase risk. Advanced cancer, intractable symptoms (such as pain), side effects from the treatment, partially treated depression, nonadherence to antidepressants, fatigue, family conflict, perceived helplessness, hopelessness, loss of dignity and meaning, and a sense of being a burden are likely to render the person suicidal. Single status and social isolation are key social determinants for mental illness and suicide in particular.

Finally, identify the **protective factors** that will mitigate the risk. Often an absence of biopsychosocial factors that are known to precipitate or perpetuate the risk of suicide are seen as protective factors. The patient may need the clinician to identify protective factors at a time when all hope appears to have been lost. The patient may hold a deeper sense of meaning and purpose, have dependent children, and have a love of

music, and the team can draw upon these factors to mitigate risk.

Step 5: Make a diagnosis and identify the imminent suicide risk.

Consider several differential diagnoses: dementia, delirium, psychiatric disorders secondary to general medical condition, substance-induced psychiatric disorders, and other psychiatric syndromes such as depression and demoralization. A high-suicide-risk patient is one with suicidal ideas, suicidal intent, and suicidal planning and has access to lethal means to commit suicide, including prescription medication.

Step 6: An approach for the management plan for the imminently suicidal patient.

The physician empathizes with the patient's suffering by saying something like "I can only imagine how you must feel looking at the scar across your chest" for a patient with a mastectomy scar. Even a well-intentioned statement like "The scar does not look too bad" may be experienced by the patient as being invalidating. The physician puts himself in the patient's shoes and views the situation, as perceived by the patient, as a means to understand the patient's distress to demonstrate empathy.

Early in the interview, the physician says something like "It is very common for people with cancer to think about death, dying, and suicide, often when they feel alone and have lost all hope." This lifts the veil of secrecy. The patient is then invited to elaborate on their suicidal thoughts and distress as a tangible sign of physician's concern for the patient. As the physician actively listens and makes an attempt to understand the patient's predicament, the patient feels understood. A curious stance goes a long way in creating a therapeutic space wherein the patient articulates their distress without fear of judgment.

The physician provides a clinician's formulation to the patient, and this facilitates rapport, and the formulation serves a road map for intervention. There are various factors that the clinician needs to take in to account in deciding how much to share with the patient. For instance, the clinician needs to be aware of the patient's general level of intelligence, their proficiency with language, their capacity to process and understand information, and their psychological mindedness in determining how much of the clinician's formulation is communicated to the patient. The biological, psychological, and social factors contributing to the patient's distress and suicidal thoughts are actively managed. Collaboratively working toward symptom relief instills hope. As stated previously, the physician-patient relationship is a key determinant in suicide risk. Drawing upon the patient's social support systems in the ongoing management may prove helpful in managing the suicidal patient. The physician challenges unhelpful thought patterns (e.g., thoughts like "There's no point"), provides information, problem solves, offers reassurance, and instills hope. The clinician obtains consent to contact family for collateral information and reviews the patient frequently. If the patient is assessed as a high risk of suicide, an immediate psychiatric consultation should be sought. The palliative care team will need to manage the patient in the interim.

The social worker may provide a formulation based on the patient's narrative or family systems theory, assess, and manage unhelpful family dynamics with a view to help the patient make sense of their situation. Interventions offered range from supportive psychotherapy to family therapy. Pastoral care workers bring to light the religious conflicts faced by the patient, for instance, suicidal thoughts may be in conflict with the patient's conservative Christian ideology. Pastoral care discusses themes of guilt, shame, and punishment in the patient's narrative with respect to religion. Involving the patient's family is a vital component of the treatment plan because they are often a source of collateral information, support for the patient, and an ally to the team.

Based on the individualized formulation, a management plan is constructed by remediating factors known to precipitate and perpetuate suicidal thoughts and building upon protective factors to mitigate risk. For the acutely suicidal patient, creating a safe environment is the immediate priority. This invariably involves treatment in an inpatient palliative care unit, if specialist palliative care is necessary. It would be

uncommon to transfer a patient with suicidal thoughts and palliative care needs from a palliative care unit to a psychiatric ward.

Management decisions need to be made by the multidisciplinary team because each member of the team may have a specific role in the ongoing management. Nursing staff may be able to provide direct supervision of the patient, administer medication, and clear the surrounds of dangerous items (e.g., belts and kitchen knives). There may be circumstances when it may be necessary to arrange a psychiatrically trained nursing staff member to engage with the suicidal patient and provide constant visual observation.

Consider the role of **psychotropic medication** in the context of a broader biopsychosocial management plan for the cancer patient (refer to Table 3 below). Pharmacological management of specific underlying psychiatric syndromes is described in the chapter entitled ▶ Chap. 85, "Distinguishing and Managing Severe Psychological and Psychiatric Distress."

The consultation liaison psychiatry service will assess the suicidal patient as a matter of urgency and suggest a **psychological therapy** depending on the individualized formulation. The ▶ Chap. 85, "Distinguishing and Managing Severe Psychological and Psychiatric Distress" details a range of psychotherapeutic approaches used in palliative care. The therapy is targeted to address the key aspects of psychological distress, which may in turn drive suicidal ideation.

When demoralization is seen to be mediating suicidal ideation, existentially-oriented and meaning-centered therapies restore much needed hope and morale (Kissane 2011, 2017). Recent randomized-controlled trials have confirmed the efficacy of meaning-centered therapies, whether using a group (Breitbart et al. 2015) or individual approach (Breitbart et al. 2018). Clinicians should pay attention to sources of continued meaning in a person's life: focus on their role within a family and the quality of their relationships; recognise the value of their life and accomplishments, making an active choice to embrace meaning and enjoy life through sources of creativity (arts, music and literature). These key areas of significance for patients all foster a deeper investment in life, despite infirmity (Lethborg et al. 2018). It remains unclear whether the above therapies directly reduce suicide rates, although there is clear evidence that there are evidence-based therapies to reduce distress and demoralization in palliative care.

7.3 Additional Issues to Consider in the Management of a Patient with a Serious Mental Illness

Societal marginalization and rejection lead the psychiatric patient to expect being rejected by their healthcare team, and staff may be anxious when admitting a person with a history of a serious mental illness. Not uncommonly, psychiatric patients have endured neglect and abuse up until they recieve holistic care during the hospice admission. Patients feel cared for and are grateful for the care. The patient with a psychiatric illness is more likely to have multiple medical comorbidities, a life-span 20 years less than the general population, and a higher cancer mortality. Howard et al. (2010) highlight issues arising in the treatment of those with a psychiatric disorder (Howard et al. 2010). Patients with schizophrenia may have thought disorder, rendering them unable to communicate their cancer-related symptoms clearly, or have auditory hallucinations that tell them to refuse treatment, or they may be amotivated leading them to miss medical appointments. The patient with schizophrenia may have disrupted frontolimbic circuits (involved in pain perception) leading to an apparent underreporting of pain. It is important to anticipate the potential challenges when planning treatment with patients with mental illness. The refusal of lifesaving medical treatment in the context of active psychiatric disorder should prompt a referral to the liaison psychiatry service.

Assertive management of the medical and psychiatric illness is vital. Consider drug interactions between psychiatric medications and anticancer treatments. In terms of the *pharmacodynamic drug interactions*, it is important to note that

Table 3 Role of psychotropics in the suicidal patient

Psychotropic medications may be prescribed for (Grassi et al. 2014).
- The treatment of emotional distress without psychiatric disorder
- A pre-existing/underlying psychiatric disorder
- For nonpsychiatric disorders such as pain disorders
- Cancer-related symptoms such as anorexia, nausea, etc.
- Non-cancer symptoms such as sleep disturbance

Other considerations before prescribing psychotropic medications.
- Constellation of psychiatric symptoms
- Comorbid medical conditions
- Efficacy data
- Safety profile
- Drug interactions and
- Cancer stage and goals of care (curative vs. end-of-life care)

	Advantages	Disadvantages
Antidepressants	Reduce impulsivity, treat underlying depression, and anxiety. Management of cancer-related symptoms such as pain (dual-acting antidepressants), fatigue (modafinil, bupropion, and reboxetine), anorexia, and insomnia (mirtazapine) may indirectly reduce suicide risk	Can cause restlessness, increase suicidal ideation, and lead to an instability in mood especially early in the treatment and with dose increments. Regular monitoring of suicidal ideation is advised
Benzodiazepines	Benzodiazepines do not reduce suicide per se but alleviate emotional distress and treat anxiety disorders. Other indications are insomnia, non-specific agitation, dyspnea, and terminal restlessness, as adjuncts to antiemetics and as antiepileptics which again may have indirect effects on suicide risk	Can rarely lead to "disinhibition or paradoxical excitement" and increase impulsivity. If prescribed with other sedative agents can be lethal in overdose. Managing the access may mitigate risk
Antipsychotics	Efficacious in the treatment of psychotic disorders and mood disorders, thereby reducing suicidality through treatment of the underlying disorder. Antipsychotics may be used in the management of behavioral disturbance in the setting of a dementia, delirium, and paraneoplastic syndromes. Haloperidol is commonly used antipsychotic in palliative care as a hypnotic, antiemetic, augmenting agent for analgesia, and in delirium	Concomitant use of antiemetics can infrequently prolong QTc. Can be subject to drug interactions. An anticholinergic delirium is a rare side effect at low doses but common in an overdose context
Ketamine	Acute antidepressant like action with rapid-onset anti-suicide properties with few side effects in the short term, in cancer patients (Reinstatler and Youssef 2015; Fan et al. 2016). Ketamine treatment was associated with a reduction in suicidal ideation independent of depression (Murrough et al. 2013).	Longer-term safety and efficacy data is lacking
Psychostimulants	Can be activating, improve attention and have a rapid onset of antidepressant activity, and are used to alleviate cancer-related fatigue, anorexia (in low doses), and poor quality of life in terminal cancer and to manage sedation secondary to opiates	Rarely used and no evidence in the suicidal patient. Often a regulated drug. Inhibit cytochrome system. Can precipitate psychosis and cause arrhythmias

(*continued*)

Table 3 (continued)

Lithium and clozapine	*Level 1 evidence for the treatment of bipolar disorder and schizophrenia but also have independent "anti-suicide" effects*	*Prescribed under the supervision of a psychiatrist. Rarely used in the palliative care context and therefore rarely studied*
Electroconvulsive therapy	*ECT has been shown to rapidly alleviate suicidal intent in almost 40% of acutely suicidal depressed patients within 1 week, and 60% by the end of the second week were no longer acutely suicidal* (Kellner et al. 2005). "*ECT is recommended as first-line treatment in extremely severe melancholic depression, particularly when the patient refuses to eat or drink and/or is a very high suicide risk, or when the patient has very high levels of distress, has psychotic depression, catatonia or has previously responded to ECT*" (Malhi et al. 2015). *There is level 1 evidence in support of ECT as an efficacious treatment option in the depressed patient with medical comorbidities and cancer is not a contraindication* (Zwil and Pelchat 1994)	

psychiatric medications and anticancer therapies impact on a range of organ systems, e.g., the liver. Concurrent medications that affect bone marrow functioning need to be considered, e.g., agranulocytosis is a known side effect of clozapine, carbamazepine, clonazepam, and a range of chemotherapy agents. Furthermore, antipsychotics, chemotherapy agents, and antiemetics (metoclopramide) can cause prolongation of the QTc, as seen on the electrocardiogram (ECG) which can increase the risk of Torsades de pointes (TdP), a fatal arrhythmia. Hepatotoxicity and renal impairment with concurrent medication usage should be anticipated, and close monitoring is advised. In terms of *pharmacokinetic drug interactions*, consider the impact of a medication on the metabolism of another. Medications may be metabolized through the cytochrome P 450 system, such as CYP 1A2, 2D6, and 3A4. Inhibitors of this system may lead to an accumulation of the substrate and consequent toxicity. Fluoxetine and fluvoxamine are potent inhibitors of CYP 2D6. Tamoxifen is a prodrug metabolized by CYP 2D6 to the active metabolite, endoxifen. Hence, inhibition of CYP 2D6 leads to an accumulation of the prodrug rather than the active metabolite, rendering treatment ineffective (Andersohn and Willich 2010). There are innumerable drug interactions, and it is prudent to check before prescribing.

7.4 Experience of Those Bereaved Through Suicide

Suicide does not occur in a vacuum. It occurs within a family and social system, and in palliative care, a suicide will also impact the treating team. Suicide is ubiquitous, and therefore, it is not uncommon to know a person bereaved after suicide: a suicide survivor. When suicide occurs in the physically well, the suicide survivors are more likely to report perplexity ("Why did he do it?"), guilt about not being able to prevent the suicide ("I couldn't prevent it."), guilt about missing the early signs ("I should have seen it coming."), a sense of rejection by the deceased ("Why did he do it to me?"), and stigma from society (people might think "What in the family caused it?") (Sveen and Walby 2008).

When a suicide occurs in the context of a terminal illness, the survivor may experience emotions similar to the ones described above. However, survivors may view the cancer suicide as an understandable response to pain and suffering, a noble act in the face of an inevitable death, and the survivor may not feel guilty because the patient would have died from the cancer in time. The suicidal patient may have the covert permission from the survivor, and in this scenario, relief may be mixed with guilt. The experience of a

suicide survivor is impacted upon by their personality, genetic predisposition, developmental stage, capacity to "make sense of the suicide," as well as the shared environmental factors such as family and social supports for the survivor (Andriessen et al. 2015). The nature and quality of the relationship and meaning of the relationship have a bearing on the experiences of the suicide survivor. In the general psychiatric literature, suicide survivors were not at an increased risk of suicide when compared to those bereaved by sudden unnatural causes, but suicide survivors were at higher risk of suicide than those bereaved by sudden natural causes (Pitman et al. 2016). Spouses bereaved by suicide were at a greatly increased risk of suicide (Agerbo 2003). It is unclear whether spouses of cancer suicide are at increased risk of suicide and whether there are differences in terminal cancer suicide versus suicides early in the cancer trajectory.

7.5 Management After a Suicide

After a suicide, the responsibility of the clinician shifts to the care of those left in the aftermath of the suicide. A designated staff member will make early contact with the family, may attend the funeral if possible, advise on what to expect in the bereavement process, suggest a grieving ritual, provide information on local suicide bereavement groups, and consider a referral to specialist services (Alici et al. 2016). The physician should take advice from a senior colleague and the medicolegal unit before speaking to the family, in order to provide accurate information and express regret at the loss of a life.

There will often be two distinct staff meetings with two distinct agendas within days of the incident. Firstly, a staff support meeting would offer informal comfort within days of the event. When attending to the emotional needs of the staff, it is suggested that staff express their feelings toward the deceased (sorrow, relief, anger, etc.) and express their feelings about their own role in the care of the patient (guilt, shame, relief, etc.) (Grad 1996). The convener of the group educates staff about the signs of emotional distress and strategies to cope with the loss while also maintaining a high standard of care for staff and other patients. Secondly, a psychological autopsy meeting is convened to ascertain accurate information regarding the deceased. This second meeting has a different membership, including senior clinical staff and operations managers. They adopt a detailed approach to examine processes and systems of care and deal with any immediate systemic issues that may compromise the care of other patients. The meetings should remain focused on the events and processes rather than people or feelings. Undue focus on people or feelings can exacerbate feelings of guilt or shame. There may be formal reporting processes within organizations involving the Quality Assurance Unit (QAU). There may be a fear that the QAU will abandon the physician so as to protect the institution and its reputation (Misch 2003). The clinician may be mandatorily required to notify systems outside the institution, such as the Coroner's Office and/or the Office of the Chief Psychiatrist. A suicide should go through multiple levels of scrutiny as part of the overall local suicide prevention strategy. The inquiry process itself is stressful for the clinician.

8 The Professional Carer

8.1 The Clinician Survivor: Physician's Experience After a Patient Suicide

Given the paucity of literature on the physician's experience on this matter, physicians may benefit from the reflections of psychiatrist survivors. The personality style (e.g., perfectionism and obsessional personality traits confer vulnerability) and their emotional state at the time of the suicide will impact on the experience of a patient suicide (International Association 2016). The quality and duration of the therapeutic alliance, professional skill base, whether there were other clinicians involved in patient care, and finally the physician's career developmental stage have a bearing on the clinician's experience (Gitlin 1999).

The quality of the doctor-patient relationship varies from one patient to another, and so the suicide of one patient may affect the clinician differently from another. In the dyad, one has unconscious and conscious feelings toward the other, which are activated at various times in the course of the therapeutic relationship. The quality of the therapeutic relationship is often changing and is dynamic. Therefore, the timing of the suicide in the context of the prevailing therapeutic relationship will have a bearing on the clinician's experience of the suicide. For example, the suicide at a time when the therapeutic relationship was strong may be experienced differently from the suicide which occurs in the context of an estranged relationship.

The suicide reactivates deep emotions from the physician's private life, often based on unconscious conflicts within the physician's past relationships. Unconscious conflicts are out of the conscious awareness, and the physician may not be able to readily articulate these deeper emotions (Misch 2003). In simple terms, the suicide death of a patient may resurrect internal emotional conflicts from the physician's past. It follows then that there is no one set pattern of how a suicide will impact upon the physician. After the suicide, a range of painful unconscious feelings may torment the physician. In the first week, the physician may experience disbelief and denial, followed by emotional turmoil that can last a couple of months. The physician experiences heightened anxiety and surreal feelings such as depersonalization and numbness. Physicians may experience a sense of shame for failing an internally set standard of care (Tillman 2003). He/she may become angry with the deceased. The doctor may experience excessive guilt, as if responsible for killing the patient. Perceived guilt may be disguised or concealed, manifesting as over-conscientiousness and excessive care of other patients. Internal conflict may lead to poorly planned discharges or overly restrictive practices so as to prevent another suicide (Little 1992). There may be an internal sense of relief disguising itself in thoughts such as the recognition that the patient is now at peace. Unconsciously, the physician could be relieved at not having to manage this once challenging patient or experience denial manifesting as forgetting vital information about the patient. The physician is likely to keep these ambivalent and painful feelings private.

The physician will also have a range of emotions that are subject to conscious awareness and can be articulated. The suicide of a patient may activate a sense of threat and/or loss.

In the short term, the doctor may experience:

- Feelings of shame and incompetence manifesting as self-doubt: "Am I good enough?", "Will I identify the next suicidal patient?"
- Fears of being exposed as incompetent or fears of persecution by the patient's family and "Will I lose my job over this?"
- A changed view of oneself and a loss of the competent self which may manifest as "I am not good enough and my colleagues no longer respect my clinical skill and I am the topic of hushed conversations."
- Loss of support from colleagues, a sense of failing to meet the standards set by one's colleagues, and meeting colleagues who no longer want to associate themselves with the management of this patient.

At this lonely hour, grieving staff may turn to literature to seek closure and meticulously read the case notes to see what could have been done differently. Speaking up can be painful and may be taboo within the unit. Staff will avoid breaking down at work because it may be misunderstood as a sign of weakness or an admission of incompetence. Staff will continue with their duties with a brave professional façade. In the longer term, burnout, depression, post-traumatic stress disorder, and substance abuse may ensue.

Gitlin (1999) suggests a few strategies to assist the clinician survivor (Gitlin 1999). Firstly, the physician should manage the sense of isolation by talking to a senior colleague, friends, or family. If appropriate, speaking to the bereaved family may be appropriate and may also reduce the sense of isolation. Secondly, the physician could educate colleagues about the management of this type of scenario. Consider a case presentation or

writing up as a case report for a journal. Writing about yourself, in third person, helps in distancing yourself from the case. Next, remind yourself that suicide is a preventable outcome in many but not all cases. Suicide rates in inpatient psychiatric units have remained fairly constant over the last 75 years, despite advances in interventions such as antidepressants, antipsychotics, lithium, and ECT (Cotton et al. 1983). From this knowledge, the physician may conclude that despite evidence-based treatments, suicide remains an undeniable reality in those with a serious mental illness. The physician can remind himself that the cancer patient is at greater risk of suicide and again suicide may be a possible outcome despite treatment. Note that suicide may be a failure of the treatment (not a failure of the physician). Suicide prediction is a flawed science with low positive predictive value and high false positives (Pokorny 1983). Little suggests a departmental review and case presentation of the incident after 2 months but before 6 months (to describe what happened) with the aim of staff education (to see what can be learnt) (Little 1992). Finally, the physician can take the lessons learned from one suicide and use it in the management of the next. Notwithstanding the turmoil experienced by the clinician, there is opportunity for emotional growth.

In summary, there is no one predictable trajectory after a patient suicide. Several factors impact on the clinician's experience of a suicide. Some of the factors are accessible to one's conscious awareness while others are not. However, there are tangible steps a clinician can take to regain a sense of mastery and control.

8.2 Physician Suicide

The physician is more vulnerable to depression and substance use; suicide rates are consistently higher among physicians than among the general population. Even though the absolute numbers of suicides among physicians is small, it would not be unusual to know of a physician who committed suicide. There are about 300 physician suicides in the USA each year (American Foundation 2016). A meta-analysis found that male and female physicians in the USA were at greater risk of suicide (suicide rate ratios of 1.41 and 2.27, respectively) than the general population (Schernhammer and Colditz 2004). More recent Australian data (Milner et al. 2016) found that suicide rates were significantly higher in females who worked in healthcare professions (doctors, nurses, psychologists, and allied health staff) in comparison to females working in non-healthcare professions. Suicide rates followed a gradient, being highest in female nurses, followed by female doctors (two and a half times more likely to suicide than females working in non-healthcare professions), followed by male nurses (who were one and a half times more likely to suicide than males in non-healthcare professions). Ease of access to prescription medication was a key risk factor and one which is of particular relevance in palliative care. The rates of suicide were comparable for male doctors and males in non-healthcare professions (Milner et al. 2016). Higher rates of suicide are attributed to two sets of vulnerability factors. Firstly, general suicide risk factors such as depression and substance misuse. Secondly, risk factors are associated with being a clinician such as personality attributes (e.g., perfectionism), gender role conflict, stress of work, workplace bullying, and harassment. There are substantial expectations of their role, their personal identity may be defined by the work, and staff may experience vicarious traumatization. Male nurses may experience stigmatization as a result of career choice, and female healthcare professionals may feel conflicted about their responsibilities at home and work. For the abovementioned reasons, the palliative care clinician is at risk. There are organizational barriers, such as rising insurance costs and restrictions on scope of practice following disclosure of mental illness, thereby reducing the likelihood of a disclosure of mental illness (Lindeman et al. 1999).

Middleton (2008), a family physician and a suicide survivor, wrote an essay on her experience of losing a colleague to suicide (Middleton 2008). She reminds us that, firstly, the issue of a physician suicide is an unacknowledged problem and, secondly, stigma prevents our profession from

managing it. The suicidal physician is under pressure to remain silent or risk being labeled as an impaired physician, a label that threatens his professional identity and dignity, right to practice, and livelihood.

After a physician suicide, colleagues are left grappling with questions like "Why didn't you ask for help. . .did I fail you?" The survivor is also under pressure to grieve in silence. Center et al. (2003) prepared a consensus statement with recommendations for physicians to address the issue of physician suicide. Center recommends ensuring healthcare for the physician, recognizing the symptoms of depression in oneself and colleagues, seeking treatment of mood disorder and substance abuse, being aware of the local services available for the mental health of doctors, and having working knowledge of the local laws regarding confidentiality and the statutory obligation to inform regulatory authorities (Center et al. 2003).

9 Conclusion and Summary

Suicidal behavior, much like an acute abdomen, is a medical emergency. The general perception in the community is that suicide in the cancer patient is an understandable response to the illness and that it is somehow different from suicide in other populations. Arising from this misperception is the notion of rational suicide in cancer. The desire for hastened death is not uncommon in palliative care and may reflect underlying suicidal thoughts. There are known general risk factors and cancer-specific risk factors. Suicide in this population represents a desperate attempt to escape internal or external stressors, and these stressors can be conceptualized via biological, psychological, and social factors or a combination of the above. Patients with cancer are more likely to have a comorbid psychiatric disorder and are at greater risk of suicide; however, death through suicide in a cancer patient is a relatively rare outcome. Suicide is a multi-determined behavior, and correspondingly, interventions also need to be multimodal to address issues such as symptom control, emotional distress, and social isolation. An individualized formulation of the suicidal patient aims to alleviate distress. The palliative care clinician, in the context of an established therapeutic relationship, is ideally placed to undertake the task of a suicide risk assessment and then arrange a psychiatric consultation if needed. As public opinion shifts, physician-assisted suicide has gained traction in palliative care. In the context of this cultural change, there is a risk that society may revert to thinking of suicide as a legitimate means to end intolerable suffering, and it is conceivable that family may assist the patient in ending their own life. Suicide prevention is a global challenge, and ongoing medical education is vital if we are to have any chance of preventing suicide at an individual level. As we focus our attention to the care of our patient, it is also important that clinicians care for themselves and each other.

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Transfer to a Preferred Place of Death

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Contents

Abstract

The preferred place of death is an important consideration in end-of-life care, especially when the dying person is definite about their choice. The preferred place of care may well be the same location, but this is not always the case. When the two venues are different, and the patient's prognosis is poor, a decision has to be made whether to move the patient or not. The expectation to not only transfer the dying person in a timely fashion but also to minimize the time in the current setting often makes the situation a palliative care emergency. However, should the move occur at all? The risk of dying in transit may be high. Furthermore, respecting the wishes of the dying person needs to be balanced with the practicalities of

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_85

safe ongoing care. These are practical and ethical decisions that should be made as early as possible.

How do we facilitate the smooth transfer from one location to another? Coordination and communication are vital in planning the process and supporting the discharge. The provision of the right medications and equipment, relevant information, and strategies for managing future problems should increase the chance of a successful transfer. Sometimes a smooth transfer will not be possible, but patients and family members will usually be happy with a successful one.

1 Introduction

The request to die in an alternative setting to the current venue of care is often stressful, until transfer to the preferred place of death has been achieved. It is not a singular decision but rather a process of considering and reviewing the relevant factors at various points in time. It is important to remember that views may change over time, e.g., due to clinical deterioration or psychosocial issues. Therefore, a careful review of any request is critical.

In order to fulfill the wish of the dying person, the process of transfer is usually deemed an emergency by palliative care teams. The aim of this chapter is to provide a systematic and practical approach for such transfers, considering the needs of all those involved. A multidisciplinary team approach will be beneficial, especially if the prognosis is limited. Last minute requests are complicated by the lack of time but are not uncommon. It may be impossible to fulfill the request of the patient/family in a limited timeframe and provides another reason for earlier referral to palliative care teams for appropriate assistance.

2 The Preferred Place of Death

Most people report that they want to die at home, and 80% do not change their mind as death approaches, although the preference to die at home varies between patients (31–87%), caregivers (25–64%), and members of the public (49–70%) (Gomes et al. 2013). Other research suggests that the views of patients and their carers do change over time, and we need to carefully distinguish between the preferred place of death and the preferred place of care (the venue in which people would like to receive most of their care) (Agar et al. 2008). In planning for end-of-life care (EOLC), healthcare professionals should be encouraged to ask and identify these venues of care; failure to do so is more likely to lead to a hospital admission (Ali et al. 2015).

Despite the desire to die at home, most people actually die in hospitals in the western world. Internationally, comparing 14 countries across 4 continents, we have found that 12–57% of cancer patients die at home and 26–87% die in hospital. The authors attribute these differences to the healthcare resources of the countries and their specific EOLC strategies for cancer patients (Cohen et al. 2015). Many healthcare services have been organized to meet the perceived demand for home deaths, especially in cancer patients, but these figures demonstrate limited success. In people with nonmalignant disease, it is likely that their preferred and actual place of death will differ, due to poor recognition of the terminal phase of disease, not establishing a preference in venue of death, and an inadequate provision of available supportive and palliative care (Billingham and Billingham 2013). Cohen et al. compared people with lung cancer and people with chronic obstructive pulmonary disease (COPD), across 14 countries, and highlighted that those with COPD were overall more likely to die in hospital or in a nursing home (Cohen et al. 2017). Similarly, people with end-stage renal disease are more likely to die in hospital, unless they are not receiving dialysis (Lovell et al. 2017).

Dying at home can be more peaceful for patients and provide less traumatic grieving for families, when compared with hospital deaths, providing the following have occurred: a discussion of the patient's preferences, the involvement of a general practitioner (GP) who can provide home visits, and the ability for the family to be given time off work to support care at home

(Gomes et al. 2015). These findings provide some insight into the challenges of dying well at home.

Furthermore, societies have changed over the years, e.g., families are more dispersed around the globe than previously. Patients may not have family nearby to care for them, but even if they do, they may not want to be a burden to them. Similarly, some immigrant communities may not have the cultural and supportive networks to remain at home. Societies have also entrusted their health in a predominantly biomedical model and believe in the "rescue culture" of medicine (Poppito 2013). These changes influence the choices about the venue of care and venue of death between the primary decision-makers, i.e., patients, carers, and healthcare professionals. The decisions may favor home, aged care facilities, hospital, or hospice settings at different times; however the impact of family wishes, cultural, and religious beliefs should not be underestimated (Lin et al. 2017; Gott et al. 2013).

From a population perspective, two studies delineate a change in where people are dying. There has been a drop in the number of people dying in hospitals in England and Wales (2004–2014) and in Norway (1987–2011). However, both studies report (during their respective periods) and predict a rise of deaths in aged care facilities (Bone et al. 2017; Kalseth and Theisen 2017). Given the aging population in modern societies, not only will the number of facilities require review, but there will also be a challenge to the provision of optimal EOLC in this sector.

As healthcare professionals, we should plan ongoing care with the preferred place of care in mind. The preferred place of death will be more difficult to determine, due to the changing views and circumstances of dying people and their families over time (Agar et al. 2008). As a result, sometimes transfers will occur more rapidly than expected. There are excellent patient transfer guides online that may be useful to review, e.g., the "National Rapid Discharge Guidance for Patients Who Wish to Die at Home" (Ireland) and the "Accelerated Discharge to Die at Home" (New South Wales, Australia). In healthcare settings, the transfer destination should provide more appropriate care for the needs of the patient. Implied in the statement is also a view that the setting from which the transfer occurs cannot provide the necessary care to the individual. A further expectation is that the person is likely to improve at the destination venue. In an end-of-life context, we need to reconsider these statements, but there is often an ethical dilemma that exists for all parties concerned.

3 Dealing with the Request to Be Transferred

Palliative care teams frequently receive requests for transfers to another setting. These patients may or may not be dying, but when the reason is to die in a desired destination, the sense of urgency increases. The first response is usually to find out more about the referral, and a phone call may be the first means of triage.

The triage process aims to determine the urgency of the referral. A written referral may not include all the relevant information, and so discussing the case with either the referrer or caregiver will help. The tone of the discussion may be enough to decide that the case is an emergency, but we need to know about the patient, their family, and any other reasons relevant to their decision. Perhaps the most common scenario involves a patient wanting to return home to die from the acute hospital ward. In this case, the referral will have been made by a junior medical officer who may, or may not, know the case well. Calling the nurse in charge of the ward may be helpful, as they may have more knowledge of the multidisciplinary team approach to the care thus far.

A similar case may involve a dying person at home, where the family prefer the death to occur in an institution, e.g., they may not want to live with the memory of the death at home, or they may not be coping with caring at home. The person may be conscious, semicomatose, or unconscious. Furthermore, the decision may be in keeping with their wishes or contrary to them. The referral may have come from the GP, or the community palliative care (CPC) team, but once

again speaking to the person with the best overall knowledge of the case will be most helpful.

So, when do these scenarios become a palliative care emergency? There are three main reasons to urgently review the case, assuming the transfer is desired:

- Firstly, if the person has a poor prognosis, e.g., days, then a greater need for action will be required. A delay could lead to death in the current venue of care, which does not meet the patient wishes and may anger the family.
- Secondly, the presence of significant distress in the current setting, from any of the relevant parties, would also increase the acuity for intervention.
- Finally, assuming the dying person wishes to be moved and/or the family are agreeable, then the referring healthcare professionals may be strongly advocating for urgent action.

Ultimately, there is a balance between meeting expectations, minimizing the time in the current venue of care, and maximizing the time in the desired venue of care. In terms of the patient and family, we therefore have a duty of care to ensure the discharge would be feasible, safe, supported, and beneficial. Modern healthcare systems can challenge the decisions we make in these scenarios, e.g., moving someone because of acute hospital bed pressures or requiring the patient to meet the specialist palliative care requirements for a hospice bed (Bergenholtz et al. 2016; Love and Liversage 2014). Overall, palliative care teams aim to respect the wishes of people who are dying as much as possible and support their families through whatever decision is made.

4 Patient Review and Family Discussions

The transition to palliative care should be a process over time, integral to the clinical handover of the patient's care. However, referrals to palliative care teams are often later than desired, despite evidence of less aggressive EOLC, improved quality of life, and reduced healthcare costs (Scibetta et al. 2016; Smith et al. 2014). The referral marks a move from living with a disease to dying from it. We need to recognize that a palliative care referral often marks a significant psychological step toward death. Patients and families may be at different stages of dealing with the illness, irrespective of the actual clinical status. It is important to establish who is the main spokesperson for the family as early as possible, in order to save time and repetition of information. How these conversations are managed, at such an emotional time, may have lasting repercussions in bereavement (Stajduhar et al. 2017). Late palliative care referrals mark an altered course in the condition and care of the patient, which requires a more rapid adjustment from previous beliefs. Hence, allowing time for people to express their concerns and wishes regarding future care is necessary (Romo et al. 2016; Smith et al. 2016).

The coping mechanisms of the family and staff at the site of care should be considered when deciding upon possible transfers. As discussed above, it is important to understand the situation we will encounter when we review the patient in person. The priority of care should be focused on the patient, and therefore any distressing symptoms should be managed urgently. Advice may have been given over the phone, so a review of the efficacy of the suggested interventions is possible when the patient is assessed in person. The family are more likely to concentrate on their conversation with the clinician, if they see attentive and effective care being given to their loved one first.

Once the patient is settled, we need to consider what information the family has been given and their current understanding of the situation. Determining the goals of care, e.g., curative/restorative, palliative, or terminal (Thomas et al. 2014), for the patient provides an excellent starting point to plan an ongoing management, as medically the parameters of care should be defined. In consultation with the patient and/or their family, the next step would be to ascertain the preferred place of death and an idea of their advance care plans. Finally, these elements should be considered in discussion with the family and the treating team, to achieve a shared decision about the planned management.

The necessary conversations may have occurred previously, but a quick review of the relevant views establishes current priorities.

The condition of the patient informs the feasibility of any transfer. Hence, clinical examination and obtaining a history of deterioration are important to estimate prognosis. In some cases, the person may not be dying, and the consultation provides an opportunity to listen to their wishes. There may be an underlying reversible cause for their deterioration, e.g., infection, opioid toxicity, or hypercalcemia, that requires discussion about potential treatment. In such cases, even though treatment is possible, a decision should be made regarding the appropriateness of prolonging life, according to the individual circumstances.

Prognostication is one of the three important skills in clinical medicine; we have honed our skills in the first two, diagnosis and treatment, but neglected prognostication by comparison (Glare et al. 2008). There may be prognostic tools to help, but in our given situation, reviewing the patient with a corroborative history is key. The family and treating team should provide a trajectory of the deterioration to make a quick assessment of prognosis. Remember that the family knows the patient better than anyone and is a valuable source of information about who the patient is and their life narrative. If there are no reversible causes and the deterioration has occurred day by day, it would be reasonable to assume a prognosis of days. However, if the deterioration has occurred in hours, then a shorter prognosis of hours is likely. Any decisions made in regard to an imminent death should be supported by clinical evidence, e.g., comatose, Cheyne-Stokes breathing, and thready erratic pulse. Hui et al. determined some useful bedside clinical signs in cancer patients, to predict impending death within 3 days, i.e., nonreactive pupils, reduced response to verbal and visual stimuli, inability to close the eyelids, drooping of nasolabial fold, hyperextension of the neck, grunting of the vocal cords, and upper gastrointestinal bleeding (Hui et al. 2015).

Should the prognosis permit a possible transfer home, we need to evaluate the stability of the patient for transfer. A useful way to approach the decision is to review the last routine clinical observations, i.e., temperature, pulse, blood pressure, and respiratory rate. If these measures, or any other clinical concerns under normal circumstances, would prompt a medical emergency team (MET) review, then clinical instability for transfer exists. Review if they have symptoms that need to be managed to facilitate a smooth transfer, e.g., pain, dyspnea, or agitation. Without addressing these symptoms, the patient suffers in transit, and their care may be viewed as suboptimal. The transfer reflects the care we provide to the patient and family; therefore how stable the patient is in transit and on arrival at the destination is a testament of that care. Hence, the decision to transfer a person who is imminently dying is a difficult balance between respecting the views of others and maintaining our professional and personal standards of care.

5 No Transfer Due to Imminent Death

Transfers are unlikely when the prognosis is estimated in hours. In the context of respecting the wishes of a patient and/or their family, delivering such a short prognosis may lead to a volatile situation. There may also be anger about the inability to fulfill the dying wishes of the patient. The clinician should be prepared to encounter and manage any reaction from the family, including potentially violent or abusive behavior. Although we may understand the grief and anger in certain situations, personal safety measures should be implemented as a priority if deemed necessary. Preempting how families may react, after assessment of the situation, may change the approach to the consultation.

The prognosis may be a relief to the family, or at least some of them, but an explanation of the reasoning behind the timeframe and the reluctance to transfer must be clear. Going through some symptoms and signs of dying may be helpful, if appropriate, supported by leaving the family a pamphlet with this information that can be reviewed as needed. Be prepared, and offer, to

repeat any information to the family. Where possible, consultations accompanied by another healthcare professional (e.g., nurse, social worker, pastoral care worker) can help with safety issues, as well as respond to the emotions of family members.

The potential of deterioration in transit should be emphasized and can act as a sobering reminder of the inherent risks of the transfer. Instances do occur where families refuse the advice to remain in the current venue of care. In a community setting, an ambulance may have been called, and the decision rests with the ambulance crew. Without prior warning, the scenario is difficult for ambulance staff that will invariably try and adopt the best approach for the patient and the family. In ward settings, the family may carry the person to their vehicle and request the help of staff to aid them. As traumatic as these events are for staff, keeping the focus on the family can sometimes diffuse the situation. Should a hospital discharge occur against medical advice, then liaison with the GP, community services, the CPC team, and other family members may provide the required support in the community.

We do have a primary duty of care to the patient, and so emphasizing that ongoing care will be provided to support family can be helpful. It may be useful to point out how comfortable the patient is at present and that moving them is likely to disrupt their stability. If possible, allay any feelings of guilt or failure in the family, and positively reinforce the efforts they have already made. Emphasize that the patient will be less aware of their actual location but may be more responsive to family around the bedside. It is a time for the family to come together and be present for the patient, as well as each other. It is perhaps more a time for them to be family, rather than adopting the additional roles of nurses, doctors, and pharmacists. Reassure them that it will be our responsibility as healthcare professionals to ensure the patient's comfort and to support their grief. Enquire how we may best support them spiritually or culturally, and do not make any assumptions. Be present, be human, and be kind – many situations will be diffused with this approach.

There are some instances when the clinical needs of the patient would automatically preclude the possibility of transfer. Examples include patients who would die soon after extubation, patients requiring high-flow oxygenation, and patients who require ionotropic support to remain clinically stable. Often these patients would be on intensive care units, and weaning or ceasing life-supporting measures occurs after a consensus decision. A period of 24h usually provides some evidence of stability for transfer if still desired. Practically, the options for venue of care/death would be, in order of clinical preference, a ward in the hospital, the palliative care unit (PCU), or home. However, there are cases where patients have been extubated at home (Unger 2016; Mann et al. 2004). The extent to which services are prepared to help home deaths can often be admirable, especially in pediatric cases (Needle 2010). However, many more cases miss the opportunity to facilitate a home death due to late discussions, referrals, and coordination of care.

6 Transfer Options

Once the decision to transfer a patient has been agreed upon, the organization of the transfer can begin. The palliative care team is often required to coordinate efforts to ensure the smooth transition from one care setting to another. A checklist can ensure that nothing is forgotten but also streamline the process and reduce the time for transfer, especially when busy. These checklists can be sent to community teams, to ensure all tasks have been completed and education continues. The Liverpool Care Pathway for the Rapid Discharge Home of the Dying Patient provided effective guidance in EOLC (Murphy et al. 2004; Ahearn et al. 2013) and has been incorporated in other EOLC guidelines, e.g., Te Ara Whakapiri: Principles and guidance for the last days of life (the New Zealand EOLC guide).

Ambulance crews can be very helpful and flexible with transfers to the preferred place of death. Importantly, a "do not resuscitate order" is vital for the transfer. They will usually need to know about access to the house, if the venue is home, in

case they need an extra person to assist in the transfer. If any charges are incurred for ambulance trips, then families should be notified of the cost. It is also important to notify the ambulance crew and the family of what should happen if death occurs in transit. The standard advice is that they should continue to the final destination, alerting those who may be awaiting their arrival. Here the family can be supported and the necessary arrangements made to manage the deceased.

Once a discharge to the community has occurred, some palliative care services have a rapid response team, allowing the enhancement of care alongside existing services. They may provide a short period of care until the CPC team can takeover or provide support for EOLC at home or in aged care facilities (Gage and Holdsworth 2015). It may also be possible to optimize EOLC in aged care facilities post-discharge using hospital subacute services that visit them. A collaborative and educational approach between palliative care, elderly care, and aged care staff can ensure patient wishes are respected.

In the following sections, we consider each possible transfer and the role of the palliative care team in facilitating the urgent relocation.

7 Transfer from Ward Facility to Designated Home Setting

A meta-synthesis of qualitative studies over 25 years (1990–2015) provides seven themes that patients viewed as important for EOLC in acute hospitals. These are expert care, effective communication and shared decision-making, respectful and compassionate care, adequate environment for care, family involvement, financial affairs, and maintaining a sense of self. Apart from the last theme, family members shared the previous six perspectives. However, the same study also found four themes specific to the views of family members. They believed that maintaining patient safety, preparation for death, bereavement care, and enabling patient choice at the end of life were important to EOLC in acute hospitals (Virdun et al. 2016). These findings perhaps give an idea of what needs to be achieved in acute hospitals to optimize EOLC. They also provide an insight into why patients and families may want to leave hospitals at the end of life.

If a transfer is deemed appropriate from a ward setting, then a hospital palliative care team (HPCT) can assist in the discharge. As stated earlier, the timing of the referral can affect the urgency and the ability of the HPCT to meet expectations. The lead clinical team on the ward should be guided in the tasks needed to transfer care to the community. Liaising with the CPC team or the district nursing team, as well as the GP, will be critical in ongoing care at home. Discharging someone home without the support in the community to continue care only increases the chances of readmission and burdens the family with unwanted stress. Early notification to the relevant community nursing services will allow the service to better prepare for the transfer home. It is often reassuring for families to know when these services will be visiting. A GP who can visit, as mentioned earlier, is integral to the network of healthcare professionals who will contribute to the EOLC at home and fulfill the lead medical role in the community.

The lead team on the ward may have notified members of the allied health team appropriately, but the HPCT should ensure that the right individuals remain involved in EOLC. These may include:

- Case managers (with essential knowledge of the patient, family, and clinicians involved in the patient's care in particular conditions, e.g., motor neurone disease patients)
- Pharmacists (both hospital and community pharmacists – to ensure appropriate medications are in place)
- Occupational therapists (to maintain daily activities as much as possible for both patients and carers, e.g., via equipment/aids to facilitate ongoing care).
- Physiotherapists (for mobility reviews if needed, soft tissue and therapeutic massage, and advice on passive movements and positioning)

- CPC teams (especially the nurse that will visit the home post-discharge)
- Music therapists (to provide support and symptom relief)
- Home-based care programs (either to cease or increase their involvement)
- Social workers (for patient and family advocacy, counseling, loss and grief support, family support, and social services support)

The involvement of these allied health professionals contributes to the holistic goals we aim to achieve in palliative and EOLC. Furthermore, there may be some continuity of care provided by these members of the healthcare team who have supported a patient and family over a number of previous hospital admissions. Their support and knowledge of the patient and family, and how they have coped with the episodic deteriorations, can provide valuable insights into EOLC.

The physical needs of the patient may require several pieces of equipment for home care. For example, a hospital bed and air mattress will aid EOLC for patients and their families; an oxygen concentrator will be required for hypoxic patients, where dyspnea is distressing. During the coordination of the transfer home, the delivery of equipment will require a family member to take responsibility to permit entry into the house and inform of access and location for the equipment. Occasionally, families may be so keen to get home that they may not wait for equipment, e.g., hospital bed, and prefer to let the person sleep in their own bed. It may be a small detail, but hospital beds are not invariably double beds that may allow the intimacy of a couple sharing their last few nights together. A pragmatic approach should be adopted, where advice should be documented, but we work to facilitate the transfer home as the main objective. Waiting for the safest transfer, at such a critical time, may jeopardize the goal – most families will wait for deliveries or pick equipment up once the patient gets home.

The family should be aware of the care that will be required at home. Although nursing a bedbound patient is often deemed easier in practical terms, performing personal care for their loved one may still cause distress. An early family meeting, involving a social worker, can clarify and inform the family of the undertaking ahead and determine if a transfer will occur. It can be helpful to highlight the shifts of professional carers involved on the ward each day, so that family and friends can be prepared for what is required once at home. The discussion should not aim to dissuade the family but to provide an informed decision about the transfer.

While on the ward, families should be given the opportunity to learn and participate in the nursing care. Pressure injury prevention, with associated safe positioning of the patient, e.g., tilt and turns, should be taught by the nursing staff, and the family should be observed in their practical involvement. Mouth cares, hygiene cares, and feeding will all be areas for education. For some families, these tasks may deter them from going ahead with the transfer. By contrast, larger families may accept and share the tasks to facilitate their planned move. Equipment for hygiene care will need to be provided, and urinary retention should be excluded. The consideration of an indwelling urethral catheter may prevent distress, readmission, and inappropriate medication usage.

There may be times when the coping mechanisms of the family, or their social supports, are not sufficient to provide optimal care from our professional caregiver perspective. At these times, the multidisciplinary team involved need to make a decision about pursuing the transfer, especially if the patient is deteriorating. Families may be adamant that they will cope, either out of a sense of duty or determination to respect the wishes of the patient. In these circumstances, challenging their decision may not be helpful. It may be better to document that there are professional concerns, which the family has been advised of, but they remain steadfast in their views. Planning for the failure of the discharge may also help the family, e.g., to know that they can return to the ward or have a direct admission to the PCU, should the care become too problematic at home is reassuring. Community teams and other services, e.g., PCUs, should be advised of all important discussions, in order to support the discharge as much as possible and coordinate care as needed in a crisis.

Syringe driver orders, breakthrough medications, and emergency medications are all likely to be required via the lead medical team. Often, junior doctors will be unsure of the right medications and lack confidence in prescribing the right doses. In such instances, the HPCT can educate and support junior doctors, either via their usual practice or in conjunction with EOLC guidelines. It is also important to instill and demonstrate an ethos of holistic care, and the provision of EOLC provides an opportunity to highlight the necessity for an individualized approach. Discussions about artificial hydration and nutrition will need to be completed, also explaining the rationalization of medications due to reduced oral intake. Some deaths will need to be reported to the coroner. It is the lead medical team's responsibility to ensure that this information is conveyed to the family, as well as the process involved. However, the HPCT should check the completion of this task and also ensure the GP and community teams are advised.

Pastoral care and cultural liaison workers, if available, should address spiritual and cultural needs, respectively. There may be instances when these considerations are critical to the transfer. For example, there may be a desire for a blessing or cultural ritual prior to the transfer to ensure a safe passage or accommodate for a death in transit. Bereavement support should also be highlighted as a future service, so that families know who will be contacting them and when. Hence, as in all care, the holistic approach can be a powerful factor in demonstrating a respectful approach to the patient and the family if the right conversations are undertaken.

Patients returning to aged care facilities may require a higher level of care than they had previously. In some countries, there may be a requirement to reassess the current level of care required before the patient can return to the facility. Here, allied health assessments are essential if the diagnosis of dying is not so clear. Even under these circumstances, many facilities will need support from GPs and CPC services. Usually staff from these facilities are eager to continue the care of their patient and keen to learn about palliative care skills to help them. As with families caring for a loved one at home, the symptoms and signs of dying may need to be reiterated, with instructions to call the GP or CPC team if needed.

8 Transfer from Hospital Ward to Palliative Care Unit

The transfer to a PCU is often managed by a HPCT. However, in the absence of such a team, admissions are arranged directly with the PCU using admission criteria. PCUs vary between those that accommodate more acute cases and those that operate solely for the imminently dying. In the USA, the latter PCU is termed a "hospice." Although PCUs differ in practice across the world, the common grounds for admission may restrict some patient transfers. For example, a family may want to continue intravenous fluids and antibiotics due to preferences for their loved one, but some hospices may not facilitate such treatment. Admission to the PCU may be dependent upon the cessation of the intravenous management and appropriate conversations with the family, hence delaying the transfer.

There are many issues to consider in these transfers. The lead clinical team on the ward will value a transfer based on their assessment of the patient, their confidence in caring for a dying patient, the family expectations, the acute bed status of the ward, and the empty beds available in the PCU. These are all valid considerations, but often the acute hospital is unaware of the demands on the PCU from community patients, as well as other hospital campuses.

PCUs should provide specialist palliative care services to those patients admitted to its care. Hence, the question often raised by the PCU staff is whether the admission from the acute hospital requires specialist palliative care management. EOLC guidelines, such as the Liverpool Care Pathway (LCP), were developed to help manage the nonspecialist palliative care deaths occurring in acute hospitals or in the community. However, misuse and media interpretation of the implementation of these guidelines has undermined the intention to improve the standard of EOLC outside PCUs. In services where a HPCT exists, many patients can be supported in

the acute hospital setting via the collaboration with acute teams. For many clinicians, the ability to continue caring for patients and families familiar to them is both personally and professionally rewarding.

Organizational imperatives, such as patient flow, are more prominent when the PCU is part of the acute hospital system. Within such organizations, the movement of patients to the most appropriate ward is a priority, and PCUs are often considered the best site for EOLC. Tensions can arise when seemingly all deaths are referred to the PCU, irrespective of their need for specialist palliative care. Determining the urgency for transfer on the basis of patient or family need should be the PCUs objective, but it can often be challenging. The organizational need for an acute bed may be the main factor behind a referral and can be difficult to defer when PCU beds are empty. Once again, a HPCT can clarify the need for transfer and ensure supportive care until the move can occur. When PCUs are not governed by the acute hospital organization, referrals can be reviewed without the same pressures and therefore ensure the appropriate patient cohort for the PCU.

Another important factor in transfers from acute hospitals to PCUs is the distance between the two facilities. The movement of a patient in the terminal phase of their illness is affected by the transit mode and duration of the transfer. The HPCT will need to decide if the person is likely to survive the trip, whether by ambulance, helicopter, or airplane. The same issues apply with regard to the comfort of the patient during transit, as discussed earlier. The balance between the stabilization of symptoms and the goal of preferred place of death often means a compromise. Pre-transfer medications are usually given to ensure comfort, but the longer the trip the riskier the transfer becomes in terms of comfort or death in transit. Hence longer trips may not be sanctioned by HPCTs.

A family meeting, led by the social worker, is the best initial process to ensure all parties understand what is happening. A member of the HPCT should attend the meeting not only to hear the discussions and meet the family but also to demonstrate a clinical handover of care. The HPCT can clarify the workings of the PCU and arrange the transfer at the most appropriate time. Some family members may not accept that death is imminent for their loved one. Acute care interventions, delayed decisions, and the fear of the PCU may all delay the transfer. Many family meetings may be required to gain a consensus plan, but transfer without such agreement will only cause more problems on the PCU.

9 Transfer from Designated Home Setting to Ward Facility

If most people want to die at home, then community services are tasked with the challenge to keep people at home, under difficult circumstances. A recent review of the essential components of quality community palliative care reports six vital requirements: integrated teamwork; management of pain and physical symptoms; holistic care; caring, compassionate, and skilled providers; timely and responsive care; and patient and family preparedness (Seow and Bainbridge 2018). These are the elements that all healthcare organizations strive toward, but the aging population remains a challenge that will increase demands and place community healthcare under immense strain.

There are two major settings to consider as a designated home for people. The first is the usual private residence, recognized as home, and the second is an aged care facility. Each has their problems in the transfer of patients into a ward, whether acute or subacute in nature. Subsequently, we shall consider them separately in the following discussion.

9.1 Transfers from Home

People dying at home may, or may not, be known to a CPC service. GPs and district nurses can usually provide support to carers at home and obtain advice from CPC services as needed. Dying at home remains difficult in the cities of the western world, as discussed earlier. In many cases the social networks are less prominent than in former years, prompting a movement for

"compassionate communities" and EOLC as a focus for public health reform (Kellehear 2013; Sallnow et al. 2017). The concept is growing from a public health perspective, to better support carers in the community and recreate links within our societies based upon compassion. Many rural and traditional communities have operated in a similar fashion for years, due to the close-knit relationships and traditions over many generations (Sallnow et al. 2010).

CPC services vary around the world in terms of personnel, provision of care, and funding. The aim may have been to facilitate dying at home, but more modern services are aware of the changing needs of the population. People may want to be admitted to a hospital or PCU for a number of reasons, and CPC teams should recognize the choices made regarding the venue of death. Early recognition of deterioration can trigger discussions about transfer from the home environment. Usually, CPC teams liaise with PCUs for an admission as early as possible. However, a PCU bed may not be available when required and hence an urgent admission via the hospital system is necessary. The emergency department (ED) should preferably be avoided, but families usually value being rescued from a crisis situation at home even if an admission must occur via the ED. There is still merit in these admissions, e.g., there may be continuity of care with the lead treating team, reversible causes of deterioration can be reversed, and patients who refuse a PCU admission can be reviewed and followed-up by the HPCT if they get admitted.

Once again, the assessment of the dying patient is critical. Home visits often encounter families who have been struggling for days to maintain the level of care required. These later reviews may find an imminently dying patient, who is too unwell to transfer. However, community teams facing such a scenario need to act calmly and quickly to deal with the situation. Families who are keen for a transfer to occur may pressurize the visiting clinician for an admission; similarly the clinician may also feel the least risky decision is to admit. Both the needs of the patient and the family can underpin these decisions, but invariably a PCU bed will be sought if possible. It should be noted that community palliative care staff might walk into unexpected scenarios of despair and distress. The consultation may be the first with the family about the seriousness of the situation, and establishing a quick rapport can be difficult. Subsequently, the clinician receiving the call from the CPC nurse should recognize the predicament the patient, family, and CPC nurse is facing.

There are times when some admissions to a PCU do not match the specialist palliative care criteria for entry. These referrals may emanate from the community, where the home option is no longer viable due to the level of care and support that are required. Recognizing this fact, PCUs prioritize community referrals above hospital referrals, where the clinical teams are available and can be supported in delivering palliative care. Clinicians triaging these referrals often understand the community situation and accept the referral, even though it may be deemed "inappropriate" for a specialist unit. The quicker the decision is made, the sooner the referring clinician can inform the family and organize transfer.

9.2 Transfers from Aged Care Facilities

Aged care facilities are the homes for many frail people in our population. In many countries they may be divided into high-level (nursing homes) and low-level (residential homes) care facilities. People with higher nursing care needs are more likely to require palliative care services; however not all facilities are served by CPC teams. CPC support may be provided for the staff at aged care facilities but may not be as "hands-on" as desired. Staff would certainly benefit from, and appreciate, the clinical experiential learning from CPC teams.

Medical support is also required. GPs may be associated with the patients by virtue of the facility or via an ongoing relationship that began before admission to the facility. Patients who want to die in the facility should be known to the GP and linked in with the CPC team. Out-of-hours care may involve locum medical staff, where acute decisions may not be underpinned by patient or family wishes. Here again the

importance of advance care planning is highlighted for those out-of-hours visits. Locums will refer people to hospital, if they are unsure of the clinical plan for the patient or the wishes of the patient/family under certain circumstances.

Ideally, patients admitted to aged care facilities should be asked about their wishes at the time of their admission to the facility. Conversations at this time, involving substitute decision-makers, will inform future care planning. Although these conversations may seem straightforward, how they are performed and updated require careful consideration. Firstly, the circumstances of the admission to the facility should highlight the more vulnerable and frail nature of the patient. A review of their deterioration can give an idea of their disease trajectory, but their comorbidities also factor into the prognosis. The GP has a major role in these conversations, to guide and coordinate the views of patients, families, and specialists in an advance care plan. How these conversations occur will determine the effectiveness of the plan created. Medically the goals of care need to be clear, and the patient's wishes need to be woven into the management plan. Conversations about death and dying may need to occur, at a time when functional change is traumatic for both the patient and members of their family. However, these conversations cannot be delayed.

Once an advance care plan is achieved, there should be accompanying medication changes to deal with the immediate care and future care. De-prescribing allows a streamlining of medications, but planning for emergencies may prevent an unnecessary admission. An awareness of potential modes of deterioration should be in the forefront of the clinician's mind when reviewing the patient. Are they likely to have a catastrophic event, e.g., massive gastrointestinal hemorrhage, or massive hemoptysis? Is a clinical deterioration in condition likely sooner or later? If so, these are further conversations that should occur with the family and staff of the facility.

A completed advance care plan will need to be reviewed and appropriately updated. When should this occur to remain up to date? Certainly, after an acute admission to hospital, there should be a review of the plan. However, it may be prudent for the staff of the facility, the family, and the GP to meet periodically to review the patient's progress and to plan for any deterioration. There may be a presumption that the patient and/or the family will prefer conservative management in the aged care facility. Once again, assumptions should not be made, and possible transfer options should be discussed. If the patient and family wishes are clear that a hospital admission should be made, then staff can respond appropriately if deterioration occurs.

Another option may be the admission to a PCU. Often, these admissions are firstly discussed with the CPC teams. Support may be provided to the facility staff and GP, but two triggers may change this approach. Firstly, the patient may display specialist palliative care needs, e.g., uncontrolled pain, dyspnea, or terminal delirium. Secondly, the family or staff may decide that care needs are not being adequately met in the facility. In the latter cases, an admission to either an acute hospital or a palliative care unit may rescue the situation sufficiently to minimize suffering and potential bereavement complications. Once again, the timeframe to plan the transfer to another venue of care can be limited.

Generally, the ambulance transfer can occur rapidly once the decision has been made. The hope is that the decision is a well-informed one and reflects the wishes, values, and expectations of the dying person concerned.

10 Transfers from a Palliative Care Unit to the Acute Hospital

Admissions to a PCU usually have a specific goal of care in mind. End-of-life care is often the main goal of care, but in the modern hospice setting, other goals may exist. For example, the admission could be for symptom management and then discharge home. For some patients, a period of assessment may be required. In such cases, the patient may eventually go home, require placement in an aged care facility, or enter the terminal phase of their disease. Time often allows the inpatient palliative care team the ability to review the prognosis and plan care accordingly.

However, in modern PCUs there may be a need to transfer the patient back to the acute hospital. A family meeting, led by a social worker, is often the best forum to discuss the transfer and prepare appropriately, if possible. There may always be the potential for the patient to die before the transfer, but the team should prepare and advise according to the discussion above. Further coordination is required with the hospital teams, in order to facilitate the best support for the patient and family.

Families may be keen for a transfer, as they may have not understood the philosophy of the PCU. Hope can be maintained by a transfer, as "more can be done" in the hospital. Some family members will find it difficult to leave the PCU, especially if they believe the decision to leave is wrong. Families often struggle with the emotions between the devotion to the dying person and their wishes, the practical issues of coping with the decisions, and the safe haven of the PCU.

Another factor to consider is the relationship the patient and family may have with their treating team in the acute setting. Many patients with chronic diseases will have developed a strong bond with the multi-professional team on the acute ward. Examples include patients with end-stage renal disease or end-stage chronic obstructive pulmonary disease. The relationship may also be reciprocal with the acute care staff, as often displayed by their willingness to care for these patients at the end of life (Gott et al. 2013).

In the current healthcare system, patients and families often have a misperception of palliative care. Without time to process the need for palliative care, it is not difficult to understand the reluctance of some patients and families to stay in the PCU. The familiarity with the acute hospital team and the environment is one factor, but the kind of medicalized care provided is another. The mismatch of expectations and experiences can prompt a request for a transfer back to the acute hospital. Sometimes the transfer may be difficult to facilitate, due to organizational systems, but invariably an understanding can be reached from a patient-centered approach.

Once in the acute hospital, the HPCT may be able to monitor the progress of the patient, collaborate with the lead clinical team, and support the family as required. Abandonment of the patient and their family can be an important factor in the delivery of care, during the terminal phase of an illness (Smith et al. 2016). Even if the HPCT is not required, the supportive role can remain significant for all concerned. The lead clinical team will require a handover, due to the complexities of care. In both scenarios, the HCPT should be involved and relevant to the supportive processes.

11 Conclusion

Transfers to a chosen venue of death require planning, clear goals of care, and empathic communication in order to facilitate a smooth transition of care. The knowledge of the patient and family wishes, as early as possible, is critical to allow the coordination of required services. The introduction of more systematized advance care planning in our communities, and increasing societal conversations about death and dying, provides useful opportunities to plan care. Ultimately, under difficult circumstances, we are trying to honor the wishes of a dying person. For those people whose goal we achieve, there is much satisfaction and gratitude. There may be instances where the goal was achieved, but how we were successful was less satisfactory. Finally, there will be times when we failed to achieve the goal and there is disappointment and anger. In each case there is an uncertainty to accept and a reflection to learn from, but how we fought to realize someone's preferred place of care and then death will live with families as a memory of our respect for their departed.

12 Summary

The preferred place of death remains an important factor in good EOLC but may not always be the home setting we are led to believe. Many people prefer other venues of death, for many reasons including societal, cultural, and psychological considerations. A recent systematic review of the

barriers and facilitators to dying at home provides a succinct overview to facilitating the preferred place of death. The facilitators include coordinated care, skilled staff, effective communication, and support for patients and HCPs. On the other hand, the barriers included a lack of knowledge, skills, and support among informal caregivers and HCPs; informal caregiver and family burden; recognizing death; unfavorable social circumstances; inadequate discharge processes; condition-specific discrepancies, e.g., the inequity of access to palliative care for people with nonmalignant conditions; and poor planning (Wahid et al. 2017).

Whatever the setting of care, the early knowledge about the wishes of the patient is important. Only then can we plan and realistically obtain a smooth transition to the venue of death. Prognostication adds to the complexity of the situation, amidst the current standards of healthcare communication. These decisions cannot be made lightly but are often made in emergency situations. Taking the time to understand the decisions of patients and the families can ensure the right choices are made in the timeframe available. The coordination of services, reduction of adverse risks, and compassionate communication help achieve the best outcomes in these situations.

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Challenging Family Dynamics

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_86

Abstract

At a time when palliative care guidelines are advocating greater respect for patient autonomy and the inclusion of patients and families in decision-making with clinicians, families themselves have become increasingly complex and more broadly defined. Some families bond internally with one another and with the clinicians to best meet the needs of the patient despite the significant stress of facing the death of one of their members; others become more obstructively dysfunctional, jeopardizing patient care and creating stress in the healthcare system. Conflict may arise from the interaction between the nature and circumstance of the patient's care and contextual family factors reflecting structure, dynamics, and prior history. Thorough family assessment can provide a basis for interventions to avert a crisis. Early recognition and management of potentially damaging family conflict is illustrated throughout this chapter by clinical vignettes. The published literature and the clinical experience of the authors are drawn upon to illustrate the management of situations that threaten to escalate out of control. The need for communication skills training for all staff involved in palliative care is highlighted.

1 Introduction

Care of the dying person has involved the family from the inception of the hospice movement (Saunders 1978). The term "family" cannot be regarded as a unitary entity (Wellisch and Kissane 2009). Families may include not only the traditional model of parents, children, extended family, but also same-sex couples, former partners, stepfamilies and blended families, adopted or fostered children, friends, partners, and caregivers who are regarded by the patient as "family." Cultural and religious factors also influence not only who is identified as family, but also the function and role of its members (Baider and Goldzweig 2012). A broad understanding of the many subsystems under the rubric of "family" that are thrust together into the physical, psychological, existential, and spiritual space of a person suffering from terminal illness is needed. Without this, health professionals will miss the opportunity to optimally ease the patient through the dying process and assist the family into the bereavement phase.

Very few families are perfectly cohesive; even "healthy" families can become temporarily dysfunctional during a normal process of adaptation when catapulted into the intensely emotional, confronting, and unchartered world of a dying family member. Family conflict is not a

unidimensional construct and can become quite complex (Kramer et al. 2006). Long-standing, entrenched, and maladaptive patterns of coping, communicating, and relating (often transgenerational in origin) are brought into high relief in the complexity of palliative care settings (Lichtenthal and Kissane 2008). Family context includes the historical issues, family structure, involvement with care and other demands and resources, as well as the presence of substance abuse, religion, culture, and belief systems and the extent to which plans or promises have been made in relation to the dying patient (Boelk and Kramer 2012; Kramer and Boelk 2015).

This chapter will discuss different palliative care service sites, setting the scene for emergencies involving families that may be more likely to arise, or more difficult to manage, in these settings. It will describe assessment of families, family typologies, attachment styles, and different models of family conflict and will present a series of clinical cases dealing with aspects of the family context, the circumstances and location of the conflict, the contributing factors, and the consequences of the conflict for patient, family, and staff. Management of these individual challenging situations will be described, and general principles of dealing with difficult family situations will be presented. Throughout these discussions, the importance of training in communication skills for all palliative care workers will be emphasized.

2 The Palliative Care Inpatient Setting

The inpatient palliative care unit can be an intense crucible where staff and families are thrown together for prolonged periods of time in situations of heightened emotional and physical suffering, disparate expectations, intimate spectacles, and little privacy. The goal of the admission may be symptom management, assessment, respite, end-of-life care, or stabilization prior to transfer to more appropriate longer-term accommodation. Whatever the circumstances of admission, patients and their families find themselves in an unfamiliar environment devoid of the comforts and routines of home and may feel unsettled, even when they are relieved that the burden of care will shift to the multidisciplinary team. Exhausted and distressed family caregivers may feel guilt and have difficulty in relinquishing their role. On the other hand, they may be more able to be present as supportive family members instead of having time and energy consumed by the practical and emotional demands of caring. The patient can experience even greater loss of dignity, autonomy, and independence in a hospital environment, which impacts on the family's perception of care. Pre-existing family conflict escapes from the privacy of family life into the public arena and draws staff members into a complex drama.

3 Community Palliative Care

Palliative care administered in the patient's home can avoid some of the disruptive elements of admission to a palliative care unit and is more often the preferred choice of patient's and family (Gomes et al. 2015). It allows the maintenance of normal family routines; the nurturing presence of family pets; a neighborly or community support network; the comfort of familiar objects; reminders of the life lived; and favorite views, cushions, and positions. Community palliative care staff enjoy the privilege of entering the patient's world, gaining insights into the needs and functioning of the family and an understanding of how best to engage them to provide optimal care. There are additional challenges, however, as staff do not have the same degree of control or certainty about the care the patient is receiving and lack the backup of a multidisciplinary team when difficulties arise. Considering the family, they have no real respite from caring, even when they have a roster of availability – they cannot "go home" after an emotionally and physically exhausting day. In rural and remote areas, community teams may have to travel vast distances to provide services. Some teams supplement their visits with Skype or FaceTime connection on mobile devices,

providing a reassuring virtual presence. Specialist palliative physicians provide regular consultancy visits to regional areas and have an on-call consultant to provide telephone advice in some countries. People requiring palliative services who belong to indigenous communities may want to be cared for by their extended family, in their own familiar landscape. It is therefore important to liaise with indigenous workers who are able to sensitively interpret the needs and wishes of the patient and family (McGrath et al. 2005).

4 Palliative Care Consultation Teams

As the concept of palliative care has become increasingly integrated into general medical and surgical units, a specialized consultation team has been developed in some of the larger health facilities. These teams assess and recommend treatment for patients with malignant or nonmalignant disease who have palliative care needs. The patient remains under the care of the admitting unit, and conflicts can arise where the treating team pursues treatments that are at odds with the palliative care team's goals of care. The palliative care consultation team has a culture of holistic care of the patient and family, which contrasts with the more medical focus of the treating team. Subsequently, the palliative care consultant becomes an important link in the medicalized hospital environment. Communication about clinical information can be inadequate between teams, unless the palliative care consultant is able to participate in the multidisciplinary team meetings of each unit. There is considerable variability in the respect shown for the palliative care consultant's perspectives and recommendations, both between the senior doctors of the same unit and between units. The stable nature of the palliative care consultation team contrasts with the rotating junior medical staff and in complex cases may provide the only source of continuity and "holding of the story" for patients and families. Medical and surgical teams are often reluctant to acknowledge that a patient is dying and generally lack the specialist communication skills training of their palliative care colleagues. As a consequence, there is often poor preparation of patients and families for death and a retreat from time-consuming interactions with families. Even when the treating team is on-board with the person- and family-centered approach to clinical care, arranging a full family meeting with members of the treating team and the palliative care consultation team can be logistically difficult; in a general hospital setting, there is often less space and fewer resources to deal with the needs of the family.

5 Assessing Families

Assessment of family structure and functioning needs to begin from the earliest contact with a patient entering palliative care. It may begin with the construction of a genogram, which notes not only the members of the family of origin and generative family of the patient (as well as others considered by the patient to be family) but also significant information about their relationships, occupation, closeness or estrangement, role in decision-making, mental and physical health, previous loss and trauma, substance abuse problems, beliefs and values, and potential sources of conflict. Having some foreknowledge of family dynamics helps the clinician to understand what might be happening when crises arise with families at a time of heightened distress and guides effective communication strategies.

Further understanding of the family functioning develops over time with skillful observation of interactions between patient and family, family members, and family and staff. Evidence of particular strengths, vulnerabilities, coping styles, and issues not initially apparent may emerge in the process of engagement with the family. These observations should be shared at team meetings so that a comprehensive picture of the patient's world can be created. Well-conducted family meetings, which are encouraged in palliative care settings (Hudson et al. 2009), allow further opportunities for observation of family dynamics. They are not only useful for discussion of goals of care, treatment options, and care planning with the patient and family but can be optimized through circular

Table 1 Strategies for conducting a family meeting in palliative care (Lichtenthal and Kissane 2008)

Strategies for conducting a family meeting[a]
Planning and prior setup to arrange the family meeting
Welcome and orientation of the family to the goals of the family meeting
Check that each family member understands the illness and the patient's prognosis
Check for consensus about the current goals of care
Identify family concerns about their management of key symptoms or care needs
Clarify the family's view of what the future holds
Clarify how family members are coping and feeling emotionally
Identify family strengths and affirm their level of commitment and mutual support for each other
Close the family meeting by final review of agreed goals of care and future plans

[a]Content reproduced with permission from Lichtenthal and Kissane (2008)

Table 2 Practical elements of the family-focused grief therapy model (Kissane and Bloch 2002)

Practical elements of the family-focused grief therapy model[a]
Build rapport with each family member to create a therapeutic alliance
Elicit concerns
Acknowledge and foster family strengths
Focus first on improving teamwork and communication and then target conflict
Remain neutral
Reframe by shifting attention away from content of arguments to underlying meaning (i.e., why they feel so heated, what the difference represents)
Pose questions that invite reflections and curiosity
Invite storytelling
Generate hypotheses about family dynamics related to cohesiveness, expressiveness, and conflict resolution
Summarize hypotheses for consideration and modification

[a]Content reproduced with permission from Kissane and Bloch (2002)

questioning to reveal how the family members relate to each other, if there are any possible conflicts or misunderstandings, and their perceptions, hopes, and fears. Good communication skills are essential for conducting a family meeting so that each member feels supported and heard. Table 1 sets out strategies for conducting a family meeting in palliative care (Lichtenthal and Kissane 2008). Practical strategies from family-focused grief therapy (FFGT) (Kissane and Bloch 2002) are outlined in Table 2 and can be used to explore family dynamics, communication patterns, and areas of conflicting views. The styles of questioning used by therapists in FFGT are presented in Table 3 and may be useful in family meetings (Kissane and Zaider 2011).

6 Typologies of Family Functioning

Four fundamental interactional concepts in families dealing with a terminally ill member described by Wellisch and Kissane (Wellisch and Kissane 2009) are:

- *Homeostasis* (the relative constancy of the family internal emotional environment when dealing severe stresses)
- *Bonding* (the ability of the family to maintain its own territory by regulating the incoming and outgoing people, objects, and ideas)
- *The family system* (whether open, closed, or random)
- *Resilience*

Kissane and Bloch (2002) introduced a different way of describing family types in their extensive study of grief and psychosocial morbidity in bereaved family members. The patterns of emotional functioning have been characterized as supportive, conflict-resolving, intermediate, sullen, and hostile. Using the Family Relationship Index, they derived scores on three key dimensions of family competence – cohesiveness, communication, and conflict resolution. The dysfunctional families in this framework are the hostile families, who show high conflict, low cohesiveness, and poor expressiveness and sullen families who had more moderate limitations in these domains. Families with moderate to high levels of cohesiveness and expressiveness and lower levels of conflict were better able to adapt to the challenges associated with a terminally ill family member.

Although not typologies of family functioning, there are other concepts of family relationship and

Table 3 Styles of questioning used by therapists in family-focused grief therapy (Kissane and Zaider 2011)

Styles of orientating and influencing questions asked by therapists in FFGT[a]		
Complementary types of questions	Description of the function and purpose of each questioning style	Typical examples use in FFGT
Linear (generally orientating and informative about individuals)	These generate a one-to-one conversation between the therapist and each individual, help to obtain information, join with and support individuals, prove useful when open-ended to take a history but are conservative in promoting family interaction.	What job do you have?What grade are you in at school?What sports do you like to play?
Circular (orientating and informative about family as a whole dynamics)	These seek observations from one family member about others, asking each iteratively to step into the shoes of one another and share diverse views that stimulate family discussion and reveal relational dynamics.	How are your spouse and children coping? Who talks to whom? Who are you most worried about?
Reflexive (generally influencing without being directive)	These encourage mutual understanding and support via greater insight and awareness of the meaning of any individual responses, can include hypotheses about dynamics inserted into the wording of the question, and seek to promote reflection upon solutions and consideration of acceptance or change.	What are your expectations about the future? How might things look difference in one year? If X were still alive, what would they ask of you? Why do you think they are becoming more irritable?
Strategic (both influencing and potentially more directive in intent)	These invite a search for a solution and aim to build consensus about future directions, including options for acceptance or change; if too directive, they may be constraining rather than generative.	How helpful might it be for Dad to reach out to old friends? What benefits would come from talking about end-of-life care? Might more open sharing of feelings which increase your sense of family connection?

[a]Content reproduced with permission from Kissane and Zaider (2011)

communication that are helpful in formulating the challenges faced in dealing with families in distress. The concept of **death awareness** is the subject of a seminal work by Glaser and Strauss half a century ago. They described types of awareness of dying between patients and caregivers:

- *Open* (where both patient and family are aware the patient is dying and are open to talking about it)
- *Suspected* (where the patient suspects, but dying is not openly discussed)
- *Mutual pretense* (where one or both parties of the dyad pretend that they do not know)
- *Closed* (where the caregiver is aware that the patient is dying, but this knowledge is kept from the patient) (Glaser and Strauss 1966)

Death awareness is a complex issue influenced by culture, spiritual and religious beliefs, family history, and the perception of the patient's or caregiver's ability to cope with the knowledge of impending death (Strada 2009).

The second important concept is **attachment theory** and its application to patient and family in terminal illness. In the 1950s, British psychoanalyst John Bowlby proposed that attachment of infants and children to caregivers was the expression of an innate drive to secure care and protection and hence survival (Bowlby 1969). He introduced the concepts of a *secure base* formed through attachment to a sensitive and responsive caregiver, a *safe haven* to go to in times of need, and *separation distress* when the attachment figure is unavailable. Individuals form an internal representation of their relationship with caregivers that endures in expectations, beliefs, and patterns of future relationships that are relevant to their experience of security.

In the 1960s, developmental psychologist Mary Ainsworth explored patterns of attachment through her strange situation research (Ainsworth

et al. 1978). She described three basic types of attachment – secure, insecure anxious/ambivalent, and insecure anxious/avoidant – to which a fourth pattern disorganized/disoriented was added by a colleague Mary Main (Main and Solomon 1990). The attachment system is inevitably activated in the situation of a dying family member, where the impending separation is irrevocable. In the decades of research on attachment theory, increasing attention has been paid to how attachment styles manifest within families and in the patient-clinician relationship. Petersen and Koehler (2006) use their observations of attachment style, evident in the first encounter with the patient and family with the powerful activator of impending separation, to inform psychotherapeutic intervention during the terminal phase. They note that even patients who have a disorganized attachment style can, with sensitive care, come to experience a secure and stable attachment for their remaining lifetime.

Milberg and Friedrichsen (2017) interviewed families during the delivery of palliative home care to patients. They found that family, friends, health practitioners, pets, and for some people God were described by patients as a source of security and trust. The comforting contact could be of a physical or nonphysical nature (e.g., by telephone). When strong, these attachments could provide a sense of security in the threat of progressive illness, and they could then focus on everyday life in the knowledge that they were being competently cared for. Some family members however experienced a fading sense of security as the ravages of illness altered the patient's personality and behavior, and this loss was accompanied by a deep loneliness. These authors recommended that each patient and close family member be assessed in relation to attachment by asking: "When you are afraid or feel insecure, who or what is a potential source of comfort to you?"

Recognizing that attachment styles affect both help-seeking behavior and the capacity to be soothed by, or accept help from, healthcare professionals, Tan et al. (2005) explored the empathic responsiveness of clinicians to specific attachment needs and fears which might significantly influence the success of the therapeutic relationship. Patients with *disturbed attachments* may find the vulnerability associated with dependency on others so intolerable that they wish to escape through death, and a tailored therapeutic response is essential. Patients with *dismissive attachment* styles may close off their feelings and maintain contradictory needs for autonomy and support. An approach allowing active participation in treatment or care decisions can enable an acceptance of emotional support on these patients' terms. Patients with *fearful attachment* styles have difficulty acknowledging their emotions, dependent needs, and feelings of vulnerability because they find them threatening and may appear to reject help. Facilitating awareness of these factors may initially be met with anger but can pave the way for a new equilibrium with family members and clinicians. The extreme anxiety that characterizes patients with *preoccupied attachment* styles can exhaust staff and family members who find these patients excessively needy, demanding, and unable to be reassured. Providing structured, reliable, and consistent time with staff and setting clear limits can reduce anxiety and fears of abandonment and lessen caregiver burden. It is important to acknowledge that clinicians bring to the relationship with the patient and family their own attachment history and need to be sensitively attuned to how this may contribute to the interpersonal dynamics.

7 Ethical Considerations in Relation to Families

When family members take on the role of "caregiver" of their terminally ill loved one, enormous stress is placed on the relational dynamic as they cope with increasingly complex care needs (Given et al. 2001). The World Health Organization (WHO) definition of palliative care states that the palliative care aims to improve "...the quality of life of patients *and their families* facing the problems associated with life-threatening illness. . ." (Alliance WPC et al. 2014).

The well-being of family members and caregivers has significance for the overall well-being

of the patient, with a meta-analysis suggesting that a reciprocal caregiver-patient dyad occurs whereby the patient is significantly influenced by the distress of the caregiver and vice versa in an "emotional system" (Hodges et al. 2005). This consideration holds even greater importance when working with challenging family dynamics, as the focus of care can become so overshadowed by conflict that failure to consider family member well-being and relational dynamics could further aggravate existing issues and distress.

The ethics of providing care for both patient and family brings up questions about boundaries of provision of support in challenging situations and the way forward can be unclear. The four general principles of medical ethics are:

- Respect for autonomy/persons (accepting the right of a person to decide what is done to them)
- Non-maleficence (do no harm)
- Beneficence (acting in the best interests of the patient and family)
- Justice (duty to treat all patients with the same dedication)

These are useful to consider in light of challenging situations. For example, a family member with a personality disorder who provokes punitive or evasive reactions in staff can cause team members to fail to observe the principles of non-maleficence and justice. Respect for autonomy can also be extremely problematic when a family member is in strong denial about the gravity of the patient's medical condition, when family members are in conflict with the patient's wishes, and where substitute decision makers are indifferent, incapable, or opposed to what the patient would have wanted if competent.

Clinicians are faced with questions such as: "How much time and service provision should be given to dependent and distressed family members?," "Should I prescribe for a family member if they are distressed and needing pharmacotherapy?," and "How much should I protect the patient if the family is obstructing treatment?" Lederberg (2010) provides clear ideas and practical guidance for navigating "ethical stalemates" when dealing with patients and family members in oncology settings which could be extrapolated to palliative situations.

The identified family of concern in these issues may include the primary carer, a recipient of supportive care from the palliative care team, proxy decision-makers, and, very occasionally, a litigator.

Ashby and Mendelson (2008) argue that instead of ethical discussion being considered only when there is an "ethical dilemma," ethical awareness should be well integrated into day-to-day discussions and embedded in clinical practice. The authors argue that while the primary clinical responsibility is to that of the patient, the family is also embraced in the palliative care model. However, they caution that not all family members wish to be the recipients of care themselves. As such, the provision of service or support to family members must only be provided with explicit consent (Ashby and Mendelson 2008).

The difficulty facing many palliative care staff in highly complex situations is that the "true" nature of problems can be hidden under layers of strong emotional reactions to cases, resulting in intransigent clinical positions. Discussions discriminating facts from beliefs or values held by staff can be beneficial in assisting staff to step back from the clinical situation to gain a more objective view. Where negotiation with all parties fails to move beyond an impasse, the patient's well-being and comfort remain at the fore, and medicolegal advice may need to be sought (Ashby and Mendelson 2008). Where the needs of a family member go beyond what palliative care teams are resourced to provide, or clearly require specialist assistance, the team need to refer the family member to the appropriate service outside of the team (Hudson et al. 2009).

8 Culture, Religion, and Belief Systems Impacting on Work with Families

In Western cultures, emphasis is placed on fulfilling the patient's wishes with secondary consideration given to the minimization of family distress. This contrasts with collectivist cultures, where decisions are deferred to the

Table 4 Cultural diversity (Baider and Goldzweig 2012)

Cultural diversity[a]
Emphasis on individualism versus collectivism
Definition of family (extended, nuclear, nonblood, kinship)
Common views of gender roles, child-rearing practices, and care of older adults
Views of marriage and relationships
Communication patterns (direct and indirect; relative emphasis on nonverbal communication; meanings of nonverbal gestures)
Common religious and spiritual-belief systems.
Views of physicians
Views of suffering
Views of afterlife

[a]Content reproduced with permission from Baider and Goldzweig (2012)

family unit as a collective rather than promotion of patient autonomy (Lederberg 2010). For instance, most Asian cultures have family-based decision-making processes; conflict within these families can impede these processes and lead to hostility among members (Lichtenthal and Kissane 2008). Muslim families believe that the ultimate decision-maker is Allah; they believe in predestination and attribute the occurrence of disease as the will of Allah. No one but Allah knows the future, which makes discussions about prognosis from a Western perspective difficult, although it is permissible to explain the natural history of a terminal illness in general terms. Decisions are made about care by the male family leader and females are unable to influence his decisions. The authority of the family overrules the patient's autonomy (Baider and Goldzweig 2012). It is important to respect the rituals of prayer that need to be accommodated into the treatment plan. In different cultures, physical and existential pain may be experienced differently; some cultures may value suffering; others may see it as God testing their faith, a divine punishment, or a mark of shame or guilt that must be hidden (Surbone and Kagawa-Singer 2013). Culture, religion, and belief systems also influence the way illness is expressed, the extent to which people seek or accept psychological help, truth-telling, and coping style. It is important not to make assumptions based on stereotypes of different groups, as there are wide variations in adherence to lore and intergenerational differences that are determined by the degree of acculturation of immigrants from another background. Table 4 demonstrates the different aspects of cultural diversity (Baider and Goldzweig 2012).

9 Context of Challenging Issues with Families

9.1 Families in Conflict with One Another

All happy families are alike; each unhappy family is unhappy in its own way (Tolstoy 1980).

With this famous philosophical line, Leo Tolstoy opens his epic novel of love and tortured family relationships, *Anna Karenina.* Families who are unhappy often exhibit conflict, defined as "interpersonal tension or struggle among two or more persons whose opinions, values, needs or expectations are opposing or incompatible" (Kramer et al. 2006), and family conflict is commonly encountered in a palliative setting. Preexisting conflict may become exacerbated by the intensity of emotions and uncomfortable propinquity around the dying family member's bedside. For all families, there are potential disagreements around aspects of the patient's care, e.g., which caregivers should be involved, the location of care, the needs of the patient, the appropriate medications to be used, who the decision-makers should be, how actively treatments should be pursued, what the patient or other family members should be told, funeral planning, and legacy issues.

Boelk and Kramer (2012) developed an explanatory matrix of family conflict at the end of life, based on their earlier qualitative research with families in different cancer and palliative care settings (Kramer et al. 2006). The matrix includes the conditions which may increase the risk of escalation of conflict; contributing factors; whether the conflict is between family members, between patient and family, or between family/patient and staff; and the consequences of the

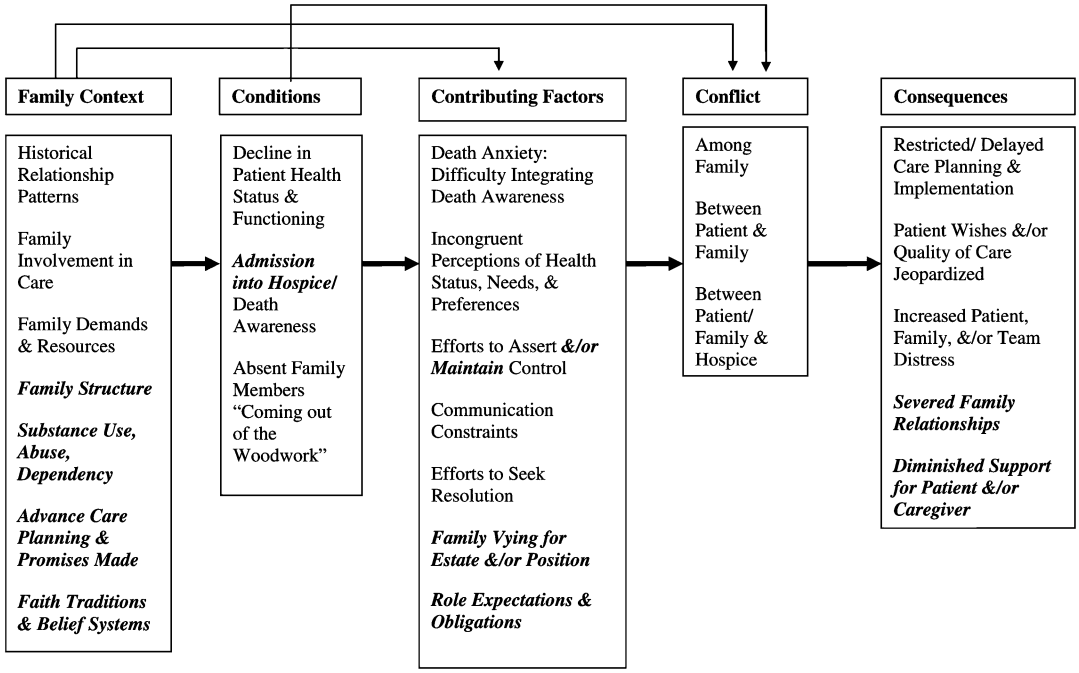

Fig. 1 Explanatory matrix of family conflict at the end of life (Boelk and Kramer 2012)

conflict. This model provides a useful way of examining the many contributing factors to family conflict (see Fig. 1) (Boelk and Kramer 2012).

Johanna, an 85-year-old woman born in Greece, was admitted for end-of-life care with several medical problems, including advanced transformed leukaemia, renal failure and diabetes. Each of her children had varying expectations and understandings of her medical state and very strong, but different views about how her treatment should be managed. The eldest child, who had medical power of attorney, became focused on the history of the diagnosis and treatments and preoccupied with which illness was causing her deterioration. Another one of her children became fixated on the dose, indication and type of medication proposed. One of her daughters wanted to ensure that everything was done, and that medical staff and the rest of the family didn't just "give up" on her too early. She was reluctant for her mother to be administered opioids, which she thought would hasten death, and wanted her to have blood transfusions, despite their no longer providing therapeutic benefit. Initially, individual children would have separate lengthy discussions with the medical staff and nursing staff but they had not formed a common view about her care.

Intervention: Medical and nursing staff held a family meeting with all the children present to provide support and education around Johanna's disease status, medications, symptom management and end-of-life care. Common ground was identified in that all children wanted to ensure that Johanna did not suffer if she was dying. Ongoing support was provided and the gentle realignment of goals were communicated consistently with clear handover among staff. The family came to understand that with the goal of care being alleviation of distress, medications would be required to achieve this. Johanna was eventually commenced on a syringe driver and died comfortably with the children by her bedside. In this case, family functioning premorbidly had not been particularly conflictual, highlighting how the stress of imminent loss of a loved one can forge divisions in any family system.

9.2 Families in Conflict with the Patient

Brochure images of a dying patient surrounded by loving family members gloss over an unpleasant reality for many families: that the end of life can be punctuated by unresolved conflicts. The dying patient may not be a "loved one." Indeed, the patient may have acted toward family members in ways that were less than loving, even abusive, creating long-standing resentment. Family members may feel angered by the neediness of the patient, and the expectation that they should now provide care and support, when they had never felt cared for or loved by the patient.

Edward was a 78-year-old married man, with no children, and was living at home with end-stage cardiac failure. He was known to a community palliative care team for symptom management in the context of increasing shortness of breath, fatigue and general functional decline. He struggled to acknowledge his increasing care needs to the team and became angry and anxious when his wife Jean was not by his side, though he denied any such emotions. His breathlessness was exacerbated by his anxiety, but he could not acknowledge any psychological component to his symptoms. Edward asserted that he did not need further assistance, despite the obvious progressive decline of his mobility, and he stated that he could 'easily' get along with the sole assistance of Jean. The team noticed that Jean was rarely present when they visited Edward, but when she was present, he would berate her for leaving his side and generally complain about his treatment. He would also criticise her housekeeping and make statements that indicated her absence was having a negative impact on the practical day to day running of the household.

Intervention: A family support worker spoke with Jean who described assuming a passive role in a "dull, lifeless marriage," in which she felt subordinated and criticised. Her current pattern of leaving the house allowed her to achieve some respite from Edward's increasingly burdensome care needs, and to "feel free of him" for several hours at a time while she played bingo. It also emerged that Jean felt a sense of triumph when leaving the house after being criticised by Edward. The support worker attempted to facilitate a couple session, which quickly broke down when Edward started to blame his wife for being unable to do "what a good wife should." Jean walked out. She phoned the support worker shortly after the attempted mediation, and stated that she could no longer care for Edward as he could no longer toilet himself and he was deteriorating. Edward was admitted to inpatient hospice care where he became belligerent and angry towards Jean, demanding to return home. The team attempted to enlist the assistance of Edward's younger brother and sister but they were "busy with work." It became clear that Edward had alienated many family members. Jean told staff that she would like Edward to be placed in a nursing home, but could not articulate this in front of him for fear of his anger. Further attempts were made to try and mediate the situation, but both Edward and Jean refused psychological support or input from the psychosocial team. Edward died in hospice care a few weeks afterwards. Jean was not present at the time of death.

9.3 The Family at Odds with the Team

Challenging situations can arise with families where the views of the family about the most appropriate care are at odds with those of the team. Such scenarios include pursuit of futile treatments (e.g., blood transfusions, repeated ascitic taps, intravenous fluids, tube feeding, or force-feeding), insistence on "natural" therapies (e.g., high-dose vitamin C infusions, homeopathy, strict exclusion diets) or alternative therapies (e.g., ozone therapy), misunderstandings about the purpose of medication, refusal to acknowledge that the patient is dying, and clashes of cultural expectations.

Anthea was a 32-year-old single woman who had returned home to live with her parents. She had

been diagnosed with uterine cancer 2 years earlier, but now had metastatic lung involvement which was causing pain, dyspnoea and anxiety. These symptoms were requiring several admissions to the palliative care unit for symptom management. During her last admission to the unit she was found to have liver metastases and it was evident that her disease was progressing rapidly. A meeting was held with Anthea's parents and three siblings, to discuss the likelihood that Anthea would die within a week. The family members were distressed and shocked because they had all seen Anthea rally on many occasions after being very ill, and they had not expected her to die so soon. Anthea's pain and anxiety were difficult to control and she was beginning to become jaundiced over the first few days of admission. The family wanted to take her home by ambulance to die at home, which was her expressed wish.

Intervention: Long discussions were held with the family during the day, allowing them to process their grief and recognise the obvious signs of deterioration, e.g. worsening hepatic encephalopathy. The loving and caring nature of the family was acknowledged, and their courage to fulfil her wishes was commended. However, they were also advised of the distress from hepatic encephalopathy when adequate and responsive titration of medication was unavailable. Anthea was requiring the addition of phenobarbitone to her syringe driver to settle her. Staff emphasised that a ride in an ambulance, across the city in peak hour traffic, would cause her additional unnecessary suffering. Since she was too ill to be taken home, the most loving thing they could do for her was to bring a sense of home to her bedside with her favourite things and the people she loved. The family came around to accepting the advice of the staff and they kept a vigil at her bedside for the next two days until she died peacefully. The consultants involved in her care met with members of the family to answer questions that had arisen for them during her care, and this helped to bring some closure to lingering fears that they may have failed her in some way.

Fardin was a 40-year-old Muslim man from the Indian subcontinent who had suffered a cerebral bleed from metastatic adenocarcinoma of the lung. His wife (Safina) was a highly educated and articulate advocate for his end-of-life care, which included caring for him at home after he became unconscious. She had hoped that he would recover enough to be able to say the prayers for the dead, a prerequisite for a better life. She not only believed she would not be forgiven, or be able to forgive herself, but also had pressure from overseas relatives and the local Muslim community in which she was culturally and spiritually ensconced. Safina believed that Allah had allowed Fardin to live before and may do so again, if it were His wish. Her role was to keep Fardin alive until Allah decided.

Intervention: The community team attempted to work with the cultural beliefs and expectations of the family, in spite of their concerns about the patient's optimal care. They understood that what they might, in Western terms, call denial of an inevitable death, was rather a manifestation of the belief that Fardin's life should be continued until Allah had called him. The team felt mandated by their own professional ethics and found it difficult to reconcile cultural awareness with their professional obligations. They accommodated some of the wishes of the family, but had difficulty dealing with suboptimal palliative care. Safina wanted to cease his subcutaneous delivery of anticonvulsants and morphine, because she believed they were making him unconscious. She told staff that suffering in their faith was an affirmation of life and that it should not be seen as a negative thing. Safina believed hydration would reverse Fardin's unconscious state and she enlisted a community doctor to set up a subcutaneous infusion of fluid. Fardin died after several days, but the circumstances of his terminal care left the community team feeling distressed and powerless.

9.4 The Return of the Former Spouse

It is not an uncommon experience in a palliative care unit to have former spouses or partners return to be involved in the care of a patient. They are often the other parent of the patient's children who are involved in the care of, or at least visiting, their terminally ill parent. This may create difficulties for a new partner who may experience a power-play with the former partner in relation to who "really knows" the patient and who has the right to have input into treatment decisions. Alliances are usually formed between the children and their parent, so that the new partner feels "pushed out" and may even be excluded from discussions with the team. Issues of rights to inheritance may also arise, particularly if the new partner has been in the relationship with the patient for a short time. The patient may feel torn and too fatigued to deal with the conflicting emotions and allegiances.

Paul was a 75-year-old man of considerable wealth, with metastatic pancreatic cancer. He was admitted to inpatient palliative care for symptom management and end-of-life care. He was in a "complicated" relationship with his second wife (Zoe), who had moved to another place of residence, but had not officially separated from Paul, telling people they were still married. Zoe left most of her husband's increasing care needs and details to his three children from his first marriage. Zoe barely acknowledged the children from the first marriage and felt that they were "just hanging out for his money," but as next of kin she allowed them to facilitate care arrangements. All three children felt Zoe was a "gold-digger" and were suspicious of her motives. Upon learning that Paul had altered his will to leave most/all of his inheritance for his children some time earlier, Zoe appeared at the inpatient unit with two solicitors. She wished to amend the will which had, according to Zoe, been Paul's wish before he entered the hospice. When Zoe came to amend the will with the solicitors, Paul was bed-bound, fluctuating in and out of conscious state, and while rousable, could not muster more than a few words, but was agreeable and cooperative to requests. A member of the nursing staff witnessed the interaction between Paul, Zoe and the two solicitors, and quickly alerted the medical team. The interaction was ceased, and a private discussion took place with the trio and medical staff. Zoe was extremely unhappy with the medical opinion that Paul no longer had capacity to sign a will, and threatened the doctor with legal action. Two of Paul's children returned, found Zoe engaged in discussion with the doctors and became angered when they were aware of the solicitors' presence and intent behind the visit. A heated argument ensued on the inpatient ward.

Intervention: The family were asked to leave the ward environment, social work engaged with the solicitors, and Paul died soon after amidst ongoing conflict.

9.5 The Distant Relative Syndrome

(Also known as the family member who "comes out of the woodwork" (Kramer and Boelk 2015) and described in the literature as "The daughter from California syndrome" (Molloy et al. 1991)).

This situation of family conflict arises when a member of the family, not involved with the patient's care, "flies in" during the late stages of a patient's illness. They are critical of the primary caregiver, undermining of the treatment plans, challenging of medical and nursing staff, and impeding of progress.

Carole was the youngest daughter of Mary, a 77-year-old woman with advanced Alzheimer's Disease and renal failure. Sue, Mary's oldest daughter, had never married and had always lived with her mother, being her primary carer for 10 years since the onset of Mary's dementia. She had left her employment as a receptionist in a medical practice to devote herself

to her mother. Carole, on the other hand, had gone to university to study law, had married a wealthy man and led an active social life in a distant state. Her only contact with her mother since Mary's seventieth birthday had been monthly phone calls until her mother became too demented to respond appropriately to the calls. Mary had been diagnosed with an invasive basal cell carcinoma on her cheek a few months previously, but Sue had agreed with the doctors that in view of her dementia and renal failure she would not be a suitable candidate for the invasive surgery required. Sue said her mother had talked to her about her wishes if she became too unwell to make decisions for herself, while she was still competent, and would not have wanted to have facial surgery. Mary was admitted to a palliative care unit for symptom control of pain and possible end-of-life care. When Carole heard of her mother's cancer she arrived within days, demanding to know why her mother's cancer was not being treated. She was aghast at the disfiguration of her mother's face and her general deterioration. She had not seen her mother for 7 years and accused Sue of neglect. She threatened medical staff with legal action if they did not surgically remove the cancer and challenged them about the opiate medication being given to Mary for pain, blaming it for her cognitive decline.

Intervention: It was evident to staff that Carole was feeling guilt about her own neglect of her mother and projected this as blame onto Sue and the treating team. She was in denial about the gravity of her mother's health and disrupted the care plan by her interference. Staff had to be aware of their countertransference feelings of anger and spend time with Carole to bring her into the clinical reality. Other staff members supported Sue and ultimately it was possible for both daughters to meet with the psychologist to speak of their very different experiences of grief over the loss of their mother. During this session Carole was able to tearfully thank Sue for the care of their mother.

9.6 The Angry Family

Patients and families bring their worlds into the treating team dynamic. Pre-existing conflicts can be augmented under the stress of forced reunions with estranged family members. Deeply buried guilt, shame, helplessness, loss of control, or emotionally charged states can bubble to the surface creating a situation ripe for misdirected discharges of anger toward staff members, who are often a "safer" target than the patient or other family members. Lifelong maladaptive relational patterns of family members can be repeated with the treating team, and the recipients of these intense interactions can experience strong countertransference reactions. In heightened angry states, family members may experience any attempts by staff to explain or clarify their concerns as an affront and can further agitate the situation. The physiological arousal of intense anger can interfere with information processing, and misinterpretation is common. Staff often find it difficult to not take it personally, and a space outside the clinical interaction is often useful to gain perspective and understand the "true" cause of the family members' anger.

Agnes was a widowed, 79-year-old lady with metastatic oesophageal carcinoma, admitted to inpatient palliative care for symptom management which turned into end-of-life care. One of her five daughters Eleanor (who was her main carer) was noted to be anxious, irritable, verbally aggressive and frequently criticised the care given by all staff in an accusatory and angry way. Barraged by angry, critical comments and a daily litany of complaints, staff become avoidant, fearful, and angry. Eleanor seemed to have an inexhaustible list of problems and had begun documenting all clinical interactions in a notebook kept by the bedside. A family meeting was held to address Eleanor's concerns. Unfortunately, any attempt to clarify or address Eleanor's concerns only seemed to fuel her rage, despite many overtures by staff to listen to and address her issues.

She continued to say, "No-one is listening to me! You're all just trying to cover yourselves!." Following the meeting, a referral to the psychosocial team was made. The psychologist engaged the daughter following the meeting. Eleanor proceeded to explain that throughout her mother's illness, treating clinicians had not paid enough attention to her mother, and "...that's why she's dying! Because no-one listened to me!." She continued to rail against "inexperienced" and "incompetent" staff she had encountered, and blamed them all for her mother's illness and decline.

Intervention: The psychologist allowed her to speak, resisting any temptation to clarify, explain, "fix" or challenge her concerns. As she continued, the psychologist noted that Eleanor began to slow her speech, sigh heavily, her volume lowered, and the content began to shift from complaints towards themes of sadness at losing her mother. Gradually her anger began to soften into a well-protected grief, cordoned off by anger and blame. The psychologist offered empathic support and enquired how the daughter was coping through all of this. Eleanor immediately burst into tears. She began to talk of her sadness at losing the "rock" in her life, her own role as a "protector" in the family, and described her propensity to accept an inordinate amount of responsibility for "fixing" everyone in the family. Yet she could not "fix" her mother's terminal illness and felt guilty, ashamed, helpless and useless – that she had "failed" her mother. After some time, the psychologist then reflected back and empathized with Eleanor's situation and role in the family, in light of the current circumstances. Once this had been offered, the psychologist then addressed the issues raised, stating that there seemed to be misunderstandings that had occurred between the treating team, and clarified some of the concerns highlighted by Eleanor. With her anger defused and a feeling of alliance with the psychologist, Eleanor was more able to engage in productive dialogue with the team.

Warren was the 35-year-old husband of Cheryl, who was transferred from a country hospital to a metropolitan palliative inpatient unit for management of pain related to her ovarian cancer. He worked in a small town as a self-employed carpenter and had not been able to complete jobs because of the need to care for his ill wife and two young sons. The couple had high hopes that the major centre would fix Cheryl's problems and they could get back to a normal life. Scans performed at the country hospital had revealed extensive peritoneal and retroperitoneal metastasis of Cheryl's disease, but this information had not been conveyed to the couple prior to transfer. The palliative care team were unaware of the couple's ignorance of her devastating rapidly progressive disease, and it was only during a bedside ward round that this became apparent. The discussion with the consultant gently moved from plans for alleviating pain to the implications of the scan findings for her prognosis. Warren watched on in shock and disbelief as his wife started to sob uncontrollably. He started to scream at the consultant, "What's the matter with you people? We came here believing you were going to make her well again and now you tell us she is going to die!" He clenched his fists as if about to punch the consultant, then abruptly left the room, yelling loudly and punched the walls of the corridor.

Intervention: The team psychiatrist was passing the room at the time these events occurred and witnessed Warren's uncontrolled rage. She had met Warren on Cheryl's admission and noted that he was highly stressed. She had some inkling about what may have triggered this display of anger from the multidisciplinary team meeting, held just prior to the ward round. She guided Warren to a quiet room and invited him to sit down, but he refused and paced around the room smashing his fist into the palm of his hand. The psychiatrist pulled two chairs into a comfortable distance from one another, without impeding Warren's space, sat down and talked in a soothing manner, speculating in general terms about what

might have transpired as Warren was unable to speak. Gradually Warren took over the story and described how cruelly his hopes and dreams had been blown apart, how angry he was that no-one had prepared them for this. He was angered by both Cheryl's oncologist in the country hospital and the heartless way the palliative care consultant had broken the news. These feelings were not challenged, but empathic statements were made about the shock he must have experienced when he had come with such different expectations. He sat down and put his head in his hands and sobbed. "Cheryl knew she was sick – she had lost 20 kg and was having these severe pains in her back which hadn't been there before. She said something bad was happening, but I wouldn't hear of it – I told her she had to be positive, that the doctors in the city would sort it out," he explained. Ultimately Warren became more composed, although he looked shattered and exhausted. "I'd better go back in to Cheryl. Thanks," he said as he left the consultation. Warren was seen on a daily basis where he continued to express his grief, and was able to start to make plans for his wife's end-of-life care and the care of his sons. Liaison with the country oncologist revealed that Warren had blocked frank discussions of the scan results – "we don't want to hear anything bad" prior to transfer. The rift in the relationship between the palliative care consultant and the couple was healed after they sat together and talked about the experience, which had been highly distressing for both of them.

A summary of the approaches that can be used to manage challenging communication is provided in Table 5 (Philip and Kissane 2017).

Table 5 Strategies for the difficult communication encounter (Philip and Kissane 2017)

Sequence of strategies for the difficult communication encounter[a]
1. Preparation – Be clear about clinical details and investigation results prior to meeting the patient. Make time
2. Listen – Using open-ended questions, allow the narrative to unfold. Develop a shared understanding of the experience, and develop shared goals from this point
3. Offer an empathic acknowledgment of the emotions expressed
4. Provide symptom relief
5. Involve experienced clinicians
6. If anger persists, reconsider approach. Important role for senior staff to guide this approach
7. and model appropriate behavior
8. Consider limit setting to the expression of emotion, where behavios present danger or disruption to care
9. Support of the team
10. Consider a second opinion or the involvement of an independent broker

[a]Content reproduced with permission from Philip and Kissane (2017)

9.7 The "Special" Family

Problems can arise in the palliative care of patients who are members of families that are famous, have celebrity status, are narcissistic, or contain healthcare professionals, important figures in public life, or religious leaders. Main wrote a classic paper on "the special patient" in "The Ailment" (Main 1957), which outlines how such a patient causes an unhealthy deviation from usual practices of staff on a psychiatric unit, with deleterious outcomes for both patient and staff. These observations are apt for "special" family members in the palliative setting.

Barbara was a 52-year-old woman diagnosed with lung cancer some years ago; a recent subacute cognitive change and subsequent MRI revealed that she had developed leptomeningeal metastases. Treatment was unable to halt progression of the disease and her care needs escalated to the point of requiring 24-h care. Barbara was in a long term, same sex relationship with a dermatologist, Nadia, and they lived together with their four children. Upon admission, Nadia made it perfectly clear to the staff that she was medically trained and able to assist with much of the care for Barbara as she "knew her needs better than anyone." The staff were very moved by the plight of the young family and the staff accommodated the

wishes of the family as much as possible. It quickly became apparent that allowing the leeway of Nadia to determine care created major problems. Nadia had little to no understanding of palliative treatments and began to accuse staff of inappropriate treatments that "bordered on inhumane." Barbara's family had indicated that Nadia was not on good terms with them, and that Barbara had separated from Nadia some years previously before returning when she became ill, but things were "less than harmonious" prior to her deterioration. Nadia refused to speak with junior doctors and only allowed specific nurses to interact with the family. When Barbara was able to voice her requests, Nadia would override them by stating that she was "confused" and she knew what Barbara "really wanted." This included attempting to withhold pain relief and rousing Barbara in order to perform physiotherapy movements (not indicated by the palliative physiotherapist). Staff were extremely distressed by Nadia's care which was causing unnecessary pain and discomfort to Barbara. When medical staff explained that her disease had progressed and the need to rationalise medications in favour of comfort care, Nadia was enraged. She demanded that Barbara be given intravenous fluids despite medical staff explaining that this would overload her lungs. Nadia again accused medical staff of "inhumane" treatment, threatened legal action and going to the media. She frequently made comments that "no-one would treat their dog this way" and berated the medical team for their "so-called expertise."

Intervention: Unfortunately, attempts at trying to address concerns with Nadia resulted in family meetings being cancelled at the last minute, outright refusal to engage with any supports (including psycho-oncology, pastoral care and social work), splitting behaviours, and increasingly entitled demands directed at younger, less experienced staff who were more likely to give in to her demands. An urgent meeting was called with the head of department, senior consultant, nurse unit manager and social worker. Nadia laughed at attempts to clarify boundaries, offers of support for her, the offer to move Barbara to another inpatient facility if she felt the inpatient care was not adequate, and agreed mockingly to the new treatment plan whereby Nadia was to have less involvement in the medical care. She would appear to agree to new arrangements, only to later question and again belittle staff, attempting to override treatment plans and take matters into her own hands.

Intervention: The staff required multiple debriefings to discuss their anger about Nadia. Many felt highly distressed that Nadia was dictating Barbara's care in a "cruel" way, and were angry at how such a situation had come to be in the first place. Reflection and unpacking revealed that the standard manner of providing care had come to be exploited and taken advantage of in this instance. Staff realised that the family-centered approach of allowing family members to participate in care, "going above and beyond" to allow the family some control, in this case served only to feed the entitled and inappropriate demands of Nadia. Senior staff were allocated to Barbara's care and the tighter boundaries seemed to contain Nadia's problematic behaviours, but she continued to denigrate staff and the quality of care. Barbara died 12 weeks after admission. Staff continued to be affected by this situation for some time and required multiple staff support sessions.

9.8 The Family with a Member Who Has Mental Illness or Severe Personality Disorder

Family members who suffer from mental illness or severe personality disorder may relapse or decompensate, under the stress of having a close relative nearing the end of life. The dying patient may have been an important part of the family member's support network and may have played a role in monitoring symptoms of relapse or medication compliance. It is important to check that the family member has support from their psychiatrist, psychologist, case manager, or GP during

this stressful time. For family members who have a history of unstable mental health, it is important to have a contingency plan in place to deal with any disturbed mental state that arises in the palliative setting. It is equally important not to fearfully anticipate difficulties with family members who have a mental illness and to afford them the same respect and opportunities for involvement in medical updates and planning meetings.

Anastasija was a 94-year-old widowed woman with end-stage heart failure. She had lived with her son Frank, who had experienced significant mental health issues for many years. Her other children had maintained a relationship with their mother Anastasija, but did not have a relationship with Frank, as he was reclusive, extremely avoidant, could become verbally aggressive, and was "peculiar" according to Anastasija's daughter, Marianne. Anastasija had survived the Holocaust in a concentration camp along with her husband, and they emigrated to Australia and raised their family. As part of her post-traumatic stress from her time in the forced labour camp, Anastasija had a long history of anxiety and hypervigilant behaviours. Prior to admission to the palliative care inpatient unit, she was admitted to hospital after phoning Marianne when she had fallen at home after a fainting episode. Frank had refused to call an ambulance at the time. Upon admission it was apparent that Anastasija was deteriorating in health, and would remain in palliative care until her death. Her children were very concerned that Frank would not cope with the idea that their mother was dying, and could decompensate or become violent.

Intervention: All efforts to make contact with Frank were unfruitful. Attempts to include him in family meetings were met with unanswered calls or letters and a failure to turn up. Staff had been informed about the possibility of Frank experiencing a relapse, and a management plan was given to staff should Frank become psychotic or distressed on the ward. Frank eventually accepted notes left at the doorstep by his sister Marianne. Given the treating team had not actually met Frank and were not aware of any current risks, it was difficult to initiate mental health crisis team involvement. His siblings reported that he had been non-compliant with mental health services previously, and had been discharged by his psychiatrist and case manager. Eventually Anastasija entered a terminal phase of illness. The treating team and Anastasija's other children remained aware of possible outbursts when Frank eventually came to say his goodbyes. He refused to engage with any staff or family, and returned to living a reclusive life at his home. The team felt quite powerless to assist or provide support to Frank; they could only provide a management plan, and offer crisis numbers to him and his family, in the hope that he would make contact if assistance was required.

9.9 The Family with a Member Who Has Drug or Alcohol Problems

Drug and alcohol abuse in the family network of a terminally ill patient can impact in a variety of ways. It can preoccupy the patient with concerns about the drug abuser, make a potential source of support emotionally unavailable and even a burden, create circumstances for abuse or diversion of medication supplied for the patient's symptom control, and create escalation of abuse through threat of loss; and the behavior of these family members in a palliative care setting may cause disruption of care delivery and increase staff anxiety.

Louise was aged 72 years and lived in a high-rise apartment with her methamphetamine-addicted 40-year-old son, Sam. She was attended by the community palliative care team, who noted that she had no food in the refrigerator and the patient's cat was not being fed. Sam was diverting her pain medication and as a result, Louise was experiencing poor pain control.

Intervention: Staff attempted to make alternative arrangements for pain medication delivery via

her GP, but Louise resisted attempts that might result in causing her son to become displeased and violent. She would not initiate police intervention in the elder abuse that was obviously occurring. The community team attempted to deal with this situation of extreme compromise by providing ongoing support for Louise. They visited Louise in pairs during this conflicted period of dependency, and attempted to engage (unsuccessfully) drug and alcohol services. Louise received no helpful advice from an online self-help group, where other contributors were not experiencing life-limiting illness.

9.10 The Abusive Family

Abuse of a patient by family members may be a long-standing pattern of behavior or may arise out of frustration with the demands and burden of caregiving by vulnerable individuals. It may take the form of neglect, rough handling, outright physical abuse, withholding of medication, oversedation, or verbal abuse. On rare occasions, sexual abuse can occur. Situations which heighten risk of abuse include personality change or cognitive decline in the patient (due to cerebral pathology, comorbid dementia, or undiagnosed psychiatric disorder), pre-existing conflict with the caregiver, substance abuse, and poor internal resources and social supports of the caregiver. When the patient is cared for at home, community workers may suspect abuse if the patient shows signs of unexplained injuries, appears neglected, or seems frightened in the presence of the carer. The community workers may not be allowed to speak to the patient alone to explore their concerns. In an inpatient setting, a patient who is being abused at home may exhibit fear at the prospect of discharge after stabilization of symptoms but be reluctant to divulge abuse because of compromising dependency on the caregiver. Sometimes it is the patient who has been abusive in the family system, and the dependency needs of progressive illness can elicit different reactions from individual family members.

Rinehart was an 83-year-old man with advanced dementia who was transferred to the palliative care unit via the emergency department, when he suddenly became unresponsive according to family members. He lived with his divorced son, and a daughter who lived close by also identified herself as one of Rinehart's main carers. Upon admission, he was found to be emaciated, dehydrated and had several pressure wounds that caused severe pain. The family would not elaborate on questions regarding the days leading up to his presentation and would not accept that he had dementia, saying he had become more forgetful as "he's an old man now." Moreover, when staff attempted to provide pain relief to Rinehart, they insisted that he would need only paracetamol. Staff were able to obtain records from a previous admission to another hospital, which indicated that the social worker had suspicions that Rinehart was a victim of elder abuse, with belongings being sold off and serious neglect of his physical health. A staff member observed Rinehart's son shaking him roughly and when they intervened, he stated that this was how he roused him.

Intervention: A family meeting was held and Rinehart's son became verbally abusive and threatening. Security was called and rules were put in place regarding the son's behaviour on the ward. He was not to handle Rinehart roughly, and he would be asked to leave if there were outbursts of anger or obstruction of treatment. Social work investigated further and found evidence of elder abuse. They were mandated to apply for a guardianship order to stop finances being drained and to appoint a third party to manage power of attorney matters. While Rinehart's son continued to be angry, he did abide by the rules and boundaries set in place by the team. Nonetheless, staff continued to feel unsafe because of his threats and unpredictability, and required regular staff support and guidance. Rinehart deteriorated and died before arrangements could be carried out regarding placement. Staff were distressed about Rinehart's condition on arrival, but were comforted that they were able to provide

him with a safe place in which to die. They were concerned that Rinehart's son would return and become violent as he had threatened, but this did not eventuate.

Helen was the 42-year-old daughter of a 68-year-old man with lung cancer admitted for end-of-life care. Her father had been an alcoholic all his life and had been sexually and physically abusive to his three daughters. Her mother had been passively collusive in the abuse and left the family, leaving the girls abandoned, unprotected and homeless at a young age. Two of the daughters went on to have chaotic lives with failed relationships, children from different partners and drug abuse; but Helen, although a single mother, had become a health care worker. Helen had been estranged from her father for many years, but when she learned of his cancer, she made contact with him and visited him daily after work. During his admission to hospital, she continued her vigil to the neglect of her work and her children. Her sisters were furious with Helen for showing compassion to "this animal" and came to the ward to upbraid her and scream abuse at their father, saying he had ruined their lives and was now getting his "just deserts."

Intervention: A meeting was held with the three sisters to help defuse and contain the intense emotions expressed on the ward. It was evident that Helen still held a fantasy of finding the "good father" and had not addressed her history of traumatic attachments, becoming a "wounded healer" in the service of others. She was encouraged to seek individual psychotherapy.

9.11 The Family Contesting Inheritance

There are many circumstances that lead to arguments about the potential inheritors of the estate of the dying patient. These can begin even before the patient's death and can be played out distastefully in a palliative setting and extend into the legal arena. They may occur around warring factions in the family, former and new partners, conflict between families of origin of the patient and partner, rejection of the patient's choice of partner by the family, and disappointment that the will is made out to charities rather than family members. The team may receive requests for evaluation of competency and other information for which motives are unclear. Staff may feel distressed by the discordance between their focus on the patient's care and the extended family's preoccupation with material issues beyond the patient's death.

Benjamin was a 50-year-old interior designer with stage IV glioblastoma multiforme. He was a divorced father of three children, and was described by his few friends as someone who was extremely "self-absorbed." He had a lifelong history of ruptured relationships and punitive gestures towards those he believed had slighted him. His former wife Rachel, had supported Benjamin by bringing their children to the hospital to visit him during his dying weeks, so that meaningful legacy work could take place. During this time, Benjamin was amiable and pleasant. However, Rachel had previously received a barrage of angry, abusive letters in the 3 years between their divorce and his admission to palliative care. The final "punishment," according to Rachel, was the "deliberately" impractical will instructions whereby Benjamin had bequeathed his superannuation death payouts to his young children in manner that precluded access to the finances. Distribution of these finances were to be legally and meticulously determined and approved by Benjamin's sister (Jane). Jane despised Rachel and had not spoken to her since the birth of Rachel and Benjamin's first child. The children had no relationship with Benjamin's family, and Rachel's attempts to contact Jane to discuss the situation were met with unreturned phone calls, blocked emails, and silence. Rachel, who had existing Power of Attorney as Benjamin had forgotten to change this, contacted the palliative care unit requesting release of records of cognitive assessment around the period of his admission date. She had mistakenly thought that he had

made his will while incompetent. However, he was in fact an inpatient at another facility at the time of making the will (which stipulated strict conditions on the inheritance for his children) and had undergone formal neuropsychological assessment, which had deemed him competent.

Intervention: Rachel was allowed to ventilate her feelings and concerns. The ongoing barrage of abuse and "punishment" of Rachel by Benjamin had continued post-death and Rachel felt distressed by the fact that "even now, he won't give me peace." Due to confidentiality and privacy laws, Rachel was provided with the information to apply for access to Benjamin's case notes via the federal Freedom of Information Act (which would indicate that neuropsychological assessment had taken place elsewhere, and that he was indeed competent at the time of writing his will). Benjamin's behaviour in spelling out his final wishes were in keeping with a lifelong narcissistic personality structure. Rachel was advised to seek legal aid, and obtain psychological support for the resurfacing of traumatic experiences in her relationship with Benjamin.

Simon, a 45-year-old stockbroker with stage IV colorectal cancer and brain metastases, was partnered to Mike, a 43-year-old physiotherapist. Simon and Mike had been in a same sex relationship for over 10 years and had lived together for over 7 years. Simon was admitted to an inpatient palliative care unit after a significant functional decline at home, and Mike's difficulty in managing Simon's care needs. During this admission, conflicts between Simon's family and Mike began to emerge. Simon's family had long expressed dissatisfaction with their relationship, trying on several occasions to force Simon to end the relationship. They had even told Simon that Mike was having an affair, and that Mike would end up "taking him to the cleaners." Simon told the psychosocial team member that he did not want his sister and nephew to visit, as they "only want to cause trouble." Mike described a telephone conversation he had with Simon's sister, where he was threatened with being thrown out of "Simon's house" when Simon died, and that he "wouldn't get a cent" of Simon's money. Mike and Simon had always had shared finances and despite Mike's name being on the title of their home, he was very distressed by the situation. Mike was unable to tell Simon exactly what his sister was saying, as he did not want to upset him further. Mike approached the psychosocial team member for advice as he was now not sleeping and struggling at work. He was afraid that every time his mobile rang it might be Simon's sister with another demand.

Intervention: The psychosocial team member encouraged Mike to obtain legal advice. Accurate information would likely reduce his anxiety, and give him space to be with his partner as he approached end of life. Simon died a few weeks later and the psychiatrist on team was approached by Simon's sister. She requested a report of Simon's competency assessment, because the will was made after diagnosis and she was planning to contest it.

9.12 Culture Clashes Within the Families of the Patient and Caregiver

Culture clashes are not only seen between the treating team and the patient's family but within the family system itself. This may arise when there are different levels of acculturation to the host culture, and it is not always the older members of the family who strictly adhere to the values and practices of their culture. Younger members who have been educated, even born, in the country of the treating culture, may be more fervent about keeping the traditions of their culture of origin.

It may also arise when there is intermarriage between different cultures, each group wanting to claim the right to determine information-sharing, decision-making, truth-telling, and rituals at the end of life.

Hanh was a 70-year-old man from Indo-China, who had arrived in the country as a boat

refugee from his mainland during major conflict. His children had been born in his new country of refuge, but still held traditional beliefs about truth-telling. Hanh was admitted to an inpatient palliative care unit with a newly diagnosed, but very advanced, neuroendocrine tumour. His son, who had achieved high qualifications in his country of birth, insisted that the medical team not divulge to his father the nature of his terminal illness. He made sure he was present for every consultation with medical teams, to enforce the withholding of information about his prognosis. On one occasion, a medical student from his culture of origin reported that he was mis-translating the guarded words from the oncologist, to provide a more benign interpretation of his illness. The issue came to a head when the patient, in great distress, asked a nurse directly (in English) "Am I dying?"

Intervention: A meeting with the son and other members of the family was convened. It was explained that Hanh had an instinctive knowledge about his condition and was more distressed by the uncertainty, rather than the reality, of his short prognosis. It was emphasised that he wanted and needed to say his good-byes and prepare a legacy for his family.

Oliver was a 40-year-old man of south Asian descent with lung cancer and brain metastases admitted for end-of-life care. He was married with no children, and his wife (Sofia), was of African descent. Upon admission, it was evident that the young man's family did not approve of Sofia as an appropriate wife for their son and brother. The pre-existing conflict had become so intense in recent times that Oliver's siblings and parents had sought legal advice, with the intent of challenging Sofia's role as medical power of attorney. The family had repeatedly accused Sofia of delaying Oliver's treatment and keeping them away from him; it was evident that they were unaware of, or in denial about, the gravity of his condition. His family's anger towards Sofia was vocalized strongly, and their repeated attempts to inform staff about his "wicked wife," in order to collude with the family against Sofia, annoyed staff. Despite wishing to appear "neutral," most were quite obviously siding with Sofia. Conflicts escalated in the ward environment and then, unexpectedly, Sofia started to become verbally aggressive and accusatory towards any staff she saw speaking with Oliver's family, and requested that they should not provide care and treatment for him. The team began to realise that the family's "denial" was due more to a lack of awareness of his condition, as they had been allowed limited access to Oliver. His father struggled with the idea of losing his only son. Not being privy to the particulars of his son's disease and illness trajectory, only fueled his anger and suspicion that Sofia had contributed to Oliver's deterioration due to neglect and improper care. As time progressed, Sofia became increasingly restrictive of the family's time with Oliver, despite their pleas for a number of bedside rituals in keeping with their cultural traditions. Sofia would only allow them to see Oliver if they promised to drop their legal demands. She set visitation restrictions and insisted Oliver could only be seen in her presence. She also requested that staff cease engagement with certain family members.

Intervention: Family meetings were stilted and uncomfortable, but all agreed that Oliver's comfort was paramount. Staff implored the family to leave conflict outside of Oliver's room, as he was quite obviously affected by the distress and arguments that took place at his bedside. All agreed that this behaviour was not in the best interests of Oliver's care, and temporary visiting arrangements were agreed upon. Psychological support was accepted by most parties. The majority of them could acknowledge that anger was "easier" than being overwhelmed by the grief of losing Oliver, but they continued to feel anger towards one another. All parties were discouraged from using existing time with Oliver to ask him questions about who he preferred in the room with him (sometimes recording his responses to be used in argument, despite his worsening cognitive impairment). They were encouraged

instead to think about how they could spend their time with him in a meaningful way. The last few days of his life were more peaceful as Sofia became exhausted and her absences meant that the family of origin could visit. Each family member devised personal ways to engage Oliver (with a favourite song, stories to recall), that allowed them to engage without conflict as the focus. Oliver's death reignited tensions however, as Sofia notified Oliver's extended family first, instead of his siblings and parents. The family were again extremely angry and felt this was Sofia's final punishment towards them. All family members and Sofia were offered post-bereavement support, but their grief was soon overshadowed by re-emerging anger as the legal threats resurfaced.

9.13 The Refugee/Asylum Seeker

Refugees and asylum seekers who are diagnosed with life-threatening illness are a particularly disadvantaged group. Often having fled war or persecution, they are separated from extended family who may have been tortured or killed. They may have poor language skills in the country to which they have fled and may have difficulty practicing the rituals related to their country of origin, particularly in relation to illness and the role of the family in provision of care.

Hasib was a 40-year-old man from the Middle East who had arrived by boat as an illegal immigrant, 18 years previously. He spent some time in a detention centre and ultimately worked in a catering business, before being diagnosed with a slow-growing brain tumour as an incidental finding following brain imaging after an accident. Neurosurgery was proposed but declined, until he developed neurological symptoms from the tumour a year later. He subsequently had four neurosurgical operations and brain irradiation over the ensuing 8 years. His admission to palliative care occurred after a gradual decline in his functional abilities. His illness course had been characterized by difficult behaviours, particularly towards women, and non-compliance with treatments and appointments. Many representations were made on his behalf to bring over his mother and brother to care for him, and to establish accommodation and community support. It was difficult to establish over this period whether the difficulties in his interpersonal interactions were related to his brain tumour, his post-surgical deficits, the steroids used to reduce intracranial pressure, his background of trauma, or amplification of symptoms to achieve the goal of bringing out his family. The only relative of Hasib lived in a distant state and he became an advocate in the latter months of his illness.

Intervention: The social worker spent an inordinate amount of time dealing with various advocacy agencies, government, and legal departments negotiating the most humane and culturally sensitive way of dealing with his end-of-life care. Hasib had a fluctuating mental state with intermittent seizures over 8 months of acute palliative inpatient care. The length of stay is indicative of the complexity of the case and the "bending over backwards" to provide care in a situation of uncertain prognosis. Although there were times over the previous months that staff thought he was deteriorating, there were no current indications that dying was imminent. He was unable to walk, almost blind and required full nursing care. Efforts to fund a medical air transport to a hospice near his only relative in the distant state were unsuccessful. Ultimately the local Muslim community gathered together to provide care in the grounds of a nearby mosque, and some members of this community came to the inpatient unit to learn how to perform his care needs. They believed that all things are determined by Allah, including whatever may eventuate from this courageous decision.

9.14 The Criminal "Family"

Everyone, from whatever background, ultimately dies – sometimes from a terminal illness, rather than a gunshot wound as in the case of many with

a criminal background. If the patient is a prisoner at the time of need for palliative services, there are protocols and procedures for management, however deficient these might be. Some patients are associated with the "underworld" without a recorded criminal history, and "the Family" visitors to the patient in a palliative care setting can cause feelings of anxiety and menace in staff.

Leo was in his 70's and dying of lung cancer. A former gangster, he had reformed and was a negotiator between warring factions of the local Mafia. He had been in the process of negotiation with these factions, when a prominent member of one of the gangs was shot in a public restaurant where the negotiations were taking place. He had been called as a witness in court proceedings and was therefore a threat to the perpetrators. The hearing had been delayed until he recovered. Captive in his hospital bed, he was a perfect target for anyone who wanted to silence him. Most of this information was unknown to staff before they started to feel uneasy in the presence of "strange" visitors and tensions in the room during the visits.

Intervention: A referral to the psychosocial team resulted in obtaining a full history of Leo's background and revealed the circumstances of his predicament. He was provided with psychotherapeutic support which allowed him to provide his life narrative, including his transformation to the "good guy," trusted by all gang members, with a secret mission of bringing an end to gangland killings. Extra security measures were introduced to protect Leo, staff and other patients, including searching of visitors and presence of security staff during any visit.

10 Principles of Management of Challenging Family Situations

- Understand as much as possible about the patient and family before contact with palliative services in all circumstances.
- Be aware of potential problems.
- Take care not to judge prematurely, despite the forewarnings – family dynamics change in the face of life-threatening illness.
- Be alert to issues that arise for the first time in the face of impending death of a family member.
- Take into consideration family dynamics, the member most trusted with decision-making, unresolved issues, and cultural/religious/belief systems in planning care.
- Discuss the approach to care with other team members/supervisors.
- Ensure clear goals of care are established with the family, and where there are different points of view, arrive at a consensus early in the contact.
- Support family members by utilizing family meetings to discuss discordant points of view and establish common goals.
- Be prepared to adapt the treatment plan according to emerging perspectives and understandings of the family as the clinical situation evolves.
- Remember that this is a process, things will change, and usually for the better.

11 Staff Support

The case scenarios described above emphasize the need for a space in which staff can "step back" from the clinical situation to consider the complex interplay of influences of a challenging family dynamic. These include the personal histories of family members, the family system including alliances and conflicts, interpersonal patterns of relating, how families express emotionality, and how the staff themselves may have been triggered emotionally.

Many studies have indicated that repeated exposure to dying patients and grieving families can leave staff vulnerable to compassion fatigue and burnout (Slocum-Gori et al. 2013; Sansó et al. 2015). When interacting with challenging patients and families in emotionally charged encounters, staff may be more vulnerable to being themselves triggered emotionally. The ensuing cascade of countertransference reactions can easily pull staff

into an intense dynamic that is not fully recognized or understood (Katz and Johnson 2016). Even the use of the "difficult" patient/family label cues the need for staff to carefully consider their own reactions as a "diagnostic barometer" and to acquire a deeper understanding of what the patient and family members bring to the clinical interaction (Philip and Kissane 2017). While some staff may happily reside in the idea that it is merely a "difficult" family, the clinical moment holds a complex, inter-relational dynamic where all parties bring their own histories, biases, patterns of relationship, communication skill level, and attunement. As staff, the need to develop greater awareness of our own emotional reactions, personal histories, biases, experiences, and personal triggers that can unwittingly eclipse our professional objectivity and clinical interactions cannot be overstated (Katz and Johnson 2016). Creating a culture of encouraged reflective practice where staff can consider personal or triggered responses can increase awareness of unexamined punitive reactions, over-involvement, helplessness, avoidance, intellectual distancing, or other defenses that staff may experience (Sansó et al. 2015; Katz and Johnson 2016; Turner et al. 2011).

11.1 Types of Support

While staff burnout can be attributed to many factors both personal, inter-relational, or organizational, higher burnout scores have been found to be associated with perceived lack of psychological support in one's place of work (Wenzel et al. 2011). Palliative care teams need to be especially mindful of provision of regular staff support, as compacted grief and other unexplored emotional consequences of palliative care work can be discharged in heightened interactions (Katz and Johnson 2016).

Staff support is multifaceted and includes discussion and education around psychological issues of patients and family members, a forum for staff to offer their "thoughts and feelings about their work," and an opportunity to provide peer support (Parkes 2000). One such model, the "Schwartz Rounds" has been increasingly adapted internationally across a range of clinical settings. The model features regularly scheduled sessions around particular cases where health providers can openly and honestly discuss the social and emotional issues they face in caring for patients and families. The focus is on the human dimension of medicine, and testimonies of the benefit of this approach can be accessed on the Schwartz Center website (www.theschwartzcentre.org).

A review of staff support in oncology health professionals indicated that promotion of staff "resilience" required a multipronged approach of both informal and formal interventions including skill development, communication skills training, provision of staff support (using expert facilitation to manage complex reactions and dynamics), reflective practice, mentorship, and supervision, as key strategies to support and educate staff (Turner et al. 2011).

12 Education and Management Strategies

Education remains a key requirement, as staff often find themselves in highly charged situations with little or no formal training regarding management of such scenarios (Turner et al. 2011; Aycock and Boyle 2009). In particularly challenging interactions, Philip and Kissane (2017) discuss important, but often overlooked, components of good communication. The importance of "staying present" with the distress of a patient and family member, even when it feels difficult or unjustified, cannot be underestimated. The subtle avoidance that staff can unconsciously promote by switching focus during an emotional discussion, to addressing physical concerns, can augment patients' and families' anger and experience of feeling misheard and disregarded (Philip and Kissane 2017).

However, while good communication skills may go a long way in defusing challenging interactions with family members, there are many times when anger or other strong emotion persists. These emotions may occur despite all reasonable attempts to defuse and calm a heightened dynamic

with family members. The focus should then shift to supporting the staff directly involved, as the intense emotional impact of dealing with challenging families can be devastating for the morale of treating teams (Philip et al. 2007; Feely et al. 2013).

Education and staff support is particularly necessary in situations where a family member has personality disorder (particularly borderline and narcissistic personality disorders). One of the most well-known defense mechanisms of an individual with borderline personality disorder is "splitting." In such cases, the family member will "split" clinicians into "all good" or "all bad," due to the inability of the individual to hold ambivalent feelings toward others (based on early caregiver attachment experiences) (Gabbard and Wilkinson 2000). This can be most commonly identified in situations where staff experience strong reactions in apparent polarity to each other. For example, anger, anxiety, punitive impulses, exist at one end of the spectrum, compared with over-involvement, wish to rescue, and feeling that the staff member is the only one who really understands the individual (Feely et al. 2013; Hay and Passik 2000). Splitting has been well documented and can create havoc within treating teams. Educating staff about the individual with borderline personality disorder includes understanding the defenses exhibited by someone with borderline personality disorder; how to set boundaries in a respectful, nonpunitive manner; providing consistency in response across the team and operating as a unified front; not colluding with attempts to downgrade other staff and not getting caught in the hubris of idealization; not taking devaluation personally; understanding that the person with a personality disorder is genuinely distressed and doing their best to navigate their suffering in their own way; acknowledging that intense reactions are likely in staff and providing a space to explore these in staff support; and where possible, enlisting the assistance of a psychiatrist or psychologist to help formulate a management plan (via the psychosocial team, consultation/liaison service, or the person's own mental health professional) (Feely et al. 2013; Hay and Passik 2000; McLafferty and Childers 2012).

13 Self-Care

In addition to promotion of personal self-care strategies (Swetz et al. 2009; Kearney et al. 2009), other interventions facilitating emotional processing of staff include "letting go" of the day's concerns using "release rituals"; (Keene et al. 2010) semi-structured staff bereavement debriefing; (Keene et al. 2010) clinical supervision; (Edmonds et al. 2015); and work environments that encourage expressions of meaning and spirituality (e.g., memorial services, rituals, etc.), which can promote staff resilience and reduce burnout (Holland and Neimeyer 2005).

14 Conclusions

The public image of a palliative care setting is a place of hushed tranquility, soft-shoed steps of compassionate nurses administering gentle care, whispered voices and sounds of birdsong, glimpses of nature through sheer-curtained windows, and delicate strains of music drifting in the background. The reality is that while it can be all these things, it is also a stage where the last drama of life is played out. The audience to this drama can experience the most intense emotions and profound moments of their lives. Staff working in this setting see people behaving at their very best and their very worst (even when the worst is the best they can be in the circumstances). In a sense, the staff and the setting have to serve as the wise and containing parent, a trusted attachment figure who provides a safe haven for those who are frightened, angry, or wretched with emotional pain. While staff are immersed in a particularly difficult family situation, they may feel hurt, incompetent, angry, and exhausted during the experience. However, with the opportunity to share with colleagues and reflect on what forces were at play in the interaction, they can emerge with a sense of privilege from bearing witness to raw, authentic human emotion. There are many ways in which professionals can ease the pain of the family, and it is in the spirit of palliative care that we employ our expertise to this end. Not only does this help the patient to die more peacefully,

but the ripple effect of poorly managed crises on surviving family members and generations to come is well known. Not only do staff develop greater self-confidence when they have managed a difficult situation well, but families too can grow from the experience. The greatest reward for staff after a particularly torrid time with a family is the family's acknowledgment of their good work.

15 Summary

This chapter has examined ways of looking at families to provide a framework for understanding what is going on in family dynamics that are experienced as challenging. It has discussed the importance of addressing family needs and assessing all families early in the palliative care context to prepare for potential problems. Apart from taking a comprehensive family history (including intergenerational issues) and being aware of the family context, culture, religious and belief systems, other concepts are important. For example, family competence and attachment styles may assist in the understanding of why some families are particularly challenging and how they may best be managed. Clinical cases illustrate a range of difficult family contexts, with interventions specific for the case outlined briefly and general management principles summarized. The importance of good communication skills training has been emphasized. Each patient and family brings their histories to the treatment setting, and there are established roles and expectations within each culture. In a situation of intense suffering and loss, staff may find it difficult to juggle and make sense of the clash of cultures between the treating system and individual families. Staff support, self-reflection, and supervision are critical components of self-care in this setting.

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Delirium as a Palliative Care Emergency

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_87

Abstract

This chapter considers delirium in the context of a palliative care emergency. It reviews screening for delirium, tools to confirm the clinical diagnosis of delirium, and diagnostic challenges. It describes both the nonpharmacological and pharmacological management of delirium. It also reviews the delirium experience and associated distress. It concludes with a brief discussion of the role of palliative sedation for refractory delirium at the end of life.

1 Introduction

Delirium is a complex and often distressing neurocognitive syndrome which commonly occurs in patients with advanced life-threatening illness. Delirium is an index of a serious change reflecting major underlying pathology and homeostatic destabilization, such as acute worsening of an existing or acute emergence of a new medical condition, medication, toxic substance, etc. (American Psychiatric Association [APA] 2000).

Delirium is often considered a medical or clinical emergency. Its sudden onset requires the clinical healthcare team to take urgent action in order to not only minimize many potentially serious negative outcomes including increased risk of falls and risk of harm to patients themselves, their families, and staff due to aggressive behavior, but also because untreated delirium is life-threatening. There is a need to identify and promptly treat reversible delirium precipitants if consistent with a patient's goals of care.

The online English Oxford dictionary defines medical emergency as "a serious and *unexpected* situation involving illness or injury and requiring immediate action" (Oxford University Press 2017). However, delirium can often be *anticipated* as it is known that certain people are at higher risk of developing delirium. This includes people with pre-existing dementia or advanced illness such as cancer, a past history of a previous delirium episode, and who are over the age of 65 years. Patients with a pre-existing "vulnerable" brain only require a comparatively small precipitating insult to develop full syndromal delirium (Inouye et al. 2014a).

Both patients and families can become extremely distressed during an episode of delirium, requiring urgent intervention, support, and education. Patients may experience psychological distress due to vivid perceptual and delusional disturbances (Partridge et al. 2013). Families may continue to have ongoing distress in their bereavement. Delirium challenges the clinical assessment of other symptoms, and often leads to patients being unable to participate in decision-making and goals of care discussion, thus potentially adding to family burden. A delirious patient can be particularly challenging to manage in the home setting, even with the availability of an "emergency kit" of medications. Family members are often exhausted due to sleep deprivation if the delirious patient is not sleeping at night. While extra homecare support will often be required, potential referral for urgent inpatient care may be needed.

The aim of this chapter is to highlight the importance of considering delirium as a clinical emergency, requiring planning for its occurrence, and immediate action at its onset to reduce morbidity and mortality. It outlines the impact and potentially ominous outcomes of this very common neurocognitive syndrome. An overview of delirium screening and diagnostic tools to assist in the clinical diagnosis of delirium is presented, as well as diagnostic challenges. A patient- and family-centered approach to delirium management which incorporates the patient's goals of care, while avoiding an inappropriately pessimistic approach to investigation and management, is

discussed. Nonpharmacological strategies used in the prevention and management of delirium are emphasized. Pharmacological management for symptom relief is reviewed in the context of recent research. Finally, the chapter discusses the importance of providing emotional and practical support to patients experiencing delirium and their families, including when a patient requires palliative sedation for refractory delirium at the end of life. The interested reader is also referred to ▶ Chap. 26, "Delirium" which provides a comprehensive description of delirium in palliative care patients, including pathophysiology.

2 Epidemiology

Delirium affects 20% of patients admitted to acute general medical care settings (Pendlebury et al. 2015), with delirium incidence increasing up to almost 29% in older patients ($\geq$ 65 years old) (Bellelli et al. 2016), 35% if >80 years (Ryan et al. 2013), and 56% in patients with dementia (Inouye et al. 2014a). Up to 20% of older persons presenting to the emergency department have delirium (Inouye et al. 2014a). Delirium is also common in palliative care patients. The prevalence of delirium on admission to a specialist palliative care inpatient setting ranges from 13.3–42.3% and increases to 88% in the last hours to weeks of life (Hosie et al. 2013). Most significantly for palliative care patients, delirium is a poor prognostic feature with an association with increase in mortality (Caraceni et al. 2000; Hui et al. 2015). In fact, delirium has even been called "a harbinger of death" in terminally ill patients, with death occurring within days to weeks of its onset (Breitbart and Alici 2008).

Delirium also causes an increase in patient morbidity, with a heightened risk of falls, longer hospital stays and associated increase in health care costs, and significant patient and family distress (see Fig. 1). In the increasingly recognized syndrome of "persistent delirium," delirium symptoms frequently continue and recovery rates are often poor in the elderly (Dasgupta and Hillier 2010). Cognitive decline after an episode of delirium is common. Delirium appears to worsen pre-existing dementia as well as increasing the risk of new-onset dementia (Fong et al. 2015). Functional decline and permanent institutionalization are also common outcomes after delirium.

3 Clinical Features of Delirium

The essential clinical feature of a delirium syndrome is impaired attention, with a change having occurred in a patient's baseline attention and awareness over a short period of time (APA 2013). Delirium usually fluctuates in severity within a 24-h period. Patients also develop disturbances in cognition, including perceptual

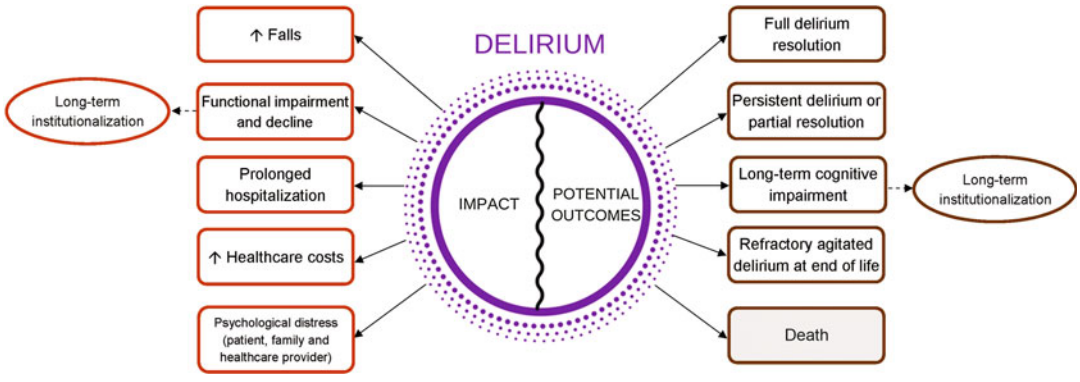

Fig. 1 Impact and potential outcomes of delirium

disturbances such as misinterpretations, illusions, and hallucinations. Other clinical features which may occur (but are not required features for a delirium diagnosis) include sleep-wake cycle disturbance, emotional lability, disorganized thinking, incoherent speech, and altered psychomotor activity (Breitbart and Alici 2012). Although not performed routinely, generalized slowing on an electroencephalogram (EEG) is a characteristic feature of delirium (Engel and Romano 1959).

Delirium is categorized into three subtypes according to the level of psychomotor activity: hyperactive, hypoactive, and mixed (with alternating features of both hyperactive and hypoactive subtypes). In a study of 100 palliative care unit inpatients with delirium whose motor activity was assessed with the Delirium Motor Subtype Scale (DMSS), almost a quarter of assessments were categorized as "no-subtype," as they did not meet criteria for the other defined subtypes (Meagher et al. 2012). The hypoactive and mixed subtypes are the most common in palliative care populations. Motor agitation is a feature of the hyperactive subtype and purposeless repetitive movements (such as plucking at bed sheets or pulling off clothes) may be observed. A patient with hyperactive delirium may be deemed to be in need of more urgent attention by the healthcare team due to visible motor agitation, but in fact patients with the hypoactive delirium subtype have a poorer overall prognosis with increased mortality (Kim et al. 2015).

After a positive result for possible delirium from routine screening or the onset of clinical signs, the diagnosis needs to be formally confirmed. Defined diagnostic criteria for delirium are codified in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) (APA 2013), and in the International Classification of Diseases (ICD-10) (World Health Organization 1992). The earlier that delirium is recognized, the sooner proactive management strategies can be put in place if previously implemented nonpharmacological strategies did not prevent its onset (see also ▶ Chap. 26, "Delirium").

4 Screening for Delirium

Back in 1959, Engel and Romano declared that: "Most delirious patients are considered either dull, stupid, ignorant, *or* uncooperative. It is only when their behaviour and content of thought *are* grossly deviant that an abnormal mental state is recognized, although [ids] not always correctly identified as delirium" (Engel and Romano 1959). Unfortunately, delirium remains under-recognized and is repeatedly missed or misdiagnosed (Clegg et al. 2011; Inouye et al. 2014a; de la Cruz et al. 2015a). Routine screening for delirium by all members of the health care team may improve its detection.

The Confusion Assessment Method (CAM) is a widely used instrument (Inouye et al. 1990). The rating of the CAM requires the co-administration of a brief cognitive assessment tool. The CAM has been validated in palliative care patients and raters require a moderate level of training to ensure reliability. Two nursing observational delirium screening tools rated at the end of each shift are the Nursing Delirium Screening Scale (Nu-DESC) and Delirium Observational Screening (DOS) Scale (Gaudreau et al. 2005; Schuurmans et al. 2003). The recently developed brief 4A Test (4AT) (available at: www.the4at.com) is designed to be used by a healthcare professional when first meeting a patient, or when delirium is suspected, as opposed to daily monitoring. It assesses for both cognitive impairment and delirium and has been validated in older hospitalized patients (Bellelli et al. 2014).

The prodromal features of delirium may provide an early warning to the healthcare team of the impending onset of a delirium episode. These early features include disruption of the sleep-wake cycle with reduced sleep at night, increased somnolence in the daytime, and also irritability, anxiety, and motor restlessness (Kerr et al. 2013). These features may occur before cognitive changes or perceptual disturbances such as hallucinations are observed. As part of the circle of care, the patient's family is also uniquely placed to identify the occurrence of subtle changes in a patient's behavior and/or cognition and should be

encouraged to report this immediately to any member of the healthcare team. The Single Question in Delirium (SQiD) asks a family member or friend "Do you think [*name of patient*] has been more confused lately?" (Sands et al. 2010).

5 Making a Diagnosis of Delirium

Delirium is listed as a "neurocognitive disorder" in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) which lists formal diagnostic criteria for delirium (APA 2013). It is a complex syndrome with varying clinical features and deleterious effects. As per the DSM-5 criteria, an essential feature for the diagnosis of delirium is a disturbance in attention and awareness, accompanied by a change in baseline cognition which cannot be better explained by a preexisting, established, or evolving neurocognitive disorder. Delirium usually develops over hours to days, and its severity tends to fluctuate within a 24-h period. Patients may also be classified as having subsyndromal delirium (SSD) if they meet some but not all the criteria for full syndromal delirium (Leonard et al. 2014).

Although the CAM was designed as a screening tool, in clinical practice the CAM diagnostic algorithm is often utilized as a "diagnostic" tool. The recent 3D–CAM, which operationalizes the CAM using a 3-min assessment, was validated in 201 general medicine inpatients ($\geq$ 75 years) in a single center (Marcantonio et al. 2014). More lengthy delirium-specific assessment tools include the Delirium Rating Scale-revised-98 (DRS-R-98) (Trzepacz et al. 2001) and Memorial Delirium Assessment Scale (MDAS) (Breitbart et al. 1997).

5.1 Potential Diagnostic Challenges

Delirium impairs patient communication. It is often challenging to diagnose delirium in a patient with reduced communication or a reduced level of consciousness, due to delirium itself or the dying phase as a result of disease progression, employing many of the currently available delirium assessment tools. Differentiating dementia, depression, and hypoactive delirium can be problematic for healthcare providers. Dementia, where a change in cognition occurs with little or no clouding of consciousness, has an insidious onset over months. Notably, patients with dementia with Lewy bodies have *fluctuating* cognitive impairment with variations in attention and alertness, complex visual hallucinations, and parkinsonism. Delusions may also be a feature (Pealing and Iliffe 2011). Delirium is also commonly superimposed on dementia, making clinical evaluation more problematic compounded by a current lack of suitable assessment tools (Morandi et al. 2017). Hypoactive delirium may present as depression or fatigue.

Hyperactive delirium may be misdiagnosed as anxiety, akathisia, or mania. With akathisia, the subjective symptoms of feeling nervous or restless and the observed movements of the body may be misinterpreted as increasing agitation due to delirium, hence the necessity that health care providers should monitor for potential medication-induced akathisia and other adverse extrapyramidal side effects (EPS) of antipsychotic medications administered to a distressed delirious patient. Agitation is not specific to delirium, so possible other causes for a patient's agitation should be considered. Urinary retention, severe constipation, or fecal impaction may aggravate patient agitation, especially in the elderly. This is often overlooked and may require urgent intervention, e.g., insertion of a urinary catheter, or rectal suppositories/microenema. Uncontrolled pain may also cause patient agitation. Valid, reliable tools to assess pain in older cancer patients with delirium are needed (Gagliese et al. 2016).

Agitation may also be the presenting feature of two distinct syndromes, neuroleptic (antipsychotic) malignant syndrome (NMS) and serotonin syndrome, where it is a more typical clinical feature in the latter (Buckley et al. 2014; Katus and Frucht 2016). Timely recognition of these potentially life-threatening syndromes is critical as urgent management is required. NMS is an infrequent, idiosyncratic, and potentially fatal

Table 1 Comparing clinical features of neuroleptic malignant syndrome (NMS) and serotonin syndrome (Buckley et al. 2014; Katus and Frucht 2016)

Neuroleptic (antipsychotic) malignant syndrome	Serotonin syndrome
Precipitated by dopamine antagonists Clinical features: Severe rigidity Hyperthermia Altered mental status Autonomic dysfunction Develops over days to weeks, and includes hyporeflexia	Precipitated by serotonin agonists Classically a triad of: (i) Altered mental status, e.g., confusion, agitation (ii) Neuromuscular excitation, e.g., clonus, rigidity, hyperreflexia (iii) Autonomic excitation, e.g., tachycardia, hyperthermia Rapid in onset, <24 h

syndrome which develops over days to weeks and is precipitated by dopamine antagonists. Some features of NMS are similar to serotonin syndrome which is precipitated by serotonin agonists with a more rapid onset of less than 24 h (see Table 1).

In palliative care settings, any sudden change in patient behavior, such as anxiety and psychological distress, should be used as a trigger for patient reevaluation to exclude delirium. A delirious patient may show signs of moaning, groaning, and facial grimacing as a result of delirium, not pain. In addition, a delirious patient may have an increased expression of pain as a result of disinhibition. If these signs in a delirious patient are misinterpreted as an increase in pain production due to activation of nociceptors, the resulting administration of extra unnecessary doses of opioids may potentially increase the delirium severity.

6 Risk Factors for Delirium

Delirium is usually multifactorial and risk factors can be broadly divided into predisposing (baseline vulnerability) and acute precipitating factors with each delirium episode having a range of 1–6 superimposed precipitants (median 3) (Lawlor et al. 2000). The development of delirium arises from the interplay of these factors: patients with a pre-existing "vulnerable" or "fragile" brain need a smaller noxious precipitating insult in order to trigger full syndromal delirium, as compared to those with a "healthy" brain (Inouye et al. 2014a). (See ▶ Chap. 26, "Delirium," Fig. 1)

The most common predisposing factors for delirium are advanced age (>70 years) and pre-existing dementia or cognitive impairment. Others include: history of delirium, depression or alcohol abuse, reduced mobility, visual and auditory impairment, fracture or trauma, malnutrition, multiple co-morbidities, and advanced life-threatening illness (Laurila et al. 2008; Inouye et al. 2014a). Studies in palliative care patients have reported the elucidation of risk factors in around 50% of delirium episodes, with rates of up to 90% also reported (Lawlor et al. 2000; Morita et al. 2001). Multiple causes for a delirium episode frequently occur at the same time (for example, opioid-induced neurotoxicity, dehydration, and hypercalcemia), so a detailed clinical assessment is fundamental, provided it is in keeping with the established goals of care.

The identification of precipitating risk factors is dependent on the extent of possible laboratory and radiological investigations which in turn is influenced by a patient's location, as well as goals of care. The precipitating factors identified in observational studies in palliative care populations depend on the clinical setting and case mix with a few consistently identified risk factors, i.e., infection, organ failure, psychoactive medication, electrolyte abnormalities, and acute illness.

Figure 2 shows common causes of delirium and Table 2 shows etiologies that are less common or potentially missed by the healthcare team.

7 Decision-Making in the Management Approach

For palliative care patients, the management of delirium should be guided by the agreed goals of care. Goals of care can be defined as "the intended purposes of healthcare interventions and support as recognized by both a patient or substitute decision-maker and the healthcare team" (Winnipeg Regional Health Authority 2011). Discussing goals of care requires clear and sensitive communication with the substitute decision-maker

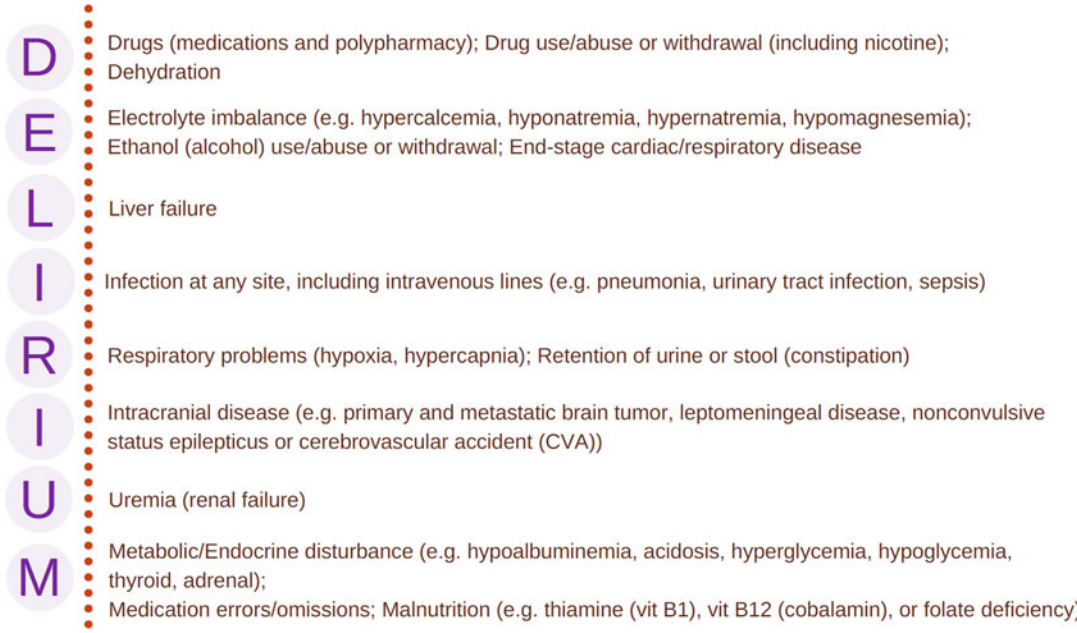

Fig. 2 Common causes of delirium

(which is usually a family member) as the delirious patient usually lacks decisional capacity, as well as an individualized approach. There is a risk of being unduly fatalistic by assuming that a palliative care patient has an irreversible delirium and subsequently failing not to investigate clinically, thereby missing potentially reversible precipitants. In such cases, death becomes a self-fulfilling prophecy and the opportunity for a period of meaningful communication between a patient and their family is lost.

It is advantageous to clarify what the patient's illness trajectory and functional status was like before the onset of delirium, to help confirm whether the patient has had a sudden precipitous change in condition, or if their condition has been steadily declining and they are in actual fact approaching the dying phase. Discussions should include the probable or suspected delirium precipitants, the potential for reversal or likelihood of nonreversal, in conjunction with ascertaining the patient's prior expressed goals of care and their possible desire to proceed or not proceed with further investigations and treatment. The burden and possible risk of inappropriate investigation and treatment should be taken into account. The conclusion of an informed decision-making process should reach an agreed management plan. As such, a timed trial of antibiotics for infection may be considered, for example. If the management plan does not aim for both delirium reversal (by way of investigation and treatment of precipitants) and symptom treatment, then symptom-directed treatment (nonpharmacological and potentially pharmacological) solely to control delirium symptoms should continue with the aim of ensuring comfort.

8 Clinical Assessment

Even with a detailed clinical assessment, delirium etiology in palliative care patients may remain unclear in approximately 50% of episodes.

8.1 Detailed History

The patient may be aware of feeling confused and report perceptual disturbances (visual or tactile hallucinations and illusions), or delusions. As part of a comprehensive past medical history assessment, an alcohol and substance abuse history should be obtained to identify delirium associated with withdrawal. A collateral history may be required from a family member or friend to

Table 2 Potentially missed and less common etiologies of delirium

Etiology
Hypercalcemia Reported calcium level within normal range, but hypoalbuminemia About 40% of the total serum calcium is bound to plasma proteins, mainly albumin "Total" calcium is reported by laboratories, and a "correction" is needed for the albumin level Measure *ionized* calcium if specific value needed
Hyperglycemia New finding in person with no preexisting history of diabetes mellitus Monitor glucose level of patients on high dose corticosteroids
Hypoglycemia
Hypoxia
Hypercapnia
Medication or substance withdrawal
Post-ictal phase
Nonconvulsive status epilepticus
Cerebrovascular accident (CVA)
Reversible posterior leukoencephalopathy syndrome (RPLS)
Paraneoplastic syndromes, e.g., paraneoplastic encephalomyelitis
Hematological, e.g., anemia, disseminated intravascular coagulation
Cytotoxic chemotherapy
Acute cerebral edema after brain irradiation
Cognitive deficits/impairment after radiation treatment/chemotherapy?

confirm the fluctuating nature and recent onset of delirium symptoms, as well as baseline mental status. Medication lists should be reviewed, not only for new medications, but also for long-standing medications and recent increases in doses. Opioid-induced neurotoxicity (OIN) is a syndrome of neuropsychiatric side effects that may occur with opioid therapy, especially if the opioid is administered in a large or rapidly increasing dose. OIN is exacerbated by dehydration.

8.2 Physical Assessment

In addition to a formal cognitive assessment and evaluation of attention, a physical examination should be conducted to look for potential underlying causes of delirium, such as infection, dehydration, and OIN. In addition to delirium and cognitive impairment, the clinical features of OIN are severe sedation, hallucinations, myoclonus, seizures, allodynia, and hyperalgesia. A patient may exhibit increased or decreased psychomotor activity. A further neurological examination of the patient may reveal abnormal movements such as asterixis, or cranial nerve deficits. In diffuse encephalopathies, signs of bifrontal dysfunction may be elicited, e.g., palmomental, snout, and grasp reflexes.

8.3 Investigations

It is less appropriate to extensively investigate for underlying causes of delirium in patients in the last hours of life. Laboratory investigations should be aimed at identifying potentially reversible causes and may include complete blood count, sodium, potassium, urea, creatinine, calcium, albumin, magnesium, random blood glucose, bilirubin, liver enzymes, ammonia levels (if severe liver impairment suspected), urinalysis, and urine culture. If suspected, tests for vitamin deficiencies such as Vitamin B1 (thiamine), B12 (cobalamin), and folate may be indicated. The patient's level of oxygen saturation should be assessed. A chest X-ray may confirm the presence of pneumonia. If in keeping with a patient's goals of care, radiological cerebral imaging may be appropriate, such as a computed tomography (CT) or magnetic resonance imaging (MRI) scan of the brain.

8.4 Management of Potentially Reversible Delirium Participants

Approximately, 50% of delirium episodes in advanced cancer patients are reversible (Lawlor et al. 2000). The decision to investigate for potentially reversible precipitants will depend on a patient's goals of care and assessment of burden of investigation and treatment, in addition to the type of care setting and availability of resources locally.

Delirium in palliative care patients is significantly more reversible if the precipitating factor is opioids and other psychoactive drugs, infection, and hypercalcemia (Lawlor et al. 2000; Morita et al. 2001). See Table 3 for the management of underlying causes of delirium. As part of good "deprescribing" practice to reduce polypharmacy, all patients' medication lists should undergo a systematic review, with a drug profile review by a pharmacist if possible, to reduce or discontinue medications, especially psychoactive drugs. Opioid rotation and discontinuation of other medications results in resolution of approximately 75–80% of episodes of drug-induced delirium. Reversal of delirium takes 2–7 days to occur. Conversely, delirium is less likely to improve in patients with an underlying dementia (Inouye et al. 2006), or if the delirium is related to hypoxic or global metabolic encephalopathy, or disseminated intravascular coagulation (Lawlor et al. 2000; Morita et al. 2001).

As delirium is often less reversible at the end of life, the challenge is discerning when attempts to reverse it are appropriate. Healthcare professionals are often inaccurate in their predictions of life expectancy, either under- or over-estimating the time left. Thus, it is important to try and identify if the person is imminently dying in order to establish the appropriateness of treating the precipitating causes of the delirium episode. However, diagnosing when a patient is entering the terminal phase can be especially challenging when viewed through the lens of fluctuating delirium signs and symptoms. Further development and research on predictive models of delirium reversibility in palliative care would assist in clinical decision-making.

9 Management of Delirium Symptoms in Palliative Care Patients

Delirium should be viewed as an acute clinical emergency requiring urgent evaluation by the interprofessional health care team. The seriousness and urgency of management to minimize its adverse effects is perhaps more pronounced if it is considered as a type of "acute brain dysfunction" (Morandi et al. 2008). The interprofessional team should work collaboratively to proactively manage patients with delirium, reduce its harmful effects, and support family members. As part of this endeavor, clear and consistent communication from the healthcare team with patients, families, and other team members is paramount. Consultation with Psychiatry or Psychogeriatrics is recommended for cases that are challenging to manage.

9.1 Nonpharmacological Management

Nonpharmacological strategies play a key role in the management of delirium, potentially preventing about 30% of delirium episodes in acute care settings (Siddiqi et al. 2016) (see Table 4). Delirious patients should be supported by frequent reorientation to who and where they are, and the names and roles of their healthcare team. Many components of existing nonpharmacological strategies constitute fundamental patient care and can be easily implemented into everyday clinical practice by the healthcare team, as well as family members with the support of the team. While evidence-based multicomponent nonpharmacological approaches have been shown to be effective in reducing delirium incidence and preventing falls in older persons $\geq$65 years (Hshieh et al. 2015), the efficacy of these approaches in palliative care populations across the illness trajectory is not known at this time (Gagnon et al. 2012).

It is important to be aware that an agitated patient with delirium is probably extremely scared. They may be experiencing frightening delusional beliefs, such as that the health care team is trying to harm them. Patients who have recovered from delirium commonly report that they feel they are not being listened to or understood, in addition to not being able to understand what staff are wanting (Partridge et al. 2013; Lawlor and Bush 2015). The healthcare team should communicate to delirious patients face to face with simple, concise, and clear sentences,

Table 3 Management of underlying causes of delirium

Underlying cause of delirium	Management approach
Opioid-induced neurotoxicity (OIN)	Reduction of opioid dose: if pain well controlled Rotate or switch opioid: with a decrease in the equianalgesic dose of the new opioid by at least 1/3 because of incomplete cross-tolerance between opioids (Indelicato and Portenoy 2002). With severe OIN, the equianalgesic dose may need to be reduced by up to 50%
Delirium caused by other medications	Consider discontinuing deliriogenic medication/s (note: this may require dose taper), or at least decreasing the dose
Dehydration	Medically-assisted hydration can be given via the intravenous or subcutaneous route (also known as hypodermoclysis – HDC) HDC can be provided with normal saline at 40–100 mL/h up to 1000 ml/day, or alternatively by giving subcutaneous boluses of 250 mL administered over 1 h, three or four times daily At this time, there is limited evidence for improving delirium with medically-assisted hydration (Nakajima et al. 2014). Hydration may be *inappropriate* for a patient who is imminently dying The risks, benefits and the values, culture, and goals of care for each person and his/her family need to be considered in each situation
Infection	For example, pneumonia, urinary tract infection, sepsis If in concordance with goals of care, consider time-limited trial of treatment with appropriate antibiotic (according to site of infection) after discussing treatment options with the patient and/or substitute decision maker
Hypercalcemia	Hypercalcemia occurs in about 8–10% of patients with cancer and is defined as a corrected calcium level of $\geq$2.65 mmol/L. Levels above 3.0 mmol/L usually cause significant problems Management (depending on the severity of symptoms, patient's wishes and estimated life expectancy) includes hydration, using saline, and additional treatment with a bisphosphonate or calcitonin (Stewart 2005) Subcutaneous denosumab, a RANK (receptor activator of nuclear factor kappa-B) ligand inhibitor, has been used to treat bisphosphonate-refractory hypercalcemia in advanced cancer patients (Hu et al. 2014). Patients should be monitored posttreatment as they may require calcium and vitamin D supplementation due to a risk of hypocalcemia after denosumab treatment (Body et al. 2017). Longer-term evaluation studies are needed
Hyponatremia	*Mild hyponatremia* (sodium levels of 126–130 mmol/L) is a common phenomenon in patients with advanced cancer and usually asymptomatic. This does not require treatment, especially in patients with very advanced disease. However, if the sodium level falls very low, then confusion and other symptoms may occur If *severe hyponatremia* ($<$126 mmol/L) occurs in a patient who potentially still has many weeks and months of life remaining, the syndrome of inappropriate antidiuretic hormone (SIADH) should be considered and confirmed or excluded with blood tests for sodium level and plasma osmolality, and also a urine specimen analyzed for urine osmolality. Management of SIADH is usually with fluid restriction, which would need to be reviewed in the context of the person's goals of care
Brain tumor or metastasis	Consider treatment with corticosteroids, e.g., dexamethasone 4–8 mg daily, in divided doses. (Higher doses of corticosteroids may be required in some patients with primary brain tumors, e.g., in patients with progressive symptoms from intracranial glioblastoma multiforme (GBM).) Depending on patient's overall condition, burden of treatment and goals of care, palliative radiotherapy may also be a treatment option
Hypoxia	Consider oxygen therapy and treat the underlying cause

using a calm voice and reassuring approach at all times. A delirious patient may misinterpret a reassuring touch from a family or team member as an act of aggression, so avoid using touch as a strategy to redirect. If delusional beliefs occur, use verbal distraction to shift the attention of a delirious patient to another topic. Rapid movements should be avoided at all times. Delirious patients

Table 4 Nonpharmacological strategies used in the management of delirium (Zimberg and Berenson 1990; Canadian Coalition for Seniors' Mental Health 2010; NICE 2010; Breitbart and Alici 2012; Inouye et al. 2014b)

Delirium management strategies	Details
Orientation: Environment	
Devices, e.g., visible clock, calendar, orientation board with name/date/location of setting	Simplify and organize patient's environment (call bell, water, telephone, and other essential items within sight and reach)
Familiar objects from home, photographs in patients rooms	
Familiar staff (continuity of care)	
Avoid frequent room changes	Single room if possible
Orientation: Verbal	
Reminders of time, day, place, who they are, who you are	Identify self every time, e.g., "I'm your nurse" – visible name badge
Family/close friends may be able to assist	Instruct family to interact in a simple, clear, and concise manner with patient
Communication:	
Face-to-face with patient Maintain a calm and supportive approach Evaluate need for language interpreters	Communication should be clear, slow-paced, short, simple, and repeated as necessary Present one task or stimulus at a time If delusional beliefs, use distraction to shift attention to another topic Explain each clinical intervention prior to instituting care or administering medication: avoid rapid movements or touching/grabbing that might be misinterpreted as aggressive
Ensure visual/hearing aids are accessible and used, and dentures where needed	Exclude and resolve impacted wax
Sleep Hygiene:	
Facilitate a normal sleep-wake pattern	For example, relaxation music at bedtime, warm noncaffeinated drinks, familiar sleepwear, minimize disruptions through the night Encourage exposure to bright natural light during the day Discourage napping during day, where possible
Environment: Avoid sensory deprivation	
Ensure appropriate lighting	For example, windowless room, excessive darkness Day-time: Shades/curtains open as much as possible during day hours Night-time: Utilize night light
Provide eyeglasses, magnifying lenses, hearing aids	
Environment: Avoid sensory overload	
Avoid excessive noise	For example, excess noise and activityImplement unit-wide noise reduction strategies, especially at night
Avoid patient over-stimulation (by staff and family)	Educate family regarding use of simple explanations and interactions with patient
Mobility:	Mobilize as patient's energy and performance status allows If unable to walk, encourage active range-of-motion exercises as tolerated Sit out of bed for meals whenever possible Minimize use of immobilizing urinary catheters, intravenous lines
Patient/staff safety: Restraint-free care as standard of care	Remove potentially harmful objects Implement a fall prevention protocol Designated sitter may be required Use of physical restraints should be avoided

(*continued*)

Table 4 (continued)

Delirium management strategies	Details
General:	
Monitor hydration and nutrition	Encourage patient to drink, if able to swallow safely Consider subcutaneous or intravenous hydration Assist patient at mealtimes Use patient's dentures, ensure diet consistency appropriate to patient's swallowing ability
Monitor bladder and bowel function	Assess for urinary retention, constipation and fecal impaction Implement interventions as needed Avoid unnecessary catheterization
Assess and monitor pain	Ensure analgesia is adequate
Consider referral to complementary services to reduce anxiety	For example, music therapy

are also hypersensitive to noise. In inpatient settings, unit-wide noise reduction strategies should be implemented (Darbyshire and Young 2013).

9.2 Pharmacological Management

(See also ▶ Chap. 26, "Delirium")

The Role for Antipsychotics

The "off-license" use of antipsychotics to treat delirium symptoms in palliative care patients has been a mainstay of clinical practice despite limited clinical evidence. Haloperidol has been the "practice standard" for many years. As one of the putative pathophysiological mechanisms for delirium development, the "cholinergic hypothesis" (with a deficit of acetylcholine and excess of dopamine) supports the dominant role of haloperidol as a potent dopamine-receptor antagonist in delirium management.

Back in 1996, Breitbart et al. reported a randomized, double-blind comparison trial in 30 adult AIDS patients (Breitbart et al. 1996). Patients who received low-dose haloperidol or chlorpromazine were reported to have an improvement in delirium symptoms as measured on the Delirium Rating Scale. Over the years, published literature has supported the use of antipsychotics in delirium management (Casarett and Inouye 2001; Michaud et al. 2007; Leentjens et al. 2012; Breitbart and Alici 2012). The National Institute for Health and Clinical Excellence (NICE) Clinical Guideline made the recommendation: "if a person with delirium is distressed or considered a risk to themselves or others. . .consider giving short-term haloperidol or olanzapine" (NICE 2010). It should be noted that this comprehensive guideline excluded "people receiving end-of-life care." In 2012, a Cochrane review found insufficient evidence for drug therapy for delirium management in terminally ill adult patients (Candy et al. 2012). Increasingly, recent systematic reviews have demonstrated a lack of evidence for antipsychotic efficacy, in addition to concerns regarding their harmful effects, especially in patients with preexisting dementia (Flaherty et al. 2011; Inouye et al. 2014b; Maust et al. 2015; Neufeld et al. 2016).

An Australian multisite, double-blind, parallel-arm, dose-titrated randomized clinical trial of oral risperidone, haloperidol, or placebo solution over a 72-h period in adult inpatients with confirmed delirium and receiving hospice or palliative care has been recently published (Agar et al. 2017). The dosing schedule for antipsychotics (i.e., risperidone or haloperidol) was age-adjusted. In the two antipsychotic arms, participants $\leq$65 years received 0.5 mg as a loading dose, followed by 0.5 mg orally every 12 h. The dose of antipsychotic was titrated by 0.25 mg on day 1, then by 0.5 mg up to a maximum of 4 mg/day. Participants $>$65 years received half the loading, initial and maximum doses of antipsychotic. All participants could receive "rescue" midazolam in a dose of 2.5 mg subcutaneously every 2 h as needed for severe distress or safety. (The dose of midazolam

was not age-adjusted.) Of the 247 participants included in the intention-to-treat (ITT) analysis, 65.6% were male with a mean age of 74.9 years, and the majority had cancer (88.3%). The baseline Australia-modified Karnofsky performance status (AKPS) ranged from 30% to 50%. Participants had mild to moderate delirium, as evidenced by median baseline Memorial Delirium Assessment Scale (MDAS) scores ranging from 13.7 to 15.1. For this study, delirium precipitants were also treated "where clinically indicated" and all participants received nonpharmacological approaches as part of delirium care. For the purposes of this study, three items on the Nu-DESC tool (assessing inappropriate behavior, inappropriate communication, and illusions and hallucinations) were combined to produce a delirium symptom score. In the ITT analysis, participants in the risperidone and haloperidol arms had significantly higher delirium symptom scores ($p = 0.02$ and $p = 0.009$, respectively) and received more "rescue" midazolam, as compared to the placebo arm. Median survival was 26 days in the placebo arm, 17 days in the risperidone arm, and 16 days in the haloperidol arm. From a post hoc analysis, the authors stated that participants "receiving an antipsychotic drug were approximately 1.5 times more likely to die." At the present time, it is not clear how to integrate the research findings from the study by Agar et al. (2017) into delirium care across the disease trajectory, in particular for palliative care patients with severe delirium, or frailer patients with a very poor performance status.

Antipsychotics are usually used to relieve perceptual disturbances (such as hallucinations or illusions) or agitation. A practical approach at this time is to maximize supportive nonpharmacological strategies for all patients, with identification and appropriate management of delirium precipitating factors where their reversal is in alignment with established goals of care. Pharmacological management approaches should be reserved for patients with severe agitation at risk of harm to themselves or if safety concerns, or to target psychotic symptoms causing severe distress. In these situations, the short-term use of antipsychotics in the lowest clinically effective dose may be indicated. This is in keeping with the pharmacological recommendation of the 2010 NICE Delirium Guideline (NICE 2010). Small starting doses of haloperidol (e.g., 0.5–1 mg PO or subcut q1hr p.r.n.) may suffice. In elderly or frail patients, lower doses should be used, e.g., haloperidol 0.25–0.5 mg, and titrated gradually. The efficacy of haloperidol should be evaluated 30–60 min after administration. Patients should also have routine assessments for akathisia and other extrapyramidal side effects (EPS). First-generation antipsychotics (e.g., haloperidol) should be avoided in patients with Parkinson's Disease or dementia with Lewy bodies (DLB), because of the risks of EPS and disease exacerbation. If treatment with an antipsychotic is required in these patients, then the second-generation antipsychotic quetiapine may be considered.

The Role for Benzodiazepines

Benzodiazepines are known to be deliriogenic, especially in higher doses, and are a risk factor for falls (Clegg and Young 2011; Stone et al. 2012). In view of this, it has been recommended that benzodiazepines are not used as first-line medications for the management of delirium that may be reversible (Irwin et al. 2013). However, benzodiazepines do have a role as first-line agents in managing agitation due to alcohol or benzodiazepine withdrawal.

Returning to the seminal trial in AIDS patients by Breitbart et al. mentioned above, only 6 of 30 patients received lorazepam, as the researchers stopped the lorazepam arm early due to concerns of treatment-limiting side effects (Breitbart et al. 1996). These included not only increased confusion, but also excess sedation, disinhibition, and ataxia. A recent study in 49 CAM-positive patients with agitation reported that a combination protocol of haloperidol and midazolam was more effective than haloperidol alone (Ferraz Gonçalves et al. 2016). The onset of action for a subcutaneous injection of midazolam is only 5–10 min. The optimal role of "rescue" doses of midazolam and other benzodiazepines such as lorazepam in the crisis management of a severely agitated and distressed delirious patient, who has not responded to nonpharmacological strategies or

an antipsychotic as first-line management, requires further study.

10 The Delirium Experience and Support

Delirium causes significant distress for patients as well as their families, countering the oft-heard description of the "pleasantly confused" patient (Breitbart et al. 2002; Bruera et al. 2009). In two studies using the Delirium Experience Questionnaire (DEQ) in hospitalized cancer patients, 54–74% of patients recalled their own symptoms after delirium resolution, and had significant associated distress (Breitbart et al. 2002; Bruera et al. 2009). Of note, patients having no recall of their delirium episode were also significantly distressed, and that hypoactive delirium was just as distressing for patients as hyperactive delirium. Patients report feeling anxious, threatened, and a lack of control, as well as feeling that they are not being listened to or understood by the healthcare team. (See also Sect. 9.1 for communication strategies with delirious patients.) As part of their delirium experience, patients also experience visual hallucinations, misperceptions, and delusions which are frequently of staff, other patients, and deceased family members (Partridge et al. 2013). Patients who have recovered from delirium may require formal debriefing to alleviate their fears.

While the presence of a reassuring family member appears to be beneficial to delirious patients, family members experience distress when observing delirium in their loved one. Spouses and nonprofessional caregivers report higher distress rating scores on the DEQ than patients (Breitbart et al. 2002). Family members often feel helpless and describe negative emotions, include anxiety and caregiver burden (Buss et al. 2007; Finucane et al. 2017). Family distress may be ameliorated if they are expecting delirium as part of the patient's illness (Partridge et al. 2013). Families have previously described a need for more informational support about delirium (Namba et al. 2007; Toye et al. 2014). Communication must be clear and consistent from all members of the interprofessional healthcare team, and tailored to the family's needs. Family members report delirium information leaflets to be a useful strategy in supporting their needs (Otani et al. 2013).

The distress of family members increases with a patient's symptom severity, terminal illness progression and declining performance status (Dumont et al. 2006). The fact that delirium can deprive patients and family members of effective communication becomes even more poignant in the face of approaching death. As delirious patients are often psychologically absent although their body is still physically present, family members may experience "ambiguous" loss (Day and Higgins 2016). In turn, this may later lead to difficulties in an individual's grief journey. The healthcare team has a pivotal role in supporting families at this time, and legitimizing their feelings of loss.

Delirium also impacts on members of the healthcare team. Nursing staff report "stress due to the unpredictability of delirium and workload," as well as safety concerns (Partridge et al. 2013). The behaviors of patients with hyperactive delirium who appear to be uncooperative or pulling at tubes and lines can be particularly challenging to care for, especially at night (Mc Donnell and Timmins 2012). Effective educational training interventions in the management of patients with delirium are required for all members of the interprofessional healthcare team, with the aim of increasing knowledge, skills, and self-efficacy, as well as providing a unified and consistent approach to care. Unit-level debriefing sessions may be required following difficult cases as part of institutional support.

11 Refractory Delirium at the End of Life

A symptom is defined as *refractory* if it cannot be adequately controlled and continues to cause distress despite the use of all other possible and tolerable symptomatic treatments that do not compromise consciousness (Cherny and Portenoy 1994). The occurrence of an irreversible refractory delirium in a physically declining palliative

care patient is a poor prognostic sign, indicating that death may occur in days or even hours, rather than weeks (Leonard et al. 2008; de la Cruz et al. 2015b). This information should be sensitively explained to the family, and patient where possible, and support provided to prepare for the dying phase.

Severe refractory delirium at the end of life may also necessitate "emergency" management by the interprofessional healthcare team. Critical action is warranted to reduce not only potential patient distress, but also importantly family distress at witnessing severe agitation in a loved one approaching the end of life which may subsequently negatively impact on their bereavement (Morita et al. 2007; Cohen et al. 2009). In the words of Dame Cicely Saunders who founded St. Christopher's Hospice in Sydenham, London in 1967: "How people die remains in the memory of those who live on." Dying patients with refractory delirium, who remain very agitated and distressed despite antipsychotics, may require additional pharmacological management in the form of palliative sedation.

12 Palliative Sedation for Refractory Agitated Delirium at the End of Life

Over the years, authors and guidelines have provided many definitions for palliative sedation, or sedation in the terminal phase (usually referring to the last days up to the last 2 weeks of life) (Bush et al. 2014). As part of a 10-point framework in 2009, the European Association of Palliative Care (EAPC) defined "therapeutic sedation" or "palliative sedation" as "the monitored use of medications intended to induce a state of decreased or absent awareness (unconsciousness) in order to relieve the burden of otherwise intractable suffering in a manner that is ethically acceptable to the patient, family and health care providers" (Cherny and Radbruch 2009). Proportionate palliative sedation is an ethically accepted intervention and does not hasten death. Palliative sedation can be administered intermittently, as temporary "respite" sedation for an uncontrolled symptom, or continuously. Midazolam is the medication most frequently used for palliative sedation and refractory delirium is the most common indication (Maltoni et al. 2012).

See ▶ Chap. 87, "Palliative Sedation: A Medical-Ethical Exploration."

More evidence is needed on the efficacy of palliative sedation for the management of refractory delirium, as well as other refractory symptoms at the end of life (Beller et al. 2015). In addition, it is important that palliative sedation guideline implementation is supported by comprehensive staff training and education strategies.

Family members require ongoing support at this time. While often feeling relief at seeing their loved one's comfort, family members may also experience distress due to patient's lack of communication, guilt over the decision-making process, in addition to anticipatory grief (Cherny and ESMO Guidelines Working Group 2014). Family members have also reported receiving insufficient or unclear information regarding palliative sedation (Bruinsma et al. 2013). Clear healthcare team communication with family members and other team members should be a priority, especially before and during palliative sedation. Families often have mixed feelings between wanting relief of the patient's suffering, but also wanting consciousness maintained (Finucane et al. 2017). As a practice point, if a patient has become increasingly agitated over the course of a day, it can be advantageous for the health care team to brief the family in advance (as well as the patient if possible) if the team anticipates that the patient is likely to require sedation overnight for their comfort. This preparation may help to mitigate some of the distress of family members if the sedated patient is not able to have meaningful conversations with them the next day.

13 Conclusion and Summary

Delirium is a clinical emergency requiring prompt assessment and management according to a patient's goals of care by all members of the interprofessional healthcare team. Delirium can be anticipated by the healthcare team if the patient is assessed to be in a high risk group, or

approaching the last hours to weeks of life. The development of validated models (specific to palliative care populations) to predict delirium development and to predict response to treatment of delirium precipitants according to a patient's goals of care will assist in this endeavor. Further research is required to ascertain the optimal management strategies of delirium, according to underlying pathophysiology and across the palliative care patient's illness trajectory. Planning for the occurrence of delirium is of immense benefit to the patient, their family, and healthcare team and, in turn, has the potential to reduce the distress associated with this common deleterious neurocognitive syndrome.

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Distinguishing and Managing Severe Psychological and Psychiatric Distress

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_88

Abstract

Severe psychological distress in palliative care patients is not uncommonly encountered by healthcare professionals. It is a manifestation of suffering requiring appropriate intervention, every bit as important as unrelieved pain or nausea. Such distress may range from transient "normal" sadness and grief to more disturbed psychological states such as severe anxiety, depression, demoralization, manifestations of serious mental illness, decompensation of personality disorder, and post-trauma syndromes. At times, the underlying cause may be organic – a reaction to corticosteroids, manifestations of cerebral pathology, or delirium.

The first section of this chapter focuses on how the clinician can recognize and distinguish different forms of psychological and psychiatric disorder which manifest as distress in palliative care patients. The discriminating features are presented in comparative tables and highlighted by clinical cases. One case is described in detail at the end of this section, where the patient suffered severe distress from different clinical syndromes over the last 8 months of his life, illustrating the need for continuing vigilance and assessment. The second section introduces therapeutic responses to patients in severe distress that every clinician can develop to reduce suffering in the moment. In so doing, the need for "emergency management" of clinical scenarios can be reduced and treatment can pave the way for specialist intervention when required. It describes the various therapies which have a demonstrated evidence base for efficacy in this population and summarizes in table form the recommended approaches for easing suffering in different forms of distress.

1 Introduction

People dealing with life-limiting disease have cumulative stress throughout the course of their illness. From the early symptoms leading to diagnosis with cancer or nonmalignant terminal disease, they undergo a series of investigative procedures and treatments, e.g., surgery, chemotherapy, radiotherapy, hormone manipulation, immunotherapies, and corticosteroids. Their lives become an emotional rollercoaster of hope and disappointment, adaptation, and crisis. Patients no longer feel authors of their own lives; they struggle to redefine their identity and role, to find new purpose and meaning in a body that is letting them down. By the time they are receiving palliative care services, the focus has moved from seeking cure to maximizing quality of life in the time remaining for the patient and family.

While some patients negotiate this journey relatively smoothly and show a remarkable degree of acceptance and stoicism, many can experience high levels of distress. Rather than being viewed as a diagnosis, distress should be considered an umbrella term, a signifier of an underlying mental state, much as fever is an indicator of underlying infection. It is a signal of patient suffering and needs to be recognized and understood. The National Comprehensive Cancer Network (NCCN) has defined distress as:

> . . .an unpleasant emotional experience of a psychological, social and/or spiritual nature which extends on a normal continuum, from common normal feelings to those of vulnerable sadness and fears, to problems that are more disabling, such as true depression, anxiety, panic, (demoralization*), and feeling isolated or in a spiritual crisis. [*author's addition]

They added "no patient's distress should go unrecognised and untreated" (National Comprehensive Cancer Network 2003).

Clinicians may not recognize the significance of distress, believing it to be an understandable and appropriate reaction to the patient's predicament. They find it difficult to distinguish between sadness and more serious clinical states of depression and demoralization. They may consider that treatment with medications will only add to the patient's burden or stigmatize them. Many clinicians may be unaware of, or unskilled in, the various psychotherapies that are available. They may feel uncomfortable about probing into the patient's psychological experience for fear of making them worse. Some clinicians do not like to get too close to the patient's pain because of their own vulnerabilities. The patient may also be reluctant to divulge emotional states for fear of appearing "weak" or burdening family or staff. Any or all of these factors may contribute to a failure in exploring the patient's distress, leading to underdiagnosis and undertreatment of psychological or psychiatric disorders causing suffering.

The consequences for the patient include impaired pleasure, meaning, and connectedness; a reduced quality of life; amplification of physical symptoms; and distraction from the emotional work of separating from loved ones, who in turn may be suffering as witnesses to the distress. Severe distress may lead to a request for a hastened death and is a risk factor for suicide, especially if the patient is depressed (Block 2000) or demoralized (Kissane et al. 2004).

2 Section 1: Distinguishing Different Forms of Severe Distress

2.1 Recognizing Distress

The clinician may recognize signs of distress through the patient's demeanor and the nature of spontaneous talk, but many patients mask or minimize their emotional stress from fear of being seen as "not coping." The importance of recognizing distress as "the 6th vital sign" (after pain) was championed in Canada and endorsed internationally in 2010 (Bultz and Johansen 2011). The NCCN recommended screening for distress in all cancer patients and developed a visual "distress thermometer" and accompanying problem list (National Comprehensive Cancer Network 2003).

The distress thermometer indicates the presence or absence of distress, as well as its intensity, and the problem list shows the domains seen by the patient as the cause of the distress, only some of which are emotional or spiritual. A second stage of screening (e.g., the Hospital Anxiety and Depression Scale (Zigmond and Snaith 1983)) and a good clinical interview with a comprehensive history are required to identify possible psychiatric disorders (Widera and Block 2012).

2.2 Distinguishing Different Forms of Distress

It is one thing to recognize that a patient is distressed, but the clinician is often unsure of the following: origin of the distress, its clinical significance in representing underlying disorders, and the appropriate intervention indicated. Responses may range from "in the moment" empathic listening, attending to social issues, involving pastoral care, or referring to more specialized clinicians for further assessment and "diagnosis." Subsequently, different forms of staff supervision, psychotherapy, family work, and/or pharmacotherapy approaches may occur.

The clinician will need to be able to distinguish:

- Sadness
- Grief
- Anxiety and panic
- Depression
- Demoralization
- Post-trauma syndromes
- Decompensation of underlying personality disorder
- Manifestations of underlying serious mental illness (bipolar affective disorder, schizophrenia)
- Substance abuse and withdrawal
- Organic mental states

The clinical features of each of these states will be described, including how they may be distinguished from other psychological states and psychiatric disorder. Some of the distinguishing features will be summarized in comparative tables.

2.3 Sadness

Sadness is a common human emotion occasioned when a person reflects on his/her situation of disadvantage, limitation, losses of future prospects, and experiences sorrow or disappointment. Everyone experiences sadness at times, and although the person may become quiet, lethargic, and withdraw themselves from others, it is a normal response. In its more severe and pervasive form, it can be a symptom of depression (see Table 1).

> **Belinda**, aged 56 years, a married mother of two teenage daughters and a former schoolteacher, was admitted into a palliative care unit for symptom management of breathlessness and increasing weakness related to Motor Neurone Disease (MND), diagnosed six months previously. She was referred to psycho-oncology because she appeared flat and at times tearful. Belinda described herself as feeling sad rather than depressed. She would look at her daughters and think about the children they would have, that she would never see. She missed working in her garden and the joy of bringing fresh flowers and vegetables into the home. She still derived great pleasure from the company of others and music was of great solace to her. She worked with the music therapist to compile a CD of her favourite pieces, which she used not only to soothe herself 'during this dreadful waiting period while I slowly die', but also as a focus point in reliving memories with her family and planning music for her funeral. (O'Callaghan et al. 2015)

Table 1 Core features of sadness and depression[a]

Sadness	Depression
Able to feel intimately connected with others	Feels outcast and alone
Feels someday this will end	Feeling of permanence
Able to enjoy happy memories	Regretful, rumination on irredeemable mistakes
Sense of self-worth	Extreme self-deprecation/ self-loathing
Comes in waves	Constant and unremitting
Looks forward to things	No hope/interest in future
Retains capacity for pleasure	Enjoys few activities
Will to live	Suicidal thoughts/behavior

[a]Content adapted from Rayner et al. (2011)

2.4 Grief

Grief is natural response to any experience of loss that restricts people by taking away possibilities and potential. In a palliative care setting, a patient's grief may be engendered by loss of autonomy, body function, social role, familiar body image, sense of dignity, and identity. The family's grief may begin well before the death of the loved one. Grief is a multidimensional phenomenon with physical, emotional, behavioral, spiritual, and social manifestations (see Table 2).

2.4.1 Grief over Loss of Aspects of Self (Clarke et al. 2005)

> **Muriel**, aged 65 years, had been prominent in the fashion industry and had been very conscious of her physical appearance. She was inconsolable because an oral cavity tumour had disfigured her face and made it difficult for her to speak clearly. She wished for an early death and would not permit visits from people who knew her from her more glamorous days. She gradually warmed to a psychologist who 'saw' her beyond her face, and delighted in regaling her with stories of her colourful past in her last weeks of life.

Preparatory Grief

This refers to grief "that the terminally ill patient must undergo in order to prepare himself for his final separation from this world" (Lindemann 1944). While Kubler-Ross (1970) saw this as a normal process in response to the perceived losses experienced by people who are dying, Mystakidou and colleagues (2008) found associations between preparatory grief, hopelessness, and psychological distress.

> **Malcolm**, a 73-year-old former businessman and child Holocaust survivor had been distressed and ruminating about things he had failed to achieve for

Table 2 Comparison of grief and depression[a]

	Grief	Depression
Nature of response	Adaptive	Maladaptive
Focus of distress	Relates to a particular loss	Pervasive
Stability of symptoms	Comes in waves Generally improves over time	Constant Unremitting
Mood	Sadness and dysphoria Lability	Protracted depression Flatness
Anger	Often expressed	Self-directed
Interest	Maybe lessened due to preoccupation	Markedly diminished
Pleasure	Capacity in certain activities	Anhedonia
Cognition	Confusion	Problems with concentration Indecisiveness
Guilt	May feel regret over specific things	Excessive feelings of guilt
Hope	Episodic and focal loss of hope Change over time to more positive orientation	Persistent and pervasive hopelessness
Self-worth	Maintained though helplessness common	Worthlessness Feeling one's life has no value
Suicidal ideation	Passive fleeting desire for death	Preoccupation with desire to die
Imagery	Vivid Fantasy	Self-punitive
Sleep	Difficulties falling asleep Episode of wakefulness Vivid dreams	Early morning wakening
Responsiveness	Responds to warmth, reassurance, and support	Limited

[a]Content adapted from Widera and Block (2012)

his family before his death from advanced renal failure. In a reparative narrative review of his life (Freadman 2015) he was able to balance some of his regrets with pride over his achievements and make plans for handing over the business more formally to his sons.

Susie, a young mother of three children, all under the age of twelve years, had metastatic melanoma and was noted by community palliative care staff to be disengaged from her children. This caused the staff considerable distress, because they had wanted her to spend as much quality time with the children as she could before she became too ill. In supervision they came to realise that, at an unconscious level, Susie was beginning to psychologically withdraw from her children (decathect) as a manifestation of her preparatory grief and protection from overwhelming psychological pain.

Anticipatory Grief

Anticipatory grief relates to the anticipated loss of a loved one (Lindemann 1944). Although originally viewed as a potential coping mechanism for a prospective loss, Fulton and Gottesman (1980) reviewed the research literature on the topic and found many methodological flaws. Whether anticipatory grief is functional or dysfunctional for a family depends upon many complex and interacting factors, including psychological, interpersonal, and sociocultural considerations.

Harry, a 75-year-old retired butcher from a country town had suffered with metastatic prostate cancer with widespread bone secondaries for twelve years, and was admitted for management of his pain. It was noticed by staff that his family would come to visit occasionally, but rarely engaged with him in conversation and occupied themselves with their phones or magazines. Harry tearfully told a nurse after a visit from his wife – "It's like I'm dead already for her. She probably looks at me and thinks – 'he's not the bloke I married'. She used to be warm and caring, but it's like she's switched off, I've been sick that long."

Complicated Grief

Although a term mostly used in the description of bereaved caregivers, complicated grief may also

be experienced by the terminally ill patient. The double effect of unprocessed losses before and during their illness can cause patients grief about the imminent loss of their own life (Alessandra Strada 2013).

2.5 Anxiety

Most individuals with advanced disease will experience some level of anxiety as they adapt to changes in their disease status. Symptoms of anxiety in a palliative setting may include feelings of foreboding, apprehension, and dread (Roth and Massie 2007) and may be experienced as emotional distress or may be somatic (Hinshaw et al. 2002) or cognitive (Roth and Massie 2007) in nature. At the end of life, these symptoms can be profoundly distressing for the patient, family, and staff.

In a palliative setting, low levels of anxiety as a response to a physical or psychological stressor are often short lived (Valentine 2014). More persistent anxiety can interfere with the individual's ability to function, significantly reduce quality of life, and lead to the development of an anxiety disorder. Individuals most at risk of developing an anxiety disorder in a palliative setting are those with a past history of anxiety disorder (NHMRC National Breast Cancer Centre (Australia) 2003), poorly controlled physical symptoms, a lack of social support or social isolation, and poor communication with their healthcare professionals (Lloyd-Williams and Hughes 2008). Higher rates of anxiety disorder have also been reported in younger patients (Austin et al. 2011).

> Kelly, a 37-year-old women diagnosed with stage 4 colorectal cancer, presented with overwhelming feelings of dread and fear soon after being diagnosed. Her symptomatology included a range of physical manifestations of anxiety, including nausea, loss of appetite and sleep dysfunction. She was well supported by her husband, and had three children under four years old. However, she lacked family support as her parents were interstate and her parents-in-law lived in a regional centre. She had a past history of anxiety, but had never seen a mental health professional. She was referred by her oncologist because she was 'not coming to terms with the news' and was seen on the ward with her husband present. Kelly described constant nausea, and presented with an acute grief reaction with high levels of anxiety around her prognosis. She focused on her mortality and her catastrophic thought processes drove her fear and exacerbated her anxiety. She interpreted her physical symptoms as a sign that her disease had progressed further, and experienced multiple panic attacks with significant shortness of breath at rest. Her physical symptoms of anxiety escalated her death anxiety.

Estimated probable cases of anxiety in advanced cancer inpatients measured using the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith 1983) range from 34% (Teunissen et al. 2007) to 44% (Delgado-Guay et al. 2009), with up to 16% of requests for psychiatric consultation based on the assessment of symptoms of anxiety (Massie and Holland 1987).

There is limited data on the prevalence of anxiety in those with non-oncological disease. In a retrospective study of stroke deaths, Ntlholang et al. (2016) reported low rates of psychological distress (1.9%) but marked levels of agitation (25.9%). Gore et al. (2000) in a comparison study of those with non-small cell lung cancer (NSCLC) and those with chronic obstructive pulmonary disease (COPD) reported higher rates of anxiety and depression (90%) in those with COPD compared to those with NSCLC (52%). While chronicity of the disease and symptom burden may explain these differences, Sorenson (2013) suggests that poorer access to quality palliation may be factor. In individuals with congestive heart failure (CHF), rates of anxiety have been stated to be as high as 63% (Moser et al. 2016).

Anxiety is often a manifestation of other psychiatric disorders, and in a palliative population, differential diagnoses include depression, delirium, and medication or treatment side effects (Roth et al. 2009). Roth and Massie postulate that depression and anxiety can be viewed as syndromes that exist on a continuum with overlap in symptomatology (Roth and Massie 2007). While depression and anxiety may coexist (Wilson et al. 2007), key distinguishing features include the hopelessness, worthlessness, and anhedonia (loss of pleasure) associated with depression, compared

with the feelings of worry, dread, and fear associated with anxiety (American Psychiatric Association 2013). When distinguishing anxiety and delirium, the key features of delirium which differentiates it from anxiety disorders include the presence of disorientation; impaired memory, attention, and concentration; fluctuating level of consciousness; and altered perceptions including hallucinations, delusions, and illusions (Wise and Rieck 1993).

It is important to remember the significant overlap between the somatic symptoms of anxiety and the side effects of treatment, illness, and the disease process (Zweers et al. 2016). A significant level of distress, anxiety, and depressive symptomatology may be attributable to the high level of physical symptom burden experienced by patients with advanced disease (Zweers et al. 2016). Uncontrolled pain is seen as a common cause of anxiety and agitation (Hinshaw et al. 2002), and suicidal ideation is common in those with uncontrolled pain (Roth and Massie 2007). In those with respiratory disease, dyspnea can cause significant distress and anxiety.

Table 3 summarizes the underlying medical causes of anxiety in a palliative setting and highlights the need to exclude other causes and manage physical symptoms such as pain, dyspnea, nausea, and sleep disturbance, in order to alleviate psychological distress (Andersen et al. 2014). While discussed in detail elsewhere, issues such as steroid psychosis and delirium should be treated as a medical/psychiatric emergency in order to reduce distress for the patient, family, and staff. Metabolic and physiological abnormalities (e.g., severe constipation and electrolyte and glucose imbalance) can lead to episodes of delirium with agitation, disturbances of consciousness, and changes in cognition. These clinical scenarios highlight that in medically compromised patients, symptoms of anxiety may be an early warning sign in relation to development of delirium (Hinshaw et al. 2002). Alcohol, nicotine, opioid, and benzodiazepine withdrawal has also been noted to cause anxiety that can lead to agitation and delirium (Irwin et al. 2005; Ginige 2016). Existential concerns such as death anxiety, fear of pain, loss of independence, being a burden, and unfinished business can lead to increased levels of anxiety in this population (Hinshaw et al. 2002).

Anxiety experienced by carers, friends, and family members can also have a profound impact on the patient's level of distress. Assessment of family distress and appropriate intervention is important, as is the provision of accurate information. Teaching the family how to manage their emotional reactions is likely to have a positive impact on the patient's ability to cope.

2.5.1 Anxiety Disorders

It is important to remember that anxiety is a symptom which may form part of several anxiety disorders, each with specific diagnostic criteria and symptomatology (American Psychiatric Association 2013). These include adjustment

Table 3 Medical causes of anxiety[a]

Uncontrolled pain	Respiratory disease/distress
Metabolic and physiologic issues	Drug induced
Hypoxia	Corticosteroids, dexamethasone, prednisolone
Delirium – hyperactive	Antiemetics
Sepsis	Bronchodilators
Blood loss	Psychostimulants
Pulmonary embolus	Caffeine
Hypocalcemia	
Hypoglycemia	
Electrolyte imbalance	Substances or withdrawal from substances (alcohol, opioids, benzodiazepines)
Undiagnosed hyperthyroidism	
Nutrition failure	Hormone secreting tumors – thyrotropic (TSH) – secreting adenomas
Severe constipation	

[a]Content adapted from Hinshaw et al. (2002); Roth and Massie (2007)

Table 4 Symptoms of anxiety[a]

Hyperarousal Restlessness Irritability	Thinking style Worry and foreboding Apprehension and dread
Panic Palpitations, tachycardia, tremor Diaphoresis (sweating) Dyspnea (shortness of breath) Gastrointestinal distress or nausea Feelings of impending doom	Recurrent unpleasant thoughts Fear of pain Fear of death Fear of dependency on others Fear of unfinished business
Sleep disturbance Initial insomnia (difficulty falling asleep) Less restorative sleep Nightmares Middle of the night or early morning waking	Negative thought patterns Catastrophization Overgeneralization Inevitability of negative outcome Helpless in hopeless situation
Changes in appetite Loss of appetite – may lead to wasting Increase appetite (mania)	Sexual dysfunction Reduced libido Erectile and orgasmic dysfunction

[a]Content adapted from Roth and Massie (2007)

disorder with anxiety, generalized anxiety disorder (GAD), panic disorder, phobic disorder, and obsessive compulsive disorder (OCD). Table 4 highlights the clinical signs and symptoms associated with each anxiety disorder. In a palliative setting, relying on rigid diagnostic criteria may lead to underidentification of disorders and has the potential to increase suffering in an already vulnerable population.

Wilson et al. (2007) in a Canadian study with palliative cancer patients reported 13.9% of respondents having an anxiety disorder, 5.5% panic disorder, 5.8% a GAD, 4.7% an anxiety disorder not otherwise specified, and 1.8% an anxiety disorder secondary to a medical condition.

Phobias

Phobic disorders should be considered especially in those who have had long episodes of illness with painful or traumatic interventions. Needle phobia is common and may have a negative impact on treatment decisions. Claustrophobia may be present in patients who are non-ambulatory or those who have extended admissions to hospital or inpatient palliative care services. Similarly, those with MND or degenerative neurological disorders may experience a phobic response associated with the fear of being "locked in" to their body. This may manifest as panic as their condition deteriorates. Individuals with end-stage lung disease and those with intractable dyspnea may find small spaces difficult and may create high levels of distress, e.g., showering may become problematic and lead to avoidant behavior. These phobias are difficult to overcome as they relate to physical symptoms that are profoundly distressing and often result in panic attacks.

> **Judy**, a 68-year-old women, with end-stage respiratory disease lives alone after the death of her husband, Ben two years before, and the suicide of her only son, Michael five years earlier. Judy is on continuous oxygen therapy and is supported with mobile oxygen when out. She had become fearful of leaving the house and while still able to drive her car, now had to drive with the windows down. She had difficulty going into shopping centres and avoided small spaces such as change rooms and public toilets. She was admitted to an inpatient palliative care unit for symptom management and a member of the psychosocial team was asked to see her. She presented with marked dyspnoea and was hunched forward in the chair. In spite of the door being open, she asked that it not be closed and that the curtain not be pulled around her. She was struggling with her admission as she described feeling like she might suffocate if she did not get fresh air. She had not showered for days and was toileting using a bedpan, as she could not face going into the small bathroom.

Generalized Anxiety Disorder

The excessive worriers who come to palliative care may have an exacerbation of anxiety but paradoxically, now there is a real threat to contend with, may have a reduction in anxiety symptoms.

Panic Disorder

Panic attacks are characterized by periods of intense fear or discomfort. Symptoms develop abruptly and include palpitations and shortness of breath dizziness and derealization (feeling estranged or detached from one's environment) and depersonalization (altered and unreal perception of self, feelings, and situation) and fear of

dying. As a combination of both physical and affective symptoms is used to diagnose panic, this can pose an issue for diagnosis in a palliative setting. The symptoms of depersonalization and derealization are more suitable for diagnosing panic disorder in those with life-limiting illness. For those with underlying shortness of breath, the fear of suffocating to death can drive panic attacks in this already vulnerable subgroup.

Death Anxiety

Death anxiety, often defined as the anxiety related to death awareness (Sussman and Liu 2014), has been described as the most profound fear and to be a driver of all anxiety. In his landmark book *The Denial of Death* (Becker 1974), the anthropologist Ernest Becker writes:

> . . .the fear (or terror) of death must be present in all our normal functioning, in order for the organism to be armed toward self-preservation. But the fear of death cannot be present constantly in one's mental functioning, else the organism could not function. . .. And so we can understand what seems like an impossible paradox: the ever-present fear of death in the normal biological functioning of our instinct of self-preservation, as well as our utter obliviousness to this fear in our conscious life.

As end of life approaches, death is no longer a distant prospect but part of rapidly approaching reality. The fear may relate to the dying process and the potential for poor symptom control especially in relation to pain or may relate to the existential nothingness and feelings of missing out that can be associated with death. A full assessment of the fears associated with end of life is important.

2.5.2 Depression

Depression is common among patients receiving palliative care but interestingly not more common than during the early stages of diagnosis and treatment and not an invariable outcome of advanced disease. A review by Hotopf et al. (2002) in 2002 and a later meta-analysis by Mitchell et al. (2011) estimated a prevalence of *Diagnostic and Statistical Manual of Mental Disorders* (DSM), defined major depressive disorder (MDD) of 15% and 14.3%, respectively (see Table 5 for summary of symptoms for DSM 5 MDD). The prevalence of DSM-defined minor depression was 9.6% and of adjustment disorder alone 15.4%. However the total prevalence of clinically significant mood disorder is estimated to be 30–40% (Mitchell et al. 2011). Many clinicians fail to recognize significant depression because of a tendency to "normalize" human responses to catastrophic situations such as life-threatening illness, leading to underdetection and therefore undertreatment (Rayner et al. 2010). The failure to recognize depression or enquire about mood is compounded by the observation that depressed patients are reluctant to volunteer symptoms (Hotopf et al. 2002).

Table 5 Summary of symptoms for DSM 5 MDD[a]

Five or more of the following, including at least one of items 1 and 2
1. Depressed mood
2. Loss of pleasure
3. Weight loss/weight gain or decreased appetite/increased appetite
4. Insomnia/hypersomnia
5. Psychomotor agitation/retardation
6. Fatigue/loss of energy
7. Worthlessness/guilt
8. Decreased concentration/indecisiveness
9. Recurrent thoughts of death/suicidal ideation/plans/attempts

[a]Content adapted from American Psychiatric Association (2013)

Adherence to strict DSM (American Psychiatric Association 2013) criteria of MDD is difficult in the palliative care context because of the overlap in symptoms of MDD and those of advanced medical illness (see Fig. 1). Greater emphasis needs to be placed on the patient's cognition and ability to experience pleasure than the somatic symptoms of depression. Some screening tools for depression omit somatic items and are more useful in the palliative care context. Two of the more commonly used assessment scales are the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith 1983; Mitchell et al. 2010), which has seven items relating to anxiety and six related to depression, and the Brief Edinburgh Depression Scale (BEDS) which has six items

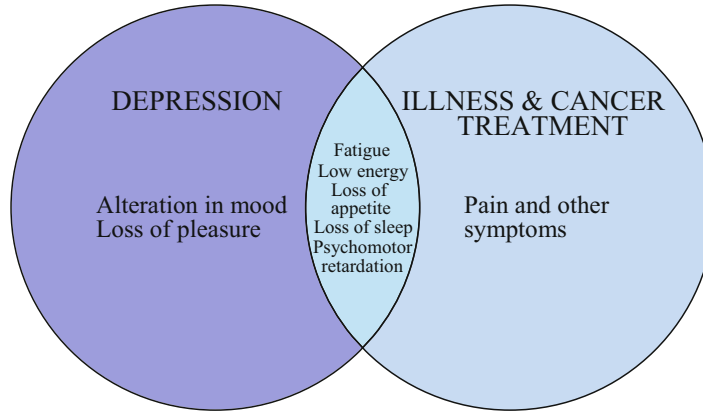

Fig. 1 Overlap between the somatic symptoms of depression and the side effects of treatment, illness, and the disease process

(Lloyd-Williams et al. 2007). Simply asking the patient "are you depressed?" (Chochinov et al. 1997) may accurately identify many depressed patients, but a two-item screen, which includes a question about loss of interest and pleasure in addition to mood and hopelessness has greater sensitivity and will pick up more cases (Mitchell 2008).

Early detection and treatment of depression is important, not only to relieve the suffering of the patient but also because depression exacerbates the physical effects of advanced disease, such as pain. Depression hinders adherence to treatment, obstructs the work of separating from the family and preparing for death, is a risk factor for high health service costs, and is associated with increased disability, poor prognosis, a higher mortality and higher risk of suicide or desire for hastened death (Widera and Block 2012; Rayner et al. 2010).

Table 6 Core features of demoralization and depression

Demoralization	Depression
Loss of meaning	Loss of pleasure
Loss of purpose	Loss of interest
Hopelessness	Hopelessness may be a feature
Helplessness	Withdrawal, isolation
Existential distress	Pervasively lowered mood
Shame	Guilt
Loss of anticipatory pleasure	
Feelings of failure or pointlessness, giving up[a]	Worthlessness
Difficulties coping and meeting expectations of self and others leading to lowered self-esteem[a]	
	Neurovegetative symptoms

[a]Proposed by Kissane as criteria for the revision of the Demoralization Scale-II and for establishment of demoralization in future editions of diagnostic systems such as DSM; Robinson et al. (2015)

2.6 Demoralization

The syndrome of demoralization, as a distinct clinical entity separate from depression and grief (Clarke et al. 2000), requiring recognition and treatment in the palliative care context and was first advanced by Kissane et al. in 2001 (2001), following the earlier work of Jerome Frank, as described by Clarke (2012). The core features of this syndrome are existential distress, loss of meaning and purpose, hopelessness, and helplessness (see Table 6). Demoralized individuals suffer immensely, lose self-esteem and a sense of mastery, see the future as pointless, and often yearn for release through death. This may lead to requests for a hastened death or suicide. Even when clinicians recognize the existential distress of the patient, they may see it as a totally understandable response to the circumstances and be unaware that the patient can, and should, receive appropriate intervention.

Although depression and demoralization share some common features, major depression is characterized by anhedonia and demoralization by loss of meaning and purpose. Patients who are demoralized can show a full range of affect and can experience pleasure in engaging in meaningful activities, although they may have difficulty in feeling anticipatory pleasure for things that are not in the here and now because they find it difficult to imagine a future without suffering. Demoralization can occur in the absence of clinical depression but when unattended can lead to depression; similarly, demoralization can become a secondary co-morbid disorder to unrelenting depression.

In a review of the literature pertaining to research of demoralization in progressive illness and cancer over the previous decade, Robinson et al. (2015) reported a prevalence of demoralization of 13–18%. It is interesting to note that, as for depression, the prevalence of demoralization is independent of time since diagnosis and stage of disease. Factors contributing to the development of demoralization include having poorly controlled medical symptoms, untreated depression or anxiety, poor social supports and social functioning, and having no partner.

The two measures of demoralization most often used in the studies reviewed were the categorically oriented Diagnostic Criteria for Psychosomatic Research (DCPR) (Fava et al. 1995), administered by structured interview and the dimensionally directed Demoralization Scale (DS), a 24 item self-report questionnaire (Kissane et al. 2004). The authors noted that the DCPR held the traditional psychosomatic notion that the mind directly causes the illness. However, in the development of the DS, Kissane viewed demoralization as a state of maladaptive coping in response to a stressor. Recently the DS was refined using classical test theory and Rasch's item response theory. The resulting 16-item, 2-component scale with 3 response options, the DS-II (see Fig. 2), has demonstrated internal and external validity; it is likely to be a useful tool in detecting demoralization and in tracking responses to meaning-centered therapies (Robinson et al. 2016a, b).

2.7 Post-trauma Syndromes

Post-traumatic stress disorder (PTSD) and other post-trauma syndromes may predate the onset of a terminal illness, be activated for the first time by the illness, or develop as a result of the experience of diagnosis and treatment of life-limiting disease itself. At times the distress manifested by the patient can be difficult to differentiate from grief, particularly if losses have been sustained in traumatic circumstances. Table 7 sets out the distinguishing features of grief and trauma. The significance of this for the patient is that there are many triggers in a palliative care context that create severe distress. The patient with pre-existing PTSD may have suffered childhood sexual and/or physical abuse, may be a refugee from a war-torn country, may have been held hostage, or may have developed the disorder from any number of traumatic experiences. People who have experienced trauma inflicted by other human beings rather than victims of natural disasters suffer more damaging consequences. Basic trust in others and the perceived safety of the world is severely challenged. The patient with PTSD experiences a cluster of symptoms:

Intrusive (memories, dissociative flashbacks, dreams, nightmares, symbolic associations)
Avoidant (efforts to avoid elements of the traumatic experience, including thoughts, feelings, memories, places, people)
Alterations in mood and cognition (dissociative amnesia, negative beliefs, negative emotions, emotional numbing, self-judgment, sense of foreshortened future, inability to feel happiness)
Hyperarousal (irritability, anger, hypervigilance, exaggerated startle response, recklessness, poor sleep and concentration)

All of these symptoms impact on the capacity to engage with staff in the setting of dependency and intimacy that characterizes palliative care. Pain, personal care, procedures, smells, and the death of other patients – a myriad of potent

For each statement below, please indicate how much (or how strongly) you have felt this way ***over the last two weeks*** *by circling the corresponding number.*

		Never	Sometimes	Often
1	There is little value in what I can offer others.	0	1	2
2	My life seems to be pointless.	0	1	2
3	My role in life has been lost.	0	1	2
4	I no longer feel emotionally in control.	0	1	2
5	No one can help me.	0	1	2
6	I feel that I cannot help myself.	0	1	2
7	I feel hopeless.	0	1	2
8	I feel irritable.	0	1	2
9	I do not cope well with life.	0	1	2
10	I have a lot of regret about my life.	0	1	2
11	I tend to feel hurt easily.	0	1	2
12	I feel distressed about what is happening to me.	0	1	2
13	I am not a worthwhile person.	0	1	2
14	I would rather not be alive.	0	1	2
15	I feel quite isolated or alone.	0	1	2
16	I feel trapped by what is happening to me.	0	1	2

Scoring Instructions:

Total score demoralization: Sum all 16 items.

Meaning and Purpose subscale: Sum items 1, 2, 3, 5, 6, 7, 13, and 14.

Distress and Coping Ability subscale: Sum items 4, 8, 9, 10, 11, 12, 15, and 16.

Fig. 2 Demoralization scale – II

Table 7 Comparison of grief and trauma[a]

Grief	Trauma
Sorrow (sadness) most prominent	Anxiety most prominent affect
Anxiety relates to separation	Anxiety is to the event and exposure to it
Preoccupations, intrusive memories, and images relate to the loss	Preoccupations, intrusive memories, and images relate to the traumatic event
Pining and yearning; seeks opportunity for contact: behavior is toward	Behavior is avoidant and withdrawing

[a]Content adapted from Raphael et al. (2004)

activators of PTSD in the palliative care setting – can interact with the patient's powerlessness and experience of being "done to" and activate post-traumatic stress. Delirium is common in the palliative care setting, and it is not uncommon for past traumatic experience to be relived during a delirium. This is distressing not only for the patient if it is remembered but for the family and staff who witness the event (Breitbart et al. 2002).

2.8 Decompensation of Underlying Personality Disorder

People who have an enduring pattern of inner experience and behavior that is maladaptive and causes significant impairment in interpersonal and social functioning are described as having personality disorder. During times of personal threat, the demand on coping strategies and need for adaptation are high. Those with personality disorder are not well-resourced internally and generally regress, with accentuation of the maladaptive emotions and behaviors. Although many types

of personality disorders are described in DSM 5 (American Psychiatric Association 2013), this section will limit discussion and case examples to three types of personality disorders patients that are most likely to experience (and cause) severe distress in a palliative setting.

2.8.1 Borderline Personality Disorder

The core feature of borderline personality disorder (BPD) is the disturbed attachments in early life, through early loss, unpredictability or unavailability of caretaking figures, or outright emotional, physical, or sexual abuse. Their vulnerabilities make them exquisitely sensitive to real or imagined abandonment, and they experience intense fears of annihilation. The distress, powerlessness, and dependency that are almost inevitable in life-limiting illness and invasive or intimate treatments and care cause severe regression and the emergence of very primitive defense mechanisms. Patients may behave in ways that are experienced as manipulative and become self-destructive in a desperate effort to gain some measure of control and channel intense, aggressive drives, and dependent needs. Their interactions with staff can cause confusion, anger, and rejection or avoidance of the patient. The BPD patient at times idealizes and at other times devalues individual staff members; sometimes certain staff are experienced as "good," while others are dismissed contemptuously as "bad." This is known as "splitting" and the dynamic becomes apparent when different members of the team have opposing views of the patient, "taking sides" for or against the patient. The BPD patient is prone not only to project feelings (such as anger) onto staff (accusing them of being angry), but also in a more subtle process, unwanted affect is taken on by the staff member unconsciously in an intrapsychic process termed "projective identification." This latter process results in the clinician leaving a patient encounter feeling unaccountably powerless, enraged, or harboring punitive impulses toward the patient (Hay and Passik 2000).

> **Pauline,** a 37-year-old divorced woman with three children from different relationships was admitted for pain management of peritoneal metastases from ovarian cancer. She had experienced childhood sexual abuse from her father from the age of 8–13 and had not been believed by her mother when she disclosed the abuse. Although she had received counselling from a sexual abuse agency in her 20's, after the birth of her first two children, her lifestyle had already developed a chaotic pattern, with unstable relationships and employment, alcohol abuse and self-harming episodes. Pauline was demanding, uncooperative and untrusting of staff. She insisted that all her care be delivered by one particular nurse who reminded her of an auntie who took her in when she ran away from home at sixteen years of age. She challenged nurses and doctors about every aspect of her care, to the degree that many staff were actively avoiding her and taking sick leave.

2.8.2 Narcissistic Personality Disorder

Patients with narcissistic personality disorder (NPD) can rankle staff because of their sense of entitlement, grandiosity, lack of empathy toward others, and contemptuous manner. They may invoke counterattack from staff whose own narcissism is challenged. The outward show of self-importance is a defense against core feelings of low self-esteem, shame, and self-doubt, and it is this vulnerability that makes NPD individuals at risk of experiencing a narcissistic wound under severe stress, sometimes with catastrophic consequences.

> **Sam** was a 48-year-old musician with metastatic colorectal cancer, estranged from his wife and children because they could no longer tolerate his self-centredness. He was angry about his illness and expressed the feeling that he would be 'better off dead' than have to rely on the incompetence of others. Although efforts were made to safely secure his environment from potential means of suicide, he was found dead in the toilet following an overdose of barbiturates which had presumably been brought to him by a visitor.

2.8.3 Paranoid Personality Disorder

The mental life of a person with paranoid personality disorder (PPD) is characterized by suspicion and mistrust of others, hypervigilance, and lack of emotional warmth. The early background is often defined by harsh, critical, and humiliating treatment by caregivers. These individuals struggle with anger, resentment, vindictiveness, and fear,

and the defense mechanisms of denial and projection make them difficult to engage. They may appear grandiose at times as everything is self-referential, and they are constantly scanning the environment to work out "what is really going on." In circumstances of life-threatening illness, the patient with PPD is precipitated into an unfamiliar situation of dependency on others and is likely to be highly critical and make angry accusations to unsuspecting staff, who are more accustomed to expressions of gratitude from the patients they care for.

Tom was a 74-year-old single man with Parkinson's Disease who was admitted to the inpatient palliative care unit for assessment, when the community palliative care team reported that he was becoming increasingly breathless. He had refused to go to his GP or a hospital for examination, but ultimately agreed to be admitted to a palliative care unit provided he could have his own room and no-one would bother him. His community care workers said that he had been very difficult to engage and would only relate to one worker provided that she kept a distance from him. He had lived alone all of his adult life and had no friends. An estranged sister told the team he was a 'difficult man, very much a loner and a bit on the paranoid side'. He had never been treated at a psychiatric hospital and community staff were not aware of any delusional thinking. From the moment of his arrival, Tom stated he was going to leave. Physical examination was not possible, nor any investigations, but he was noted to have swollen ankles and it was speculated that he may have cardiac failure. He became increasingly distressed with so many patients and staff around him that he abruptly left the unit in great distress on the third day. There were concerns for his safety as he had no medications at home for his Parkinson's Disease, so the community team called on him that evening only to find he had changed the locks and would not answer the door. Consideration was given to involving police to gain access to the house to perform a welfare check, but it was ultimately decided that such an intervention would be too distressing for him in view of his paranoid tendencies. The community team visited the following morning and were able to talk to him through the window, successfully winning back his trust over the following week.

2.9 Symptoms of Serious Mental Illness

Approximately 1% of the population suffers from schizophrenia: a further 1% from bipolar affective disorder (manic-depressive illness) (Miovic and Block 2007). As a group, people with serious mental illness are known to receive poor primary care, have inadequate screening for medical problems, have a high rate of medical comorbidities, lead lifestyles that may contribute to poor health (smoking, lack of exercise, alcohol abuse, use of marijuana and other illicit substances), and present later with cancer diagnoses, so that palliative rather than curative treatment is the only option. Other medical conditions related to serious mental illness that may lead to terminal illness include the metabolic syndrome, cardiomyopathy from antipsychotic medications, and lung or liver disease from smoking or alcohol abuse, respectively. In addition to these factors, the person with serious mental illness may have poor insight, difficulties in communication, cognitive disturbance, disturbed abstract reasoning and troubling or traumatic experiences of the world, and others during psychotic episodes and mental health treatments. They frequently experience disruptions in family relationships and social connectedness, homelessness, and interruption of the "normal" developmental trajectory with consequent deficits in sense of self. The entry of a person with serious mental illness into an unfamiliar healthcare system with a different language, culture, and technology creates a particularly acute vulnerability for the individual and anxiety and fear in professionals who often feel out of their depth. When such a patient shows evidence of severe distress, it can be difficult to determine whether it is related to these factors, relapse of the mental illness or the disease and/or the treatments.

Ray, aged 77 years, had been a loner all of his life, but had no previous psychiatric history. He presented with symptoms of breathlessness and was found to have lung cancer with metastatic disease to his brain. Radiotherapy could palliate his symptoms, but there was a question of his capacity to consent. Although Ray had delusional explanations of his illness (which revealed a long-standing and undiagnosed paranoid psychosis) and could not give informed consent, he expressed a desire to have available treatment for his disease. An empathic interview with a psychiatrist included the communication 'I can see what a hard-working man you are, and how you have always tried to do the right thing by other people. To be here with little sense of the reason why, and not to be in control

must be unbearable. I will tell the team about you and make sure they are able to think about you when decisions are being considered'. Treatment proceeded after an application under the relevant act for procedures or interventions when the patient is not mentally competent.

Erica aged 27 years, suffered from Bipolar Affective Disorder (BAD). She rejected her diagnosis of lymphoma, became manic and was difficult to engage in treatment for a potentially curable disease. When she was stable enough to commence chemotherapy, she was administered steroids to reduce the swelling around the lymph nodes in her mediastinum which were causing breathlessness and had an acute steroid-induced mania. She subsequently developed a delirium secondary to toxicity from her mood-stabilizing lithium medication. Her compliance with treatment was erratic and her disease progressed, ultimately involving the central nervous system. Her palliative care management was complicated by the diagnostic challenges of multiple aetiologies of her fluctuating mental state.

Cyril was a 74-year-old single man with a long history of paranoid schizophrenia managed successfully by his GP for thirty years without relapse of his symptoms. He was admitted with end-stage renal failure for end-of-life care after ceasing dialysis, and in the second week became aggressive and paranoid towards staff. He was initially thought to have a delirium secondary to the accumulation of toxins that his kidneys were failing to excrete, but there was no disturbance of attention and orientation. Further investigation revealed that his GP had ceased his long-term depot antipsychotic injection when he withdrew from dialysis and as a result Cyril had been unmedicated for his psychosis for six weeks.

2.10 Substance Abuse and Withdrawal

Estimates of the prevalence of alcoholism in different palliative care settings range from 7% to 27%. Over one third of head and neck cancer patients meet criteria for alcohol dependence, and a further 6.5% meet criteria for abuse. Lung cancer patients have a prevalence of alcohol dependence of 6.5%. Point prevalence for other substance use disorders in the general population is 0.5–1% each for benzodiazepines, opioids, amphetamines, cocaine, and marijuana (Reisfield et al. 2009). Palliative care staff may neglect to enquire about alcohol and drug use, and the appearance of withdrawal symptoms may be unrecognized or misinterpreted (Irwin et al. 2005). The most dramatic of these is delirium tremens, which characteristically appears 3–5 days following abrupt withdrawal from heavy alcohol use. It can present as a psychiatric emergency, with physiological hyperarousal, agitation, paranoia, visual and auditory hallucinations, disorientation, and impulsive behavior that is driven by fear. It carries a high risk of mortality and requires prompt attention with a combination of diazepam, haloperidol, and thiamine and adaptations in the environment to secure the patient's safety.

Family members may also have alcohol and drug abuse problems. Methamphetamine (ICE) abuse is an increasingly encountered problem in health settings. These may lead to problem behaviors on the ward and abuse or neglect of the patient in the home environment. A particular issue for community palliative care workers is the potential for diversion of opiate medication by drug-abusing family members. This problem will be discussed in the ▶ Chap. 83, "Challenging Family Dynamics."

2.11 Organic Mental Disorders

It is imperative that healthcare professionals are mindful of possible organic causes of severe distress. In a palliative care context, these include delirium, drug-induced states (steroids, ketamine), and cerebral disease (primary or secondary cancer, leptomeningeal involvement, paraneoplastic syndromes). In delirium, the onset is usually rapid, the course fluctuating, and the symptoms worsen in the late afternoon and evening. A "quiet" or hypoactive delirium may go unrecognized, and the patient's distress about abnormal experiences may therefore not be addressed. This state may rapidly change to a hyperactive or mixed state. Attentional deficits, disorientation, mood disturbances, and perceptual abnormalities may become more apparent in agitated patients. In a drug-induced abnormal mental state, there is a clear relationship to the administration of the medication and a resolution when the drug is ceased. Corticosteroids (e.g., dexamethasone, prednisolone) can induce mania, depression, anxiety, paranoid psychosis, delirium, agitation, and wakefulness, while ketamine can cause unpleasant dissociative experiences in the doses

used for refractory pain, and opiates can trigger a delirium. Mental state changes indicative of cerebral or meningeal involvement can be subtle and include odd behaviors, speech disturbance, and confabulation to cover up deficits. The essence to diagnosing these developments is alertness to changes in the usual mental state and a preparedness to listen to family members' observations of change.

2.12 Suicide

Ideas of suicide, suicide attempts, and completed suicide can occur in severely distressed patients who see no other way of ending their suffering. As we have noted, the demoralized, the depressed, and the narcissistically wounded are at special risk. The topics of suicide, suicide attempts, and requests for assisted suicide are discussed in separate chapters in this textbook, but Fig. 3 summarizes pathways to suicidal ideation and suicide.

What follows is a detailed description of one patient's changes in mental state during the last 8 months of life, illustrating features many of the disorders discussed above and concluding with the development of symptoms and signs of cerebral disease.

2.13 The Story of Arno

Arno was a 75-year-old man with recurrence of lymphoma, first treated 15 years previously. At the time he came to be assessed for severe distress, he had been receiving a targeted therapy in regular intravenous infusions for 2 months.

Arno had come to Australia from Holland with his family as a teenager in the early 1950s. As a child during World War II, he had witnessed his village being occupied by the Nazis and the disappearance of a lot of his Jewish neighbors, including his special friend. He did not understand the significance of these events until after the war. The atmosphere in the home was always very tense and volatile – father could be violent and mother was anxious and rarely left the house, spending long periods in bed. It fell to Arno as the eldest child to care for the five younger siblings. Both parents were communists, and although nominally protestant, religious practices were not observed in the home. Arno learned as

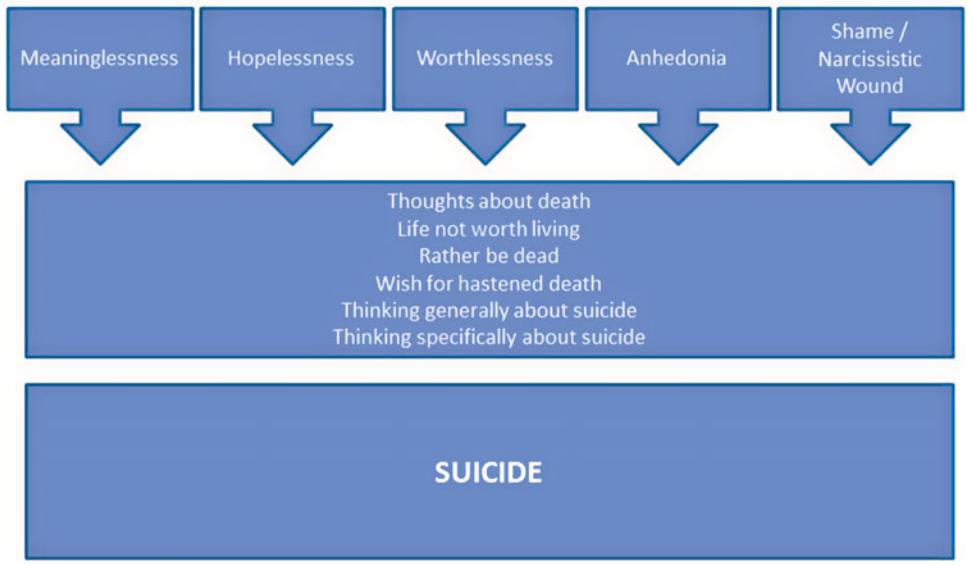

Fig. 3 Pathways to suicide

an adult that his maternal grandmother was Jewish and that he too would have been considered Jewish through the matriarchal lineage. With this knowledge came an understanding of the unspoken terror in the family relating to the fear of discovery and their relative isolation from the outside world. It also helped to make sense of his identification with Jewish people, to the degree that his school mates bullied him and called him "Levi the Jew-lover." He stood up to his bullies on one occasion and was never bothered again.

In Australia, Arno studied hard and obtained several degrees and diplomas. He worked as an engineer on a hydroelectric development that had created employment for many postwar European migrants. He had a traumatic experience of discovering bodies with their feet encased in concrete at the bottom of one of the dams but had never spoken about this to anyone. He married an Australian woman and had two children to whom he gave "old testament" names. He had one granddaughter whom he adored – "the light of my life."

Arno left engineering to become a shop steward and union man for a family business, a job he held until his retirement some years after his early illness. He was well-respected at work and had a reputation for being able to settle an argument "with a certain look I have." He had never been physically violent to others. He was known for his compassion; he and his wife would regularly take in and care for drug addicts, prostitutes, and homeless people. This was very much part of Arno's identity and he saw his actions as a way of reparation for the ugliness he had witnessed in human behavior. He considered his own life as fortunate. He had never been a smoker and drank alcohol only rarely.

2.13.1 Different Manifestations of Distress During the Last 8 Months of Arno's Life

Arno was referred as an urgent assessment after he had abruptly fled the chemotherapy unit, knocking staff and equipment in his path. He had been commenced on the monoclonal antibody rituximab because his lymphoma had progressed and was not responding to standard chemotherapy. Arno described classic features of a **panic attack** and felt he had to get out of the unit or he would die. He had already received three treatments without incident, but significant **death anxiety** was emerging since the news of his recurrence.

Over subsequent sessions a picture emerged of an underlying **major depression** somewhat masked by his stoic mien, with loss of pleasure and interest, irritability, tearfulness – "like a blubber-baby" – and poor appetite. He also described a long history of nightmares and flashbacks of his traumatic wartime experiences and episodes of cruelty and violence he had witnessed in his life. He avoided anything related to war, violence, or "bad things" happening to people and was always hypervigilant, "on the lookout" for people mistreating others. His wife complained of his emotional numbness in their marriage. He had a comorbid **post-traumatic stress disorder** which he had long managed through avoidant behaviors.

Arno responded very well to **mirtazapine** with improvement in mood, sleep, and appetite, but a month later he started to appear slumped and dejected in his sessions and conveyed a sense of shame. He said: "I just can't be the man I used to be. I feel useless. The men I used to look out for hardly call me anymore – they used to ask me for advice or just have a yarn or a whinge. . .I'm not well enough to look after the street people. I used to stand tall – have a certain presence. . .but now I feel invisible. I'm a waste of space. On the scrap heap." Arno had become **demoralized** even though his depression had improved, and the therapy started to focus more on a review of Arno's achievements and helping him to create new meaning and a sense of mastery.

Several months later, Arno developed pneumonia and became disoriented, agitated, and paranoid, while his intravenous antibiotics were being infused. Some of his post-traumatic experiences emerged in the **delirium,** and he misinterpreted messages over the public address system, believing that patients were being taken down to the basement to be shot or gassed. Medical staff in

the private hospital did not recognize the delirium and contacted his psychiatrist to say that he had become psychotic. His delirium responded well over 24–48 h to parenteral haloperidol and the treatment of his pneumonia.

Six months into therapy, Arno came to a session in a highly distressed state, having canceled his session the previous week. His face was suffused; he was trying very hard to stifle his emotions, and he had great difficulty gaining composure enough to be able to speak. Eventually he began to sob and told the psychiatrist that his daughter's marriage had broken up. "Things will never be the same for little Essie – this isn't supposed to happen in my family – I won't be there to support them." Arno was displaying acute symptoms of **grief** over the loss of a secure future for his beloved granddaughter and although initially inconsolable, he became more soothed as the psychiatrist discussed with him the importance of his role in Essie's life right now.

Almost 8 months into therapy, Arno missed several sessions because of influenza. After a break of 5 weeks, he came to his session looking haggard and disheveled. He appeared wobbly and reached out for the walls and furniture to get his bearings and steady himself. His voice was thick and he had difficulty finding the right words. He said he had been sleeping more and not eating much, forgetting to take his medication. His thoughts were rambling. He said he thought he had "thrown in the towel" because he had been so unwell with the flu. The psychiatrist believed Arno was showing evidence of an **organic mental disorder** and arranged for an MRI, which revealed leptomeningeal infiltration of his lymphoma. Arno died in a private palliative care unit 3 weeks later.

2.13.2 Key Issues from the Story of Arno

- The underlying cause of severe distress can vary over time in the same patient.
- Demoralization is a distinct syndrome that can arise independently of depression.
- Accurate assessment and diagnosis are essential for the appropriate management of the underlying cause of distress.
- Not all distress is related to the illness – other life events occur.
- The clinician must always be mindful of organic causes of distress.

3 Section 2: Managing Different Forms of Severe Distress

3.1 General Approaches

The transition to palliative care can be a time of great distress for patients and families as they cope with a lack of information, communication issues, and feelings of abandonment associated with changes in their medical team. The establishment of a therapeutic relationship based on trust and dignity is important, and the healing power of this relationship should not be underplayed. While many of the psychological interventions specified further in this chapter require specialist training, it is important to recognize strategies that all members of the healthcare team can utilize to reduce distress. All members of the team should maintain a dignity-focused, patient-centered approach that fosters open communication. This includes the use of empathic engagement and a therapeutic presence (Chochinov et al. 2013) that goes beyond basic communication and counseling skills. It is the capacity to "sit with" suffering and "bear witness" to the narrative of the person's experience, pacing the encounter so as not to stifle or threaten. While open communication should be fostered in all clinical relationships, the need for honesty and compassion is ever present in a palliative setting. There is a need to acknowledge distress and engage in empathic, reflective listening practices. The clinician's task is to maintain the patient's trust and hold confidences, all the while working within individual competencies and referring as needed (see Table 8). While communication skills training is important in all areas of healthcare, the need for ongoing training for all members of the palliative care team is essential.

Concepts from mindfulness and dignity therapy can be used by all members of the treating team to reduce distress and existential suffering. Basic relaxation techniques should be

Table 8 When to refer to the psychosocial team

Diagnostic uncertainty or complexity	Consultation for appropriate medication
Moderate-severe symptoms	Assessment of competency to make decisions
Preexisting serious mental illness	Evaluation of changes in mental state
Suicidal ideation or risk factors	Need for specific skills, e.g., clinical hypnosis
Desire for hastened death	Need to understand difficult behaviors and interpersonal difficulties
Failure of initial interventions	Complex or conflicted family dynamics
Need for psychotherapy	

implemented for those with high levels of physiological arousal, and techniques such as focused breathing strategies will reduce distress and assist with emotional downregulation.

3.2 Treatments for Specific Disorders

The treatment of specific psychiatric disorders in palliative care generally involves a combination of psychotherapy, medication, family involvement, and a multidisciplinary approach to holistic care. Disorders may be mild, moderate, or severe; some general approaches to treatment apply at all levels of severity, but the type and level of specific interventions may change according to the degree of suffering. Table 9 summarizes the approaches used for anxiety, depression, and demoralization. Details about the different forms of psychotherapy that may be appropriate and guidelines for the choice of medication follow.

3.3 Psychotherapies

A range of psychotherapeutic interventions have been developed for use in a palliative setting (Kumar et al. 2012; Rodin 2009; Stagg and Lazenby 2012; Dunlop 2010; Freeman 2011; Kissane et al. 2010; Okuyama et al. 2017). Manualized interventions have been the focus of randomized controlled trials to demonstrate efficacy (Smith et al. 2012). In practice, therapists need to be highly skilled in a range of therapeutic modalities to meet the presenting needs of the patient group. These needs will determine the choice of therapy. Other factors to consider are the individual's personality style, performance status, and prognosis. In a palliative setting, in depth, long-term psychotherapy may not be appropriate, and those with shorter life expectancies will benefit from shorter interventions. The importance of single therapeutic encounters or therapeutic moments should also not be overlooked.

The therapist must adapt to the rapidly changing world in which the patient functions and meet the patient where they are, rather than coming in with a preconceived idea on what the therapeutic encounter will look like. Due to the high burden of disease, "homework" for patients in this setting is inappropriate and has the potential to increase feelings of hopelessness and worthlessness. Inexperienced therapists may further traumatize already vulnerable individuals, highlighting the need for those working in this area to undertake specialist training. Therapists must have knowledge of the illness process and treatment side effects, practice a non-purist approach, be flexible and holistic, and foster a dignity-conserving orientation.

While those with advanced disease (Kirk et al. 2004) and their carers (Hudson et al. 2004) need information in many areas, e.g., prognosis, likely symptoms, treatment and side effects, disease progression, grief and loss, as well as the dying process, it is important that the patient and their family drive the delivery of this information. This prevents the patient and family being overwhelmed by information and reduces the potential for a negative impact on well-being.

Individuals with life-limiting illness juggle the demands of treatment, and their physical capacity may make it difficult for them to be available for regular therapy sessions. The therapist needs to be flexible and may have to travel to the patient, rather than insisting that the patient attends consulting rooms. In a palliative setting, reducing distress may involve attending to practical concerns including helping patients sit up, fluff a

Table 9 Treatment of anxiety, depression, and demoralization

	Treatment of anxiety[a]	Treatment of depression[b]	Treatment of demoralization[c]
General	Exclude medical causes; attend to contributing discomfort, e.g., pain, nausea Engage the patient in an empathic discussion of how he/she is feeling Assess contributing factors, e.g., family, financial, or spiritual concerns – refer to social work, pastoral care according to these concerns Assess the nature and severity and intervene/refer as appropriate	Exclude organic disorder; attend to contributing discomfort, e.g., pain, nausea Engage the patient in an empathic discussion of how he/she is feeling	Foster a therapeutic presence and dignity focus to reduce shame, feelings of aloneness, and disconnection Use active listening to deepen the therapeutic relationship Reassure the patient in stressful situations to reduce apprehension, panic, and perception of threat Encourage active problem solving to reduce helplessness, increase mastery, and self-esteem Promote adaptive coping in times of uncertainty Encourage help seeking to reduce hopelessness Explore meaning and purpose to reduce existential despair and meaninglessness Assess and treat comorbid depression Monitor suicide risk and desire for hastened death
Mild	Provide psychosocial and/or family support Consider brief interventions, e.g., problem-solving, relaxation strategies, guided imagery, cognitive behavioral interventions, mindfulness, hypnosis Provide patient with self-help materials – apps, CDs Engage music therapist If persists, consider introducing anxiolytics	Provide psychosocial support Assess contributing factors, e.g., family, financial, or spiritual concerns – refer to social work, pastoral care according to these concerns Provide family support Consider brief interventions, e.g., problem-solving, life review, meaning or dignity therapy, cognitive behavioral therapies If persists, consider introducing antidepressants	Utilize empathic listening and supportive psychotherapy Acknowledge the patient's difficult situation in an empathic manner Normalize grief and distress as appropriate responses in a challenging situation Focus on the individual's strengths and sense of resilience Encourage adaptation Nurture a focus on living in the moment
Moderate	Observe the recommendations above Assess for comorbid depression Consider introducing appropriate antidepressant Continue anxiolytic, change dose and scheduling as needed Consider hypnotic if insomniac Engage patient in psychotherapy with a member of the psychosocial team If persists, consider change of antidepressant	Observe the recommendations above Introduce appropriate antidepressant Consider anxiolytic if anxiety prominent, hypnotic if insomniac Engage patient in psychotherapy with a member of the psychosocial team If persists, consider change of antidepressant or augmentation	Engage a combination of therapeutic frameworks including cognitive, existential, and meaning centered approaches Acknowledge unhelpful thinking styles and challenge/reframe where appropriate Foster a life focus rather than a mortality focus Encourage the individual to live in the moment Explore gratitude in the individual's life Encourage engagement in sources of meaning Encourage family

(*continued*)

Table 9 (continued)

	Treatment of anxiety[a]	Treatment of depression[b]	Treatment of demoralization[c]
			communication, teamwork, support, and adaptive coping Educate and support the family in relation to their caregiving role and the patient's expectations of care
Severe	Observe the recommendations above Ensure antidepressant is titrated to adequate dose Consider small dose antipsychotic if agitated Continue psychotherapeutic support Monitor closely for suicide risk If persists, review diagnosis – death anxiety, terminal restlessness, delirium, steroids	Observe the recommendations above Ensure antidepressant is titrated to adequate dose Introduce small dose antipsychotic if agitated Continue psychotherapeutic support Monitor closely for suicide risk Consider augmentation of antidepressant Electro-convulsive therapy (ECT) can be necessary for a severely agitated and tormented patient	Ensure adequate symptom control to reduce distress and suffering Use narrative approaches to establish hope and meaning Assist in therapeutic life review and legacy activities Foster realistic hope while acknowledging grief Support the patient in finding new purpose Assist the patient to redefine meaningful roles Encourage supportive relationships Reframe negative beliefs with cognitive behavioral techniques Use family meetings to promote family cohesion and protect against family demoralization

[a,b]Refer to pharmacotherapies section for guidance in choice of medication
[c]Content adapted from Clarke (2012); Watson and Kissane (2017)

pillow, or pour a glass of water. It may also involve bearing witness to existential distress and immense suffering. Somatic issues can be a cause of profound distress, and anxiety and panic associated with dyspnea, nausea, or pain require immediate attention. The role of the health professional may be to act as coach in relaxation and mindfulness interventions or as an advocate in family meetings for those who are marginalized. As suffering in this setting can take multiple forms, skills in a variety of interventional strategies are required.

Many psychotherapeutic approaches have been adapted for a palliative setting, and Table 10 contains a summary of the psychotherapeutic interventions most frequently used, with a focus on mindfulness, supportive, narrative, existential, and meaning-based interventions. Creative therapies such as music, art, and movement are also highlighted.

3.4 Pharmacotherapies

Good-quality research concerning the use and efficacy of psychotropic medications in palliative care settings is scarce. The population itself is very heterogeneous, time frames for treatment variable, and multiple interventions are often initiated at the one time in the provision of care, confounding outcomes. A 2017 Cochrane Review could find no studies about the efficacy of drugs used to treat anxiety in adult palliative care patients and only two that showed some promise for a future update (Salt et al. 2017). The European Palliative Care Research Collaborative published guidelines on the management of depression which included a section on the choice of antidepressant (Rayner et al. 2011b). A separate systematic review and meta-analysis were devoted to antidepressants in the treatment of depression in palliative care (Rayner et al.

Table 10 Psychotherapeutic interventions

Psychotherapeutic approaches used in palliative care[a]			
Supportive and supportive-expressive psychotherapy (incorporating active problem solving and information provision) (Rodin 2009; Lederberg and Holland 2011; Hinshaw et al. 2002)	Therapeutic approach • Described as a framework and the "single most important tool" of the therapist in palliative care • Validates individual experience and provides support • Encourages expression of emotion, self-understanding and reinforces strengths • Promotes adaptive coping and resolution of core conflicts	Therapeutic techniques • Establishment of the therapeutic relationship and building of rapport • Bearing witness to the patient's experience, life, and suffering • Empathic listening and encouragement • Development of narrative meaning as a way of managing distress and trauma • Provision of information in a format and language that is appropriate • Education and communication with patients and families • Focus on strengths • Encourage adaptive coping • Use active problem-solving in a structured, step-by-step way	Use in a palliative setting Anxiety, demoralization, depression, end of life, fear of dying, grief, guilt, legacy work, spirituality, transition to palliative care, and trauma
Mindfulness-based interventions (Sharplin et al. 2010; Bates and Bartley 2011; Hales et al. 2010; Beng et al. 2015)	Therapeutic approach • Nonjudgmental, focus attention in the present moment, increase awareness Therapies Mindfulness-based stress reduction (MBSR) • Focus on reduction of stress, pain, and other issues (manualized) Mindfulness-based cognitive therapy (MBCT) • Integrates elements of cognitive therapy into MBSR MBCT – Ca • Palliative adaptation of group-based intervention Managing cancer and living meaningfully (CALM) • Brief individual psychotherapy Mindfulness-based supportive therapy (MBST) • Palliative care specific intervention	Therapeutic techniques • Mindfulness meditation including body scan and breath awareness • Mindfulness movement, e.g., yoga, tai chi, qigong • Supplement with CDs and apps Mindfulness-based cognitive therapy (MBCT) • Helps the individual to gain distance from thoughts Mindfulness-based supportive therapy (MBST) • Uses five components: mindful presence, listening, empathy, compassion, and boundary awareness	Use in a palliative setting Anxiety, depression, grief, management of physical symptoms, e.g., pain and sleep, and reduce suffering

(*continued*)

Table 10 (continued)

Psychotherapeutic approaches used in palliative care[a]			
Existential and meaning-based approaches (Mount 1993; Breitbart et al. 2004; Breitbart and Poppito 2014a; Breitbart and Poppito 2014b; Rosenfeld et al. 2017; Lethborg et al. 2008)	Therapeutic approach • Based on Viktor Frankl's work • Therapeutic process is to challenge individuals to find meaning and purpose through suffering, work, and love Therapies Meaning-centered group psychotherapy • 8-Week intervention (manualized) Individual meaning-centered psychotherapy • 7-Week intervention (manualized) MaP therapy • A brief 4 session intervention (manualized) • Revised and extended to 8 session intervention with evaluation work currently in progress	Therapeutic techniques • Individual or group interventions • Acknowledge the importance of an orientation toward life • Encourage a focus on living in the moment as opposed to anticipating the future • Encourage connection with the patient's sources of meaning • Use paradoxical intention, dereflection, and diversion techniques • Reduce cognitive dissonance between the individual's pre-illness expectations of life and their current reality • Utilize positive reappraisal, benefit finding, and the revision of beliefs/goals	Use in a palliative setting Death anxiety, demoralization, depression, and grief
Cognitive and behavioral interventions (includes cognitive, cognitive behavioral, and behavioral therapies) *Cognitive and behavioral interventions* (Mallick 2009; Akechi et al. 2008; Moorey and Greer 2002; Freeman 2011) *Acceptance and commitment therapy* (Low et al. 2016; Sussman and Liu 2014)	Therapeutic approach • Present based • Teaches self-efficacy and a sense of personal control Therapies Cognitive behavioral therapy (CBT)[b] • Identifies and challenges maladaptive thoughts and behaviors Adjuvant psychological therapy (APT) • Brief, cognitive behavioral therapy designed for use in an oncological population that has utility in those with advanced disease Acceptance and commitment therapy (ACT)[c] • Tolerate problems, acceptance of what is out of the individual's personal control, and focus attention on the present rather than focusing on the future • Psychological skills such as mindfulness are used to effectively deal	Therapeutic techniques Cognitive behavioral therapy (CBT) • Acknowledge unhelpful thinking styles and challenge/reframe where appropriate • Use mental distraction – behavioral task distraction and inattention • Bring focus to the now • Use adaptive ways of coping with distress and anxiety, e.g., relaxation therapy or guided imagery • Encourage active problem solving when high levels of uncertainty and complex decisions Acceptance and commitment therapy (ACT) • Focus on what is in the individual's control • Observe uncomfortable thoughts Behavioral interventions • Behavioral activation and activity scheduling esp. for depression and demoralization	Use in a palliative setting *CBT useful for* anxiety, demoralization, depression, grief, an increased confidence in decision making, an increased sense of control and mastery, physical issues, e.g., pain, nausea, vomiting, sleep disturbance, and dyspnea ACT may be helpful for death anxiety Relaxation strategies used for anxiety and panic at end of life, distress, pain and physical symptoms and stressful situations, treatments or procedures

(*continued*)

Table 10 (continued)

Psychotherapeutic approaches used in palliative care[a]			
	with painful thoughts and feelings	• Focus on what can do rather than what cannot Relaxation techniques • Breathing techniques such as breath reregulation and pacing • Guided mental imagery and progressive muscle relaxation • Anchoring the person to keep them focused on the now • Role of the health professional as a coach is important in these situations	
Narrative approachesNarrative therapy (Mount 1993; Noble and Jones 2005)	Therapeutic approach • Through the individual's story, meaning is found during times of suffering • Therapeutic work is done by the patient "re-authoring" their story • Individual puts the experience of illness into the context of their whole life	Therapeutic techniques • Encourage patients to share their life stories, memories, and experiences and record them in way that is meaningful to them • Assist in life review and legacy activities	Use in a palliative setting Anxiety, demoralization, depression, grief, legacy, and preparation for death
Narrative approaches Dignity therapy (Chochinov 2012; Chochinov and McKeen 2011)	Therapeutic approach • Principle of bedside care in line with existential principle "To be known is to matter" • Reflects on how the individual wishes to be remembered by focusing on the patient's life story and memories • Uses dignity-conserving therapy question protocol to obtain information about the patient's life and what and who is important to them • The interview is recorded, transcribed, edited, and refined into a narrative document	Therapeutic techniques Dignity-conserving therapy question examples • Asks patients to talk about their life history and the parts they consider to be most important • When they felt most alive • What are their hopes and dreams for their loved ones • What have they learned about life that they would want to pass along to others	Use in a palliative setting Anxiety, demoralization, depression, existential distress, grief, and legacy
Narrative approaches Reminiscence and therapeutic life review (Keall et al. 2015; King et al. 2005; Stagg and Lazenby 2012)	Therapeutic approach • Provides a way of addressing existential and spiritual concerns Therapies Reminiscence • Descriptive and involves thinking about	Therapeutic techniques • Encourage participation in biography or life review programs, where available • Assist in the writing of biography as a form of legacy	Use in a palliative setting Reminiscence reduces depression, improves adaptation to life and quality of life Therapeutic life review reduces depression and improves quality of life at

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Table 10 (continued)

Psychotherapeutic approaches used in palliative care[a]			
	life and recalling memorable aspects • Biographical in nature Therapeutic life review • Evaluative with a focus on examination, addressing, and resolving or rectifying conflict • Helps the individual look for meaning in the events of their life • Utility when life expectancy is less than 6 months	• Individuals describe important life events • Use statements like "thinking of your life as a series of photographs, what ones would you choose to describe your life and why?" • Utilize activities such as the creation of scrapbooks, cookbooks, and family stories • Techniques can be incorporated into individualized psychotherapy • Provide individuals ways of addressing issues or starting conversations with family members	end of life and spiritual well-being Legacy activities reduce fear of being forgotten
Narrative approaches Expressive writing (Bruera et al. 2008; Freadman 2015)	Therapeutic approach • Focus on writing about thoughts and feelings associated with an event • Assists in trauma processing • Reparative writing involves encouraging the individual to develop, revise, and expand the writing of their illness story so that it becomes "less generic and more authentic"	Therapeutic techniques • Use journaling and more formalized interventions that can be conducted individually or in group settings	Use in a palliative setting Anxiety, depression, and trauma
Clinical hypnotherapy (Brann 2015; Brugnoli 2016; Willmarth 2017)	Therapeutic approach • Induces an altered state of consciousness with increased suggestibility • A state of deep relaxation can be achieved • Recognized by the National Institute of Clinical Excellence (NICE)	Therapeutic techniques • Engagement, induction, deepening, establishing response sets, introduction of metaphor according to the themes of the goal of hypnosis, checking in, posthypnotic suggestion, closure, and disengagement	Use in a palliative setting Anticipatory anxiety related to medical procedures, and the management of pain and phobias
Family-centered approaches (Kissane and Bloch 2002)	Therapeutic approach • Based on the family as a system and includes the needs of children • Interventions include family therapy and family-focused grief therapy	Therapeutic techniques • Encourage family communication, teamwork, and adaptive coping • Educate and support the family in relation to their caregiving role	Use in a palliative setting Improve communication, cohesion, and conflict resolution
Brief psychodynamic approaches[b] (Macleod 2009)	Therapeutic approach • Focus is on the individual's unconscious processes	Therapeutic techniques • Concepts such as transference, countertransference,	Use in a palliative setting Those already oriented to psychotherapy or where

(*continued*)

Table 10 (continued)

Psychotherapeutic approaches used in palliative care[a]			
	• Goals of therapy are client self-awareness and the influence of the past on present behavior	regression, and attachment used to understand the psychological processes involved in dying	psychodynamic issues have arisen
Other interventions *Music and art-based therapies* (McConnell et al. 2016; O'Callaghan et al. 2015) *Art therapy* (Fenton 2008) *Drama therapy* (Redhouse 2014) *Eye movement desensitization and reprocessing (EMDR)* (Udo and Gash 2012) *Sleep* (Hajjar 2008) *Physical activity and somatic therapies* (Lowe et al. 2016; Selman et al. 2012; MacDonald 2016; Falkensteiner et al. 2011)	Music therapy • Well established with reduction in depression and anxiety Art therapy • Assists those approaching end of life make meaning of their situation and helps to provide legacy Drama therapy • Used to create life story Eye movement desensitization and reprocessing (EMDR) • Recommended by National Institute of Clinical Excellence and the American Psychiatric Association for use in PTSD • Effectiveness in reducing hypervigilance, re-experiencing the experience and consequent avoidance associated with response to trauma, and may have relevance in those with life limiting disease Sleep • Important in the maintenance of mood is well established • Routine around sleep maintained even as end of life approaches • Structure sleep hygiene strategies important including maintaining sleep routine (arising and retiring at approximately the same time each night), techniques for thought dumping prior to bed, relaxation, or meditation techniques to get to sleep and to stay asleep. Physical activity and somatic therapies • The role of physical movement rather than exercise • Use of physical and somatic therapies such as dance, yoga, pilates, walking, and massage		

[a]Content adapted from Kissane et al. (2010) and Watson and Kissane (2017)
[b]Cognitive and behavioral interventions: Evidence for use in a palliative setting with cancer patients, Parkinson's disease, end stage respiratory and cardiac disease and dementia
[c]Limited evidence in a palliative setting, feasibility trial underway

2011a). They comment that in many studies they reviewed, people with poor physical health were excluded and that treatment decisions for depression at the end of life is guided by research in populations with better prognosis.

Farriols et al. (2012) reported an increase in prescription of benzodiazepines, antidepressants, and antipsychotics over a 7-year period from 2002 to 2009 in a palliative care unit in Barcelona. They noted that inclusion of a psychiatrist on the multidisciplinary team had probably improved recognition and treatment of psychiatric disorders and that new drugs and new routes of administration had become available during this period. The published literature on psychotropic drug use in palliative care inevitably lags behind the development and use of new drugs.

The choice of individual drugs is influenced by factors independent of efficacy. These include drug interactions, the presence of active metabolites, possible routes of administration, time to onset of action, adverse side effects, and beneficial effect profile which may be exploited to treat other symptoms such as nausea, anorexia, vomiting, insomnia, or neuropathic pain. In addition, the availability of drugs varies between countries, as does the different forms of preparation of the drug. Drug-regulating bodies determine which drugs are approved for a specific use and which qualify for pharmaceutical benefits schemes. Different centers have developed their own culture of prescribing practices, and individual clinicians often have their own "favorite" medications.

What follows below is a synthesis of the available literature and the current prescribing practices in major palliative care centers in Australia.

3.4.1 Anxiolytics

Anxiolytics are the most commonly prescribed psychotropic medications in palliative care. Farriols et al. (2012) reported that 84% of patients were prescribed a benzodiazepine (BZDP) in 2009, increased from 72.6% in 2002.

- ***Lorazepam*** is the most commonly prescribed BZDP. It has an intermediate half-life and provides good anxiolysis at low doses (0.5–1 mg) without excessive sedation.
- ***Oxazepam*** (7.5 mg, 15 mg, or 30 mg) is a little more sedative but is a useful alternative as it is cheaper and the patient may already have been prescribed it in the community.
- ***Midazolam*** is the second most commonly prescribed in a palliative care setting. It is very expensive and has a very short half-life. It is able to be administered parenterally and is commonly used with morphine in a syringe driver as a subcutaneous delivery in terminal sedation. It is also prescribed for catastrophic events, some distressing procedures, and with an antipsychotic in an agitated delirium.
- ***Diazepam*** has an active metabolite, nordiazepam which has a long half-life and can accumulate in frail patients with impaired metabolism. It should be reserved for management of delirium tremens, people with motor restlessness, and those who are BZDP-dependent with the objective of reducing the dose gradually. It has greater muscle-relaxant properties than the above BZDP and is more likely to cause amnestic effects.
- ***Clonazepam*** has a very long half-life and can accumulate in the body over days, causing ataxia. It is available in an oral solution (2.5 mg/ml, 0.1 mg/drop, 25 drops/ml), and some patients experience a greater sense of control over their anxiety by being able to titrate the number of drops according to need. It is also a powerful anticonvulsant and can be helpful in patients who have brain tumors in reducing agitation and seizures. Administration via PVC tubing has been shown to result in significant loss of drug. A syringe driver using non-PVC-based tubing should be used.
- ***Alprazolam*** is a very short-acting BZDP with a rapid onset of anxiolytic effect and a rapid offset; it creates a cycle of relief and exacerbation of anxiety which can lead to increasing doses, tolerance, dependence, and abuse. It can cause amnestic effects and disinhibited behaviors. Because of these factors, it has become a restricted drug in Australia. Patients already taking alprazolam when they come to palliative care should be changed over to a longer-acting BZDP.

3.4.2 Hypnotics

Insomnia is a common problem on a busy inpatient unit and is a symptom, not a diagnosis. Sleep hygiene factors need to be addressed and pain, nausea, or delirium managed accordingly. Where initial insomnia is the result of worry or noise levels, sleep tapes of hypnosis, guided imagery, or music may be a useful means of inducing sleep. If medication is required, a higher dose of the same BZDP used for the management of anxiety (e.g., **lorazepam** or **oxazepam**) may suffice. The short-acting **temazepam** commonly used in medical units is also used in palliative care units when no regular BZDP is prescribed for anxiety. It is important to avoid charting four or five different BZDP as the effects are cumulative. There is some benefit in initiating **mirtazapine** 7.5 mg or 15 mg in patients who are thought to be sleeping poorly because of depression. Some patients cannot sleep because of an agitated depression and may need a small dose of a sedative atypical antipsychotic (e.g., **quetiapine** 6.25–12.5 mg or **olanzapine** 2.5 mg) in addition to adequate doses of antidepressant medication. **Nitrazepam** is not used in most settings. Non-BZDP omega 1 hypnotics, **zolpidem** 10 mg, and **zopiclone** 7.5 mg are used in some centers, but there are reports of amnestic effects, dissociation, and unusual behaviors with these drugs, particularly with **zolpidem.** **(**Olsen 2008**)**

3.4.3 Antidepressants

In palliative care, time is short and antidepressants are increasingly being introduced early in the care of patients with depression, even when they may have syndromal depression rather that a DSM diagnosis of MDD. In part this is because some antidepressants have an effect profile that addresses other problematic symptoms. In a systematic review and meta-analysis (Rayner et al. 2010), antidepressants were superior to placebo at every time point measured and the difference increased over time.

- **Mirtazapine** is the most commonly prescribed antidepressant in palliative care (Farriols et al. 2012; Cipriani et al. 2009). It is classified as a NaSSA (noradrenaline and specific serotonergic agent) and is related to the tetracyclic mianserin but has a unique mechanism of action. It boosts both serotonin and noradrenaline neurotransmitters: it blocks alpha 2 presynaptic receptor, thereby increasing noradrenaline neurotransmission; blocks alpha 2 presynaptic receptor on serotonin neurons (heteroreceptors) thereby increasing serotonin – novel mechanisms independent of noradrenaline and serotonin reuptake blockade. It blocks 5HT2A, 5HT2C, and 5HT3 serotonin receptors as well as blocking H1 histamine receptors (Stahl 2014). It has a relatively rapid onset of action, improves sleep, reduces anxiety, acts as an antiemetic, reduces nausea, stimulates appetite, increases food intake and promotes weight gain, and acts as an adjuvant in pain control (Alam et al. 2013). It also alters serum inflammatory cytokines and has been studied in cancer related cachexia and anorexia (Riechelmann et al. 2010). Doses of 15–45 mg given at night lead to a rapid and sustained improvement in depressive symptoms. Vivid dreams are occasionally reported and liver enzymes may become mildly elevated, but mirtazapine is well-tolerated in patients with advanced disease.
- **SSRIs** (selective serotonin reuptake inhibitors) may be the first choice for the treatment of MDD in cancer (Li et al. 2017), but side effects of diarrhea, nausea, lowered seizure threshold, and insomnia, as well as their propensity for drug interactions through the cytochrome P450 (CYP450) enzyme system, make them less attractive in people who are on multiple medications and may be already struggling with these symptoms. The CYP450 metabolizing system has more than 50 enzymes, the most significant of these being CYP3A4 and CYP2D6; polymorphism is responsible for the variations in drug response among patients of different ethnic origin. Drugs can be inhibitors or inducers of enzymes, causing unanticipated drug interactions with severe adverse effects or therapeutic failure (Lynch and Price 2007). SSRIs in combination with other serotonergic drugs (e.g., ondansetron, metoclopramide, pregabalin, morphine, fentanyl, tramadol, methadone, warfarin, methylphenidate, and antidepressants – all common in palliative care) can cause potentially fatal serotonin toxicity, characterized by high body temperature, agitation, headache, increased reflexes, tremor, sweating, dilated pupils, and diarrhea (Sun-Edelstein et al. 2008). At normal doses, SSRIs can cause a distressing symptom of psychic and motor restlessness known as akathisia. They can also lower platelets, as well as cause a syndrome of inappropriate antidiuretic hormone (SIADH) resulting in hyponatremia. In addition, if doses are missed or reduced, SSRIs can cause an unpleasant discontinuation syndrome of flu-like symptoms, insomnia, nausea, imbalance, odd buzzing sensations in the head, and anxiety. Where they are prescribed or continued in palliative care, the most common SSRIs are **escitalopram** (10 mg), **citalopram** (20 mg), and **sertraline** (50 mg). **Paroxetine**, **fluvoxamine,** and **fluoxetine** should be avoided because of the high propensity for CYP450 drug interactions. The CYP450 system is very complex and the clinician is advised to check for possible interactions through drug information services or a reputable website (Flockhart 2007).
- **SNRIs** (selective serotonin and noradrenaline reuptake inhibitors) may be associated with higher remission rates for depression than SSRIs. Like the SSRIs, they are more

activating than mirtazapine and are commonly prescribed in the community. **Venlafaxine** (75–150 mg), its enantiomer and major metabolite **desvenlafaxine** (50–100 mg), and a third SNRI, **duloxetine** (30–60 mg), are among the most commonly prescribed of this group in the general population with MDD. **Venlafaxine** is metabolized by CYP2D6, unlike desvenlafaxine which is largely renally excreted. Both **venlafaxine** and **duloxetine** can increase blood pressure, and **duloxetine** may cause deranged liver function. **Venlafaxine** has been associated with an unpleasant discontinuation syndrome. **Duloxetine** has some benefit for neuropathic pain.

- **Tricyclic antidepressants** have no role in the treatment of depression in people with advanced disease. They have a strong anticholinergic profile which increases the risk for delirium (especially in patients on opiates), urinary retention, constipation, dry mouth, and blurred vision, and their alpha 1 adrenergic blocking activity causes postural hypotension. There is also a considerable time lag (4–6 weeks) before a therapeutic response in the treatment of depression. Small doses of **amitriptyline** (10–25 mg) or **doxepin** (10–25 mg) may be used at night as adjuvant treatment for neuropathic pain.
- **Others. Ketamine** is a N-methyl-D-aspartate (NMDA) receptor antagonist commonly used as an anesthetic agent. In addition to blocking NMDA receptor channels, it interacts with other calcium and sodium channels, cholinergic transmission, noradrenergic and serotonergic reuptake inhibition, glutamate transmission, synapse formation, and mu, delta, and kappa opioid-like effects. These other actions may contribute to its usefulness in pain and depression. **Ketamine** is inexpensive and well-tolerated and has a rapid onset of antidepressant action. Some people experience mild dissociative effects within an hour of receiving the drug, and blood pressure may spike. Concerns about long-term use in treatment-refractory patients with major depression are not an issue in a palliative care population. Several sites are investigating the use of daily oral ketamine for the treatment of depression and anxiety in patients receiving hospice care (Irwin et al. 2013). The results are promising and ketamine may prove to be a useful alternative to the treatment of depression with psychostimulants. This latter group of drugs, particularly methylphenidate, is used to achieve a rapid improvement in mood when the patient's prognosis is days to weeks (Hardy 2009). It is usually initiated at 2.5 mg in the morning and, if tolerated, may be titrated up to 5 mg morning and midday. However adverse effects such as restlessness, tachycardia, delirium, nausea, loss of appetite, and insomnia may occur.
- **Monoamine oxidase inhibitors** are contraindicated because of the likelihood of drug and food interactions. **Agomelatine**, **reboxetine,** and **vortioxetine** are not discussed because of the lack of evidence and clinical experience in this setting.

3.4.4 Antipsychotics

Haloperidol remains the drug of choice in the treatment of delirium because its properties are well-known and it is available in parenteral as well as oral form. As second-line treatment or where the patient has an agitated delirium, a more sedative atypical antipsychotic such as **quetiapine** or **olanzapine** may be preferred. **Risperidone** is favored in some units but can cause dyskinesias. **Levomepromazine** is a relatively weak antipsychotic but is popular in palliative care units as a third-line treatment for agitated delirium, terminal sedation, and in some very agitated patients with psychotic illness (Dietz et al. 2013). The management of delirium is discussed in a separate chapter. These atypical antipsychotics are also helpful in an agitated depression in combination with an antidepressant. If a patient suffers from a serious mental illness, it is best to continue the antipsychotic the patient has been treated with prior to admission. If a patient with schizophrenia has been treated with **clozapine**, weekly monitoring by the strict protocol

must continue because of the risk of blood dyscrasias, myocarditis, and cardiomyopathy. Dose reduction or cessation may be required as the patient nears the terminal phase.

3.4.5 Mood Stabilizers

Mood stabilizers may be used in the palliative care setting where the patient is already receiving treatment for bipolar affective disorder or may be introduced to help manage manic effects induced by steroids or brain tumors. **Lithium carbonate** is difficult to manage in the medically ill, and the choice is usually made for **sodium valproate** over other drugs such as **carbamazepine** and **phenytoin** which have more problematic side effects. **Lamotrigine** is useful but may cause a Stevens-Johnson syndrome; it needs to be titrated up slowly and ceased immediately if a rash appears. **Gabapentin** and **pregabalin** have weak mood-stabilizing effects though they may have anxiolytic effects and are more often used in the treatment of neuropathic pain. **Levetiracetam** is commonly prescribed in patients with brain tumors but can cause anger, irritability, depression, and self-harm rather than stabilize mood (Thekdi et al. 2012).

3.5 Staff Education About Management of Patients with Personality Disorder

3.5.1 Borderline Personality Disorder

The scenario described in the case of Pauline in Sect. 2 can cause havoc on a ward and can be very destructive to a normally well-functioning team. Explanation of the origin of borderline dynamics and how regression and the primitive defenses mobilized under extreme stress impact on staff goes some way toward creating a framework for understanding the patient. In a team meeting, it is useful to have each staff member articulate their strong feelings about the patient and to understand that these feelings are useful data; it will become apparent then that each staff member carries a "fragment" of the disturbed inner world of the patient and a picture of the "whole" person can emerge. Patients with BPD find it hard to tolerate warmth, kindness, comfort, or intimacy. It is important to develop an empathic stance that is attuned to what the patient really needs and is able to tolerate, without loss of boundaries. Overly sympathetic responses may feel dangerous to the patient and promote withdrawal, further regression, or acting out. A few clearly defined and realistic limits may need to be set with the patient; it is important that the whole team participates in ensuring adherence to these limits because the patient will invariably test them to determine whether staff really care about them enough to contain them. While it is important for the clinician to have an understanding of the internal dynamics of the patient in order to form a collaborative and respectful relationship, it is equally important to avoid confronting and interpreting the patient's rage or entitlement, as this may lead to escalation of emotions. The primary focus of management of the BPD patient is education and support of staff who struggle with the rapid shifts in the patient's mental state and behaviors and may feel depleted, angry, incompetent, and sadistic or have personal vulnerabilities triggered by the encounters. Regular group supervision and reviews of management are necessary, and it should be recognized that some staff are unable to maintain their professional boundaries in working with BPD. It is worthwhile to remind staff that, while the behavior of BPD patients is dysfunctional, it is the best they can do under the circumstances.

While treatment of comorbid anxiety, depression, or substance abuse is indicated, psychotropic medication is not advised for the emotional dysregulation nor is psychotherapy for the traumatic early life helpful in a palliative care context unless requested. Enhancing self-regulation and self-control through techniques described later in Sect. 3 are of most benefit to the patient.

3.5.2 Narcissistic Personality Disorder

As the case of ***Sam*** in Sect. 2 demonstrates, any threat to the health and integrity of the body in individuals who place great store on how the outside world sees them can be experienced as a

narcissistic wound. The person with NPD keeps others at a distance with displays of grandiosity and dismissiveness, hiding in shame the tenuous sense of self. The narcissistic rage that ensues when these defenses break down can turn against the fragile self and lead to suicide, often in dramatic circumstances. Nursing staff had learned, with supervision, to cope with his demanding behaviors by meeting his needs with prompt and efficient service while setting limits on his less reasonable expectations. Staff can be left with feelings of responsibility, guilt, challenged professional competence, emptiness, and low self-esteem, some of which mirror the patient's disavowed and projected inner sense of self. These impacts must be managed with great sensitivity in staff support sessions.

3.5.3 Paranoid Personality Disorder

In dealing with PPD, staff need to be aware that these patients have difficulty tolerating intrusions into their personal space. A formal, respectful, and courteous manner needs to be maintained in spite of a barrage of criticism and accusation. It is important to elicit the patient's understanding of what is happening and to explain any procedures and their rationale carefully, repeating explanations if necessary. Staff need to ensure that what they tell the patient will happen ("I will be back with your newspaper in an hour") does indeed happen. Keeping unnecessary interpersonal interaction to a minimum avoids pushing the patient into an overstimulated state which amplifies the defensive projections. In spite of these considerations, **Tom** could not withstand the ward environment and could not be adequately assessed. When the crisis of his abrupt departure arose, the senior members of the team had to make a decision based on non-maleficence and respect for his autonomy despite the potential risks.

3.6 Family Interventions

In the palliative setting, families are important collaborators in care and sources of information and observation for staff. Supporting family members who become distressed by the suffering they witness in their loved one is an important role of the team and can help to reduce the burden on the patient. Family meetings help to share information, establish goals of care, and plan care delivery (Hudson et al. 2009). They can also provide opportunities to explain the causes of the altered mental states families witness (e.g., delirium, cerebral irritation) and may reduce misunderstandings within the family. They provide a window through which the functioning of the family can be observed and may reveal deep conflict between members which requires more specific intervention. Challenging family dynamics are discussed in a separate chapter.

3.7 Staff Support

Working in a palliative setting places individuals at risk of empathy fatigue (compassion fatigue), burnout, and vicarious trauma. The incidence of each of these in this setting is unclear due to methodological differences between studies. Compassion fatigue has been cited as the cost of caring (Boyle 2015; Figley 1997; Sinclair et al. 2017). Remen (2002) states that:

> The expectation that we can be immersed in suffering and loss daily and not be touched by it is as unrealistic as expecting to be able to walk through water without getting wet. This sort of denial is no small matter. The way we deal with loss shapes our capacity to be present to life more than anything else. The way we protect ourselves from loss may be the way in which we distance ourselves from life and help. We burn out not because we don't care but because we don't grieve. We burn out because we've allowed our hearts to become so filled with loss that we have no room left to care.

The need for self-care strategies is well recognized as having a protective function for those working in a palliative setting (Mota Vargas et al. 2015). Supervision and skills training need to be embedded in the organizational structure, and staff support sessions around challenging clinical care should be available to staff on a regular and as needed basis.

4 Conclusions

Patients facing life-limiting illness are vulnerable to a vast array of psychological and psychiatric disturbances. These may be related to their existential plight, the impact of the illness on their life trajectory, the ravages of the disease process itself, or the interventions required to treat it. Unfortunately, many patients, families, and staff view suffering as inevitable and understandable – even "normalizing" severe distress given the patient's predicament. There is no place for therapeutic nihilism about our capacity to relieve suffering. There are powerful psychotherapeutic modalities that can be employed to help the patient to negotiate the challenges of living while dying. These may be employed on an ongoing basis by trained clinicians, but some of the concepts from different forms of psychotherapy can be introduced in the everyday interactions with patients and families. It is important to embrace the idea that every clinical encounter is potentially therapeutic, not only for the patient but also for the staff member who may feel helpless in the face of another's suffering. There are also psychotropic medications which have good efficacy in treating anxiety and depression along with a greater readiness to introduce medication early. An awareness that "something **can** be done" leads to better recognition of distress, more thorough assessment of the underlying cause, and more appropriate and timely treatment. The multidisciplinary nature of palliative care allows for whole person care, which includes attending to physical comfort and mobility, engagement with music and art therapies, and attention to spiritual and culture-specific needs.

5 Summary

This chapter has explored the various manifestations of severe distress in patients receiving palliative care for malignant and nonmalignant disease. It has demonstrated the distinction between the normal distress of sadness and grief and that associated with problematic anxiety, depression, demoralization, post-trauma syndromes, decompensating personality disorder, serious mental illness, drug and alcohol abuse and withdrawal, and organic mental states. It has endorsed the NCCN statement that "no patient's distress should go unrecognized and untreated" and has provided the clinician with ways of distinguishing the different psychological and psychiatric disorders that can manifest as severe distress. General and specific treatment approaches have been outlined, with descriptions of the most helpful psychotherapies in the palliative population. Guidelines for the use of various psychotropic medications have specifically focused on the rationale of choice for patients with advanced disease, rather than provide an exhaustive list of possibilities. The importance of all staff receiving communication skills training and becoming familiar with some of the concepts of psychotherapies for incorporation into everyday communication with patients has been emphasized. Engagement with the family and supervision and support of staff is stressed as an essential component of palliative care.

6 Key Points

- Distress is often unrecognized, underlying causes not assessed, and disorder untreated.
- Distress is often "normalized," causing unnecessary suffering.
- Acknowledging distress is an essential first step.
- Every clinical encounter with a patient has the potential to be therapeutic.
- Nonspecialist staff can provide very helpful "in the moment" interventions.
- Early intervention is essential.
- Refer according to recommendations.
- Provide supervision and support to reduce compassion fatigue and burnout.

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Part VIII

Ethics of Palliative Care and End-of-Life Decision-Making

End-of-Life Decisions

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_91

Abstract

This chapter deals with the topic of medical decisions and decision-making that occur at the end of life and have the potential to allow the patient to die or hasten death. These decisions include: withholding and withdrawing treatment, intensified management of pain and other symptoms, active shortening of life without explicit patient request, euthanasia, physician-assisted suicide, and voluntary stopping eating and drinking. Evidently, such decisions are subject to considerable ethical deliberation and scrutiny, apart from their applicability in the legal framework of some jurisdictions. In this contribution, the main ethical principles – autonomy, beneficence, nonmaleficence and justice – are considered in the context of end-of-life decision-making. We go on with a discussion of intensely debated special topics such as: proportionality, the principle of double effect, (medical) futility, nonabandonment, and vulnerability. Next a glossary is provided of the most pertinent issues inherent in each type of end-of-life decision. Examples include: opioid phobia in pain management, the "slippery slope" argument in the assisted dying debate, and the relationship between palliative care and assisted dying. Finally, attention turns to a number of important topics related to communication in end-of-life decision-making: truth-telling, shared decision-making, advance care planning & advance directives, conflict, and cultural issues.

1 Introduction and Aims

Over the past decades, momentous progress has been made in the form of changes in living conditions and substantial and significant advances in science and technology, including in the realm of medicine. This has brought about important epidemiological, demographic, and social changes and hence also new challenges. Everywhere, but nowhere to the same extent as in the developed countries of the Americas, Australasia, central and western Europe, and the Asia-Pacific basin, life expectancy has risen sharply and consistently since the 1950s and will continue to increase (Kontis et al. 2017). Increased life expectancy, which might break the 90-year threshold in 2030, is accompanied by global population ageing. Both the increase of life expectancy and the growing proportion of people at old age – outnumbering younger generations – will globally challenge key aspects of health-care management.

Improved medicine and living conditions have changed not only the manner in which people live but also the way people die. Old age often brings frailty and failing health and illnesses with a heavy symptom burden. Death nowadays comes more often – generally in about two third of all cases – after a chronic, protracted illness trajectory with mostly noncommunicable conditions such as cancer, dementia, cardiovascular disease or lung disease, rather than suddenly due to communicable infectious disease or violence (accidental or conflictuous). Death is very often foreseeable and expected. This can be seen as the downside of medicine having provided us and continuing to provide us with the means to overcome health crises and prolong our lives. The corollary of many more life years for much of the population is that at a certain stage in a person's illness trajectory the "standard" or "straightforward" decision of providing life-saving, life-sustaining, or life-prolonging treatment can become disputable, undesirable, and/or unadvisable. Over the years, the extended period of declining health preceding death has incited people to become more involved in discussions and decisions on how they want to live in the final stages of life as well as how they want to die.

Historically, the dominant paradigm in medicine has been geared toward preservation of life at all costs, even in the very late stages of severe, incurable, and even terminal disease. Particularly when it comes to people with advanced chronic illness, this focus on "quantity of life" has recently become questioned and is being challenged by a movement – a societal movement, but also within medicine itself – advocating a shift in focus and perspective toward "quality of life" (Gawande 2016). This socio-cultural perspective shift is within medicine mainly represented by the palliative care movement, which has developed considerably in the past decades. As concerns treatment plans and decisions to be made in advanced illness and/or when death is approaching, considerations about quality of life and comfort care will increasingly come into play. The focus on life prolongation and therefore the relevance and appropriateness of burdensome and costly treatment for patients will increasingly be disputed. In this context, end-of-life decisions (i.e., decisions that allow the patient to die or that have the potential to hasten death) will be made primarily between the physician and the patient, and with the patient's family and other involved caregivers. These decisions will range anywhere on the spectrum between withdrawal of futile treatment and active life termination.

While there is a wide variety of clinical situations and ensuing therapeutic attitudes, and a great many variables need to be considered in each individual end-of-life decision, there are a number of tenets and ethical principles underlying each type of decision. The aim of this chapter is to provide an overview of the various types of end-of-life decisions and to discuss the ethical considerations and dilemmas (whether or not grounded in a specific legal framework) that come up in each of them. This will give the reader some insights into the complexities and pitfalls of end-of-life decision-making. Given that it remains a highly contested topic in academic, medical, and legal circles, this chapter will also highlight the fault lines of debates about acceptability and applicability of the conditions of certain types of end-of-life decisions.

2 Typology of End-Of-Life Decisions

Recognizing that medical practice at the end of life is extremely complex and does not always lend itself to clear-cut categorizations, classification is nonetheless necessary for an orderly discussion of the ethical and practical aspects. Though there is some occasional academic dissent, the typology of end-of-life decisions used in this chapter is widely accepted, largely uncontroversial, and empirically validated in research. The following types are discerned:

- *Withholding or withdrawing medical treatment*

  These are decisions forgo or discontinue (potentially) life-prolonging treatment. Examples of such decisions include forgoing radiation or chemotherapy, artificial respiration, resuscitation, antibiotics treatment, artificial administration of food and fluid, etc. Physicians can decide to withhold or withdraw treatment taking into account that the patient may die or explicitly intending to allow the patient to die.
- *Intensified management of pain or other symptoms*

  These decisions concern the administration of drugs for pain and/or symptom relief in doses that may also have a life-shortening effect. Life shortening can in these cases be taken into account as a foreseeable but unintended side-effect, or cointended.

  A special form of this type of end-of-life decision, in fact the most far-reaching form, is palliative or terminal sedation. If applied appropriately, i.e., according to professional and ethical guidelines, this practice will not influence the moment of death. However, when due care criteria are not followed or when applied in patients with special risk factors, a life-shortening effect cannot be precluded. The next chapter is focused solely on this practice (see ▶ Chap. 87, "Palliative Sedation: A Medical-Ethical Exploration").
- *Euthanasia*

  Euthanasia can be defined as the administration of drugs by someone else than the

patient with the explicit intention of hastening the patient's death, at the patient's explicit request.

This definition excludes "passive" decisions such as withholding or withdrawing life-sustaining or life-prolonging treatment, which have often been termed "passive euthanasia." This is a misnomer. Similarly, "nonvoluntary euthanasia" or "involuntary euthanasia," oft-used terms for the act of administering lethal drugs without the patient's explicit request, constitute misnomers. Euthanasia is by definition active and voluntary.

- *Physician-assisted suicide*

  Physician-assisted suicide can be defined as the physician's act to supply or prescribe a lethal dose of drugs to be taken by the patient him/herself, with the explicit intention of hastening the patient's death, at the latter's explicit request.
- *Voluntary stopping eating and drinking*

  This is the conscious and voluntary decision of the patient to halt all food and fluids intake with patient's explicit aim of hastening his/her death.

The pervasive issues in each of these end-of-life decisions will be discussed extensively further in this chapter. Euthanasia and physician-assisted suicide are often subsumed together under the umbrella terms "assisted dying," "medical assistance in dying," or "physician-assisted dying." For the remainder of this chapter both practices will be discussed together.

Perhaps not unexpectedly – but nonetheless important to point out here – it appears that there is an inverse relationship between the ethical contestedness of an end-of-life decision and its actual incidence in end-of-life practice. Though euthanasia and assisted suicide are by far the most controversial of all end-of-life decisions, and illegal in most parts of the world, empirical studies show that even in jurisdictions where they can be legally practiced they make up only a small minority of all deaths. Hence, the vast majority of end-of-life decisions concern cases of withholding or withdrawing treatment and cases of intensified management of pain or other symptoms, regardless of jurisdiction or medical culture.

Empirical studies into end-of-life decision-making have also pointed to considerable overlap, grey zones, and even confusion among physicians and other clinicians regarding the various types of end-of-life decisions (Deyaert et al. 2014). Vignette studies on and studies into the labelling of end-of-life decisions, for instance, have revealed faulty interpretations and a potentially problematic lack of understanding of differences between types of end-of-life decisions (Smets et al. 2012). On the other hand, these studies also show that clear-cut classification of end-of-life decisions in clinical practice is wishful thinking. Readers should keep this in mind at all times in this chapter.

3 Legal Contexts

Before discussing the various ethical principles and rationales, it is important to note upfront that the legal and regulatory context in a jurisdiction or country form the stage for practical ethical reasoning and concrete medical decision-making in that jurisdiction or country. There is extreme variation across countries worldwide in the legal status of the various end-of-life decisions, not only with regard to what is legally permissible and what is not but also to what extent relevant aspects for end-of-life decision-making are explicitly regulated. This latter aspect signifies that there are a great number of countries where the legal status of end-of-life decisions is undetermined and therefore uncertain. This compounds the difficulty of making such decisions. An oft-cited example concerns the legal status of withdrawing life-sustaining treatment in a patient in persistent vegetative state. In some countries this may be explicitly illegal, in others the permissibility needs to be determined through court rulings, while elsewhere it might be legally permitted by means of laws on patient autonomy and self-determination (Schneiderman 2011). Generally speaking, (legal) permissibility of end-of-life decisions in more developed countries is higher than in less-developed countries.

Obviously, it is imperative for clinicians and other involved actors to be well-informed on the permissibility of various end-of-life decisions, as well as the specific legal criteria and interpretive intricacies. For instance, in countries that allow medical assistance in dying, the patient must fulfil a number of substantive criteria and the physician must follow mandatory procedural criteria for due care in decision-making. Also, in some jurisdictions withdrawing treatment will only be permitted under a number of specific circumstances. Awareness of specific legal frameworks is vital in order not to expose oneself to criminal charges and to avoid overly aggressive and/or unjustified treatment courses. Moreover, the legal context may conflict with the personal stance and individual ethical standards of one or more of the actors involved, e.g., when the patient or family request a hastened death, at which point the physician can explain that this is not a legal option. Legal developments generally tend to lag behind ethical and philosophical debate.

4 General Medical-Ethical Principles in Relation to End-of-Life Decisions

Medical decision-making is also ethical decision-making: there are always several ethical considerations to be reckoned with. As concerns medical end-of-life decision-making, this is particularly true given that these decisions are made literally about life and death. Though the main ethical principles are systematically taught in clinical education (Beauchamp and Childress 1979) and widely known by clinicians, it is worth repeating in short here the content and the context of the basic four ethical principles that permeate all end-of-life decisions and that should always be heeded when forming end-of-life decisions.

4.1 (Respect for) Autonomy

The most fundamental of medical-ethical principles is respect for autonomy. It is increasingly recognized that patients have the last word in judging and deciding on the often many available treatment options and their consequences that are submitted to their informed consent. Basically, this entails that the patient has sovereignty over their own body and what does and does not happen to it. In the end-of-life context, this translates into the right of the patient to determine which treatment that is medically indicated according to the physician may be given and which may not. The final decision for a clinical course thus ultimately lies in the hands of the patient who is to receive it. This presupposes that the patient should be always fully informed about diagnosis, prognosis, and the benefits and drawbacks of the treatment plan.

The right to autonomy has not always been as central as it is today. It has gained considerable momentum in the past decades, as part of a societal and cultural shift from medical paternalism to patient and physician shared decision-making, the focus on quality of life, self-determination, and individualism. For this movement, the wish for self-control is considered fundamental as individuals are seen as planning agents, not only of their life but also of their death (which is inherent in life itself). In this context, openness and acceptance of death as well as the concept of "good death" (i.e., with dignity and according to one's personal preferences, which mostly feature being free from pain, dying at home, being surrounded by loved ones, being conscious until the final moments, being at peace, etc.) have come to centre-stage. In the philosophy of palliative care – and in its various definitions – attention to the needs and respect for the wishes of the patient (i.e., person-centeredness) is paramount. Many countries have even set legal parameters for patient autonomy, like the Patient Self-Determination Act in the USA or the Law on Patient Rights in Belgium. Lastly, advance care planning, advance directives, and living wills are aimed at allowing patients to exercise their autonomy in case or in anticipation of becoming incompetent (see below).

The counterpart of autonomy is usually termed paternalism – whereby someone else than the subject decides about what is in the interest of the subject and what is to happen to him/her. A sometimes useful distinction is between

"strong" paternalism, where decisions are taken against the wishes of the subject end "weak" paternalism, where the subject has not expressed wishes. With the ascent of autonomy as the overarching principle in medical ethics, paternalism has been increasingly imbued with pejorative connotations and has an aura of being undesirable and unethical. Particularly in the case of "vulnerable patient groups," i.e., groups that are less well able to stand-up for themselves and thus more prone to medical misconduct such as the elderly or the cognitively impaired (see below), the issue of paternalism is heavily discussed. Recent academic contributions have attempted to requalify this negative perspective, e.g., claiming that the perspectives of other involved moral agents – such as the physicians, care team, and the family – are also highly relevant in decision-making. They argue that the ethical pendulum may have swung too far in the direction of patients' autonomy (Wancata and Hinshaw 2016) and that patient autonomy should not supersede physician responsibility, which must not be dodged (Roeland et al. 2014; Levy 2014; Specker 2016). Middle-ground solutions such as shared decision-making are discussed further in this chapter.

4.2 Beneficence and Nonmaleficence

Beneficence signifies that the physician and involved care team are at all times concerned with "doing good" for the patient and acting in the patient's best interests. Nonmaleficence is closely related to beneficence and signifies that, above all, a physician should refrain from inflicting harm upon the patient. Beneficence and nonmaleficence can be served by active (doing well) versus passive (omission of doing harm) behavior. Both beneficence and nonmaleficence represent a fundamental tenet in the code of medical ethics. Especially in cases where the patient has not clearly communicated his/her preferences or wishes, the physician must adhere to these principles to ensure ethically sound end-of-life decision-making and the patient dying with dignity. These principles should for instance shield patients from the potential pitfalls of strong paternalistic decision-making.

In real-life clinical end-of-life situations, the application of the principles of beneficence and nonmaleficence is not always as straightforward as one would perhaps expect. The best course of action often hinges on a multitude of factors on various levels, rendering medical end-of-life decision-making highly complex. In such instances, they are essentially cost-benefit judgments. Dilemmas often arise e.g., when improving a patient's situation entails inflicting considerable harm upon the patient. Naturally, medical-ethical debate has focused on the central question concerning what constitutes a "harm" for the patient. In the context of end-of-life decisions, the question becomes whether death itself should be seen by definition as a harm (Clark et al. 2002). A corollary of this is that in some cases, some patients can see further irreversibly suffering life as a harm. Adherents of the recent cultural and societal paradigm shift toward quality of life over quantity of life may formulate permissive stances toward allowing patients to die, accepting potential life-shortening effects of medical actions, and in some cases even intentional ending of life. Diametrically opposed to this view and at the other extreme is the religiously inspired sanctity of life doctrine, rooted in the conviction that life is a gift from the Supreme Being, and therefore cannot be put at risk or given up but needs to be protected at any cost.

4.3 Justice

The principle of justice or fairness relates to the equal treatment of patients under equal conditions. It is more of a transversal principle that can be formulated and applied on two levels: the level of the individual and the societal level.

At the level of the individual, the tenet requires that patients are treated fairly and adequately. This applies particularly to the most vulnerable in society who are most at risk of not receiving the treatment they need, while others in similar situations would receive that treatment. In such cases, patients are denied access to adequate healthcare

and services by virtue of a characteristic that should be irrelevant in the decision whether or not to treat. A prime example of this is ageism i.e., different treatment of older people based purely on their age. However, the line can be very fine. For instance, age can arguably be a contributing factor in end-of-life decisions, so long as it has demonstrable relevance in the clinical parameters underlying the decision. An illustration of this is the decision not to operate on a patient when their advanced age entails an unacceptable risk.

At the societal level, the principle of justice translates into a just distribution of (scarce) healthcare resources. It regulates fair and equal treatment of patients from a higher level by rationing interventions based on the costs of end-of-life care and the available resources. It is the duty of governments, clinical networks, and medical institutions and departments to continuously strive for adequate allocation of resources based on the needs of the population and/or on issues of equality.

4.4 Usefulness of General Principles in Clinical Practice

As mentioned above, the general medical-ethical principles are commonly known among healthcare practitioners. They are the backdrop of ethically sound decisions; much care must be taken to arrive at a defensible decision. However, to apply them adequately requires quite some rigor and experience. "Principlism" certainly also has its limitations in clinical practice. At best, it constitutes a practical heuristic on which to base the reasoning toward an end-of-life decision. The principles can be seen as fundamental though not absolute, as they can easily come into conflict with each other, and the hierarchical relative weights they are ascribed will likely lead to different end decisions and outcomes. In any case, the principles are represented in basic clinical criteria for treatment decision-making: every treatment must be directed toward alleviating a clear indication (= beneficence, achieving benefits), the treatment goal must be achievable (= nonmaleficence, avoiding unnecessary harm) and informed consent must be obtained from the patient or the proxy decision maker in case the patient is no longer capable (= autonomy). (Justice is more of a relational ethical principle and is presupposed in clinical treatment decision models.)

5 Special Considerations in End-of-Life Decision Making

To further the application of the general medical-ethical principles, there are a number of special considerations central to ethical, clinical, and academic debate on end-of-life decisions. These considerations are germane to the ethical intricacies inherent in medical treatment decisions at the end of life.

5.1 Proportionality

Proportionality denotes the idea that the choice whether or not to provide a treatment should be based on a harm-benefit judgment. It requires one to weigh the potential benefits of the treatment against its potential harms and burdens for the patient. In view of the general clinical situation of a patient, the prognosis, all available treatment options and their consequences in terms of achieved or foreseen benefits should outweigh the harms, i.e., be proportional to the harms. Only then can the treatment be suggested to and discussed with the patient. In the end-of-life context, harms will most often relate to disproportionally prolonging the dying process and consequently the suffering of patients, with an unacceptably low quality of life. As a basic rule, treatment that fulfils the proportionality principle may be chosen in agreement between both the physician and the patient, and disproportionate treatment should be forgone. Even if this results in hastened death, there is no obligation to provide disproportionate treatment (Ko and Blinderman 2013).

Naturally, identifying and weighing the harms and benefits of a given treatment will never be a straightforward task. It presupposes the ability of the physician and care team to estimate the

outcomes of the treatment, including among others the likelihood of success, the severity of potential side effects, the impact on the intended treatment goal and knock-on effects for the patient's well-being. Also, the judgment of the patient plays a cardinal role in deciding on the relative values of the benefits and harms. For instance, to one patient nausea may be a totally intolerable side effect of palliative chemotherapy whereas another may feel it is an acceptable price to pay to live a while longer. These considerations make proportionality decisions at the end of life a highly complex process requiring accurate information and extensive discussions between healthcare professionals, preferably from various disciplines, between physicians and their patients and the patients' relatives.

The proportionality principle has largely replaced the concept of distinguishing between "extraordinary" and "ordinary" treatment as a means to make end-of-life decisions – with extraordinary treatment being more difficult to justify. The distinction proved not useful in clinical practice because it was unclear as to which criteria (usualness, complexity, artificiality, availability, cost) should be used to define "extraordinary" treatment.

5.2 Double Effect

The principle of double effect was first formulated by Thomas Aquinas (thirteenth century) to justify homicide in self-defence. An agent applies the principle of double effect when he/she wishes to do good but cannot do so without also causing harm. In its most stringent classic formulation, the principle of double effect can be licitly applied if all of four conditions are fulfilled: (1) the nature of the act must be morally good or neutral, (2) the harmful effect may be foreseen but should not be intended, (3) the good effect is not the product of the harm, and (4) the good effect must outweigh the harmful effect (cf. above: proportionality, the benefit must be proportional to the harm) (Mangan 1949).

The doctrine is applied mainly in the context of administration of opioids and/or sedatives, e.g., when mechanical ventilation is withdrawn or when pain and other symptoms become extremely discomforting for the dying patient, where the dosages are high and where causation of death due to e.g., respiratory depression, may be foreseen or expected by the physician (Thorns and Sykes 2000; Boyle 2004; López-Saca et al. 2013).

An authoritative study of intention in general has shown that it is a brittle criterium for acting morally (Anscombe 1958). There is an old utilitaristic tradition of criticism on the originally catholic doctrine of the double effect (Mill 1863). Though the concept has been often used in the justification of rapid dose increases in symptom treatment near the end of life, beyond philosophical considerations, its practical usefulness and appropriateness in clinical situations has been disputed (Quill et al. 1997). By involving the notions of redescription (alternative definitions) of acts and proportionality of consequences, a "weak" form of double effect principle has been proposed (Boyle 2004).

Whereas in criminal law intention is crucial, e.g., to distinguish manslaughter from murder, it is a disputed criterion for the ethical acceptability of end-of-life practices. First, is "absence of intention" a serious proposition when it contradicts or denies a high probability and a reasonable expectation, as when life support is forgone? When one relies on intention, one is dependent on self-reporting and risks self-delusion. People can fabricate an intention they at heart do not have or to obfuscate an intention they do have. The double-effect principle relies heavily on the individual clinical-ethical stance of the physician and supposes that physicians will always be conscious, honest, and clear about their ethical motives. This is problematic as it is extremely difficult or even impossible to cognitively separate intention to hasten death from expecting or foreseeing a hastened death. This applies to the person who makes the decision, and even more so to third parties such as the family. Secondly, the same action can be described in different ways, without there being an objective way to determine which description is correct. In many end-of-life situations, there are multiple layers of intention, and these layers, like a cascade, are related by a chain of causalities and consequences. For example, in

euthanasia, the proximate intention is killing, the next is relief of suffering, and the next respect for patient autonomy. Similarly, for end-of-life sedation, the proximate intention is reducing consciousness, the next is relief of suffering, and the next respect for patient autonomy if it is done at the patient's request. If the patient has expressed no wish, the physician's beneficence is applied paternalistically. Which level of intention is privileged can thus be highly subjective. Acts almost always serve multiple intentions. Establishing a hierarchy between them is very difficult (Quill et al. 1997).

Thirdly, the rule obviously refers to the intention of the physician. This disregards that multiple actors are involved in palliative care, foremost the patient, but also nurses, other paramedics, informal caregivers, clergy, etc. and these different actors may well have different intentions. Focusing solely on the physician's intention is unduly paternalistic and ignores the concept of care as a *process* involving multiple parties (indeed a central tenet of palliative care). The intentions of the person who is dying cannot be ignored, and those requesting the withdrawal of life-sustaining treatment or continuous deep sedation may intend to hasten their death, even when their physician harbors no such intention.

As such, invoking the principle of double effect can be an obfuscation of the "elephant in the room" and a weak safeguard against abuse of the practice of intentionally hastening the death of the patient through administration of medication. Actually, the only effective and somewhat objectifiable aspect of the double-effect principle may be the proportionality criterion which could be a sufficient condition. The necessity of the principle of double effect comes into question for commentators who submit that it is sufficient to let care of the dying patient be guided by patients' informed consent, the degree of suffering and the absence of preferable alternatives.

5.3 Futility

Futility, simply put, can be understood as the opposite of utility, which is the result of beneficence, i.e., the state of meaningfulness or benefit. An act is futile when it generates no utility, or when its performance entails drawbacks that exceed its benefits. Deciding that something is futile requires a judgment. This judgment can be by the person performing the act, by the person undergoing its consequences or – ideally in clinical settings – jointly by both.

At the end of life, futility relates foremost to unwarranted initiation or continuation of disease-directed treatments, thereby forgoing or delaying palliative care. Secondarily, especially in jurisdictions (countries and states) having depenalized-assisted dying, some patients may (come to) declare (further) palliative care futile and request assisted dying.

We will successively deal with these two cases of futility at the end of life.

There comes a time when during the disease-directed therapeutic stage of a fatal disease the pursuit of, e.g., chemotherapy or of life support is judged futile. Qualitative research suggests that, e.g., oncologists are well aware of the minimal response rate at the cost of nonnegligible drawbacks of aggressive treatments in many cases of advanced cancer. However, they feel that they cannot deny patients even largely illusory hope. The motives to discourage or curb medical futility are at the same time clinical, ethical, and economical (Bagheri 2014). It has proven a difficult task because of poor acceptance of death: both public expectation of what medicine can achieve and professional perception of what ethics and law require drive an unhelpful alliance that often results in futile courses of medical action (Ashby 2011). As for fee-for-service remuneration of doctors and health-care facilities, we are not aware of data supporting the contention that it is associated with more medically futile interventions, but, logically, such remuneration might compound the problem.

The use of the concept of futility in clinical practice has its problems as there are many complications in attempting to define or operationalize it. Futility may lie in the total lack of a physiological benefit for the patient, e.g., treatments that would not *at all* alter the course of the disease, the time of the fatal outcome or the prevalence or

intensity of symptoms and complaints. .Such a binary judgment is often based on objective and evidence-based criteria and is thus relatively feasible for well-trained doctors and well-informed patients. More frequently, futility is quantitative, a continuous variable. It can relate to an unacceptably low probability of success, or to so small a benefit that it is outweighed by the drawbacks of the course of action. This type of futility draws on proportionality and the balancing of benefits and drawbacks. Treatment can also be deemed futile if the financial cost is too great to justify the low probability and/or magnitude of the effect. The goal of this higher-level approach is cost control and justice in the allocation of resources (Baily 2011). The overarching principle for these considerations is the obligation to always do a cost-benefit analysis, where costs can be both economical and clinical (e.g., side effects and other adverse consequences of treatment), and benefits can be physiological, psychological, or social. Cost-benefit analysis can be considered as belonging to the obligatory means of clinical practice.

"Physiologically" futile treatment at the request of the patient or proxies poses a difficult problem of conflicting interests: the values of the requesting agent are then at odds with the physician's. Most cases ought to be resolved by complete information and full deliberation.

Uncertainty also abounds according to *who* decides whether a certain course of action is useful or futile. Ideally, after a process of shared decision-making all those involved concur, but when they differ, problems arise. A decision of forgoing a course of action that is medically futile, if taken unilaterally by the physician, can be closely related to paternalism: "strong" if against patient preferences or "weak" if without input from the patient. As long as the decision is based on clear physiological or clinical indicators, and the patient has declined involvement in decision-making, such reasoning may be perfectly justified. But, of course, it is always advisable to consult with the patient and others. A judgement of futility should not serve as a justification to forgo difficult but ultimately beneficial conversations to address unrealistic expectations and prepare for the end of life. Conversely, medical futility may be a judgment by the informed patient against the "physiologic" judgment of the physicians. This is what has been termed "normative futility" (Youngner and Arnold 2016) or "qualitative futility" where a treatment may be physiologically effective but not psychologically beneficial (ten Have and Janssens 2002).

The second issue on futility at the end of life is whether there is such a thing as "palliative futility" and, if so, whether in permissive jurisdictions this justifies a request of assisted dying. A debate is ongoing regarding the (non)sense of the concept of "palliative futility." It has been argued that "meaningfulness" is not absolute, but inseparable from the question "for whom?". Caregivers, for whom palliative care is always meaningful, will always offer it, but a patient not. According to this reasoning, one can take a hard look at any a priori subordination of the view of the patient to that of the caregiver. Such a hierarchy, it is argued, violates the central position and autonomy of the patient (Bernheim and Raus 2017). Especially in jurisdictions with legal assisted dying, some patients may consider the initiation or continuation of palliative care as futile, and request assisted dying (Bernheim et al. 2008; Bernheim and Raus 2017). In general, respect for patients' autonomy encompasses patients' fundamental right to refuse perceived futile treatment (Bagheri 2017). Logically, this also applies to palliative care. However, many dispute that palliative care can ever be futile (Jaspers et al. 2009; Materstvedt and Bosshard 2013). This is also the formal European Association of Palliative Care's (EAPC) normative stance: "Palliative care is provided up until the end of life and is by definition never futile" (Radbruch et al. 2016). A reconciliating consideration could be a distinction between palliative "treatment" which may for the odd patient be or become futile and palliative "care" which is always meaningful from a human solidarity perspective (ten Have and Janssens 2002). In Belgium, for instance, palliative caregivers may see euthanasia as a last exercise of care and refusing further palliative care does not disqualify a patient from assisted dying (Vanden Berghe et al. 2013).

In any case, the question is particularly pertinent in the assisted dying debate: if palliative care can always alleviate all suffering, then a standard condition for eligibility for assistance in dying, i.e., that suffering cannot be alleviated, is never fulfilled. Conversely, if palliative care is not always able to sufficiently alleviate suffering and if some patients consider (further) palliative care as futile, then at least some requests for assisted dying could be considered legitimate and legal in permissive jurisdictions. In the Benelux countries with depenalized euthanasia and/or assisted suicide options, some patients' well-considered perception of further palliative care being futile can be honored and acted upon (Bernheim et al. 2008, 2013; Bernheim and Raus 2017).

5.4 Nonabandonment

Another oft-cited ethical consideration related to end-of-life care and decision-making relates to the idea of nonabandonment, also referred to as fidelity, on the part of the physician and care team toward the patient. It entails a duty of responsibility and accountability of the physician and the care team toward continued care for their patient. This may seem evident, yet there exist a number of not infrequent situations in which this duty conflicts with other values or priorities.

One situation very often encountered in palliative and end-of-life care relates to patients feeling a sense of abandonment from their physician when a decision needs to be made to focus treatment on palliation – instead of cure or life prolongation – or the withdrawal of life-sustaining treatment. This is closely tied to the reluctance of physicians to bring such a message and "take away hope."Nevertheless, this communication is important and when it happens the patient needs to be reassured that any change in treatment goals and any withholding or withdrawal of treatment will be accompanied by an appropriate and effective care plan focusing on the patient's comfort. This also implies that a physician will not abandon the patient by failing to consult the necessary palliative care experts when they themselves do not possess this expertise. A special case of this is when the physician has to refuse a request of futile treatment.

A different type of situation concerns the case in which a palliative patient explicitly requests a certain course of action that goes against the morals or beliefs of the physician. This will concern assistance in dying in most but certainly not all cases; a patient's refusal of clinically beneficial treatment, for instance, may also be difficult for a physician to accept. If clear and explicit communication does not reconcile the conflicting views, the physician may decide to withdraw from the therapeutic relationship on grounds of conscientious objection. In the Benelux countries there is no legal obligation to transfer the patient into the care of another permissive physician, team or unit, thus assuring the patient continuity of care whilst preserving one's personal ethical principles. However, it has argued that failing to do this in order not to be an accessory of something one disapproves of, comes near to abandoning one's patient (Vanden Berghe et al. 2013). A final type of situation relates to the physician being faithful in following the choices and decisions of the patient and even defending them when the patient can no longer speak for himself or herself.

5.5 Vulnerability

Vulnerability constitutes an important reflection in palliative care and end-of- life decision-making, closely tied to the ethical principle of justice. Over and beyond the fact that severely ill and dying patients are by definition vulnerable, physicians need to pay special attention to the protection of people who are unable or not sufficiently able to defend their own interests. Categories often mentioned in this regard are: children; the elderly; the disabled; the mentally incapacitated; psychiatric patients, cultural, and ethnic minorities. Referring to the nonabandonment consideration discussed above, physicians can be expected to defend these interests in lieu of the patient. Particularly those with reduced competence or complete incompetence are most vulnerable to unethical and unjust treatment. Persons from a cultural or ethnic minority might lack the

necessary health literacy or language skills to navigate their way to appropriate, tailored care. These persons also adhere to specific belief systems different from the cultural majority of a country and are therefore more at risk of receiving treatment that is inappropriate to their moral values.

6 Notes on Specific End-of-Life Decisions

In this section, a number of points particular to the specific types of end-of-life decisions are highlighted and discussed. These points are nonexhaustive but give the reader an understanding of the "lay of the land" with regard to modern academic, ethical, and clinical debate on each decision.

6.1 Withholding and Withdrawing Medical Treatment

Medical treatments that are commonly withheld or withdrawn at the end of life are: cardio-pulmonary resuscitation, intubation, mechanical ventilation, artificial nutrition and hydration, kidney dialysis, surgery, and antibiotics treatment. However, a nontreatment decision may also concern the decision not to run diagnostic tests or not to transfer the patient to hospital, as the finality of these conscious choices is to no longer pursue curative or disease-directed options for one or more given problems.

Many philosophers, ethicists and legal scholars have long studied the existence, necessity and/or usefulness of a moral distinction between withholding treatment and withdrawing treatment. This is referred to as the act-omission or commission-omission distinction. While the general debate does not look to be settled for some time, the consequentialism-inspired consensus view related to end-of-life treatment seems to be geared toward moral equivalence between withholding and withdrawing. Jurisprudence in most developed countries has ruled in favor of this view as well. This said, while there may not be a legal or ethical distinction, a considerable psychological and moral effect for the physician and others involved can be expected. It is arguably much more difficult and confronting to remove mechanical ventilation than it is to not initiate it. This psychological and moral impact should not be ignored in clinical practice.

The legal status of nontreatment decisions (withholding and withdrawing treatment) varies greatly from country to country. In most modern industrialized countries, they are largely unproblematic under the necessary conditions, though even recently some cases elicit heated debate and legal proceedings are necessary to clarify the possibility of treatment limitation. The most thought-provoking cases concern withdrawing life support or artificial nutrition and hydration in people in a persistent vegetative state, especially minors (cf. the Alfie Evans case in Britain, in which the parents of a terminally ill toddler in a semivegetative state lost their legal battles over the hospital's decision to withhold further prolonging life support as well as the option to transfer their son to a Vatican hospital in Rome for further treatment (Evans 2018)). In less developed and non-Western countries the law might severely restrict clinicians' possibilities to forgo life-saving, life-sustaining, or life-prolonging treatment. Clinicians are strongly advised to inform themselves about the legality in their country of forgoing various treatments at the end of life.

According to some, artificial administration of nutrition and hydration represents a special case in end-of-life treatment, as it can be regarded as standard and obligatory practice to provide food and water to the patient. It also has particular symbolic meaning; the argument states that while it does entail a technical intervention, it does not constitute a medical treatment but rather basic human care. While this is an understandable perspective on the issue, the consensus view disputes this, arguing that artificial nutrition and hydration, just as any other medical treatment, must adhere to all standard requirements: a clear indication, a reasonably achievable treatment goal and informed consent (Ko and Blinderman 2013). If not subject to these requirements, artificial

nutrition and hydration, a notably invasive treatment, could be performed against the wishes of the patient. Moreover, studies have shown that providing it at the end of life does not procure much benefit and that in end-of-life settings starvation is extremely unlikely (Druml et al. 2016). As not providing nutrition and hydration may seem harsh and unacceptable, especially for the family, it is important to reassure them – as well as the patient – of these medical requirements and that adequate comfort care will be provided to prevent unwanted effects of dehydration.

6.2 Intensified Management of Pain or Other Symptoms

As mentioned above, intensified pain and symptom management at the end of life mostly concerns the administration of increasingly high doses of morphine and/or sedatives, as these drugs are thought to contribute to a hastened death in certain doses.

The literature describes the reportedly widespread phenomenon of "opioid phobia." This term refers to a fear or reluctance on the part of physicians to provide morphine or other opioids in high or even only moderate doses. Outside the end-of-life setting, this concern is also based on fears of causing addiction and dependency in patients, but in an end-of-life situation the concern lies mostly with patients developing tolerance leading to ever higher doses being needed, and with the possibility that high doses will cause respiratory depression in already very weak patients and lead to a premature, nonnatural death. While such fears are reasonable, cf. the sharp increase of unintended deaths due to prescribed opioids in the USA (López-Saca et al. 2013), according to experts, the effects of high-dose opioids in general are largely overstated, especially in patients where the dosage increase is gradual (in opioid-naïve patients, however, more caution is needed) (Thorns and Sykes 2000). Notwithstanding the complexity of calculating dose equivalences between the various opioid products, opioid rotation, i.e., switching regularly between opioids, is recommended as in order to avoid tolerance and the need for rapid dose increases. The importance of assuaging unsubstantiated fears in physicians to use opioids in adequate doses cannot be overestimated: opioid phobia could well lead to undertreatment and therefore ineffective relief of pain (and other symptoms) at the end of life (Macauley 2012).

Of course, there will be instances in which e.g., respiratory depression under treatment with opioids occurs. These and other situations are typical examples of where the proportionality principle, the rule of double effect and risk-benefit balancing are highly useful to justify high dosages of opioids. Respectively, the reasoning goes as follows: the administered dose is as high as necessary to alleviate the patient's pain (proportionality), the objective is achieving adequate pain relief, with respiratory depression and death as an unintended but acceptable consequence/effect (double effect) and the risk of hastened death is of less importance than the need to avoid protracted suffering. As discussed in the section above, it is may be important to communicate clearly with all involved – patient, family, and care team alike – about the explicit treatment goal and the possibility of unintended consequences.

At the end of life, high doses of sedatives (mostly benzodiazepines, or sometimes barbiturates) are increasingly used to achieve palliative or terminal sedation. Here, the same considerations of proportionality and double effect apply in order to avoid misuse as "slow euthanasia," as research has suggested. Therefore, guidelines for adequate performance have been issued, and in some countries there are initiatives to register the practice (e.g., Belgium) and it has even be legally regulated (i.e., France's *Loi Leonetti*). See ▶ Chap. 87, "Palliative Sedation: A Medical-Ethical Exploration" for a thorough discussion of palliative sedation.

6.3 Euthanasia and Assisted Suicide (Assisted Dying)

An increasing number of countries and jurisdictions are legalizing assisted dying. Euthanasia is, at the time of this writing, legal in six jurisdictions

worldwide: the Netherlands (since 2002), Belgium (since 2002), Luxembourg (since 2009), Colombia (since 2015), Canada (since 2016), and Victoria in Australia (as of 2019). In the Netherlands, the legalization of euthanasia was preceded by a period between the mid-1980s and 2001 of legal tolerance of the practice, as long as certain requirements of careful practice, suggested by the Royal Dutch Medical Association, were complied with (Griffiths et al. 1998). The first jurisdiction to have legal euthanasia was actually the Northern Territories in Australia in 1995; however, the law only held 9 months and was overturned by the federal Parliament of Australia. The legalization in Canada was a result of a ruling of the Supreme Court in the Carter versus Canada case, which ordered the provinces to draft laws legalizing euthanasia by February 2016, later extended to June 2016. Medically assisted suicide, but not euthanasia, is legal in a number of states in the USA and in Switzerland.

Euthanasia and assisted suicide – for the remainder of the chapter together referred to as "assisted dying" – are arguably the most controversial topic in end-of-life debates today. Heated discussion continues to rage whether or not assisted dying can be morally acceptable at all. Obviously, for proponents of assisted dying (notably the "Right to Die" or "Pro Choice" movement) the autonomy and right to self-determination of the patient takes primacy over any other ethical principle. However, they also argue that assisted dying need not violate the principles of beneficence and nonmaleficence as death can be considered as the curtailing of unnecessary and pointless suffering – suffering that cannot otherwise be alleviated – and thus as beneficial and a good in itself. Moreover, similarly to other bioethical issues such as in the sexual or reproduction domains, assisted dying belongs to the personal province, and its legalization, as is argued, does not impinge on the rights and values of those who want no part in it.

Invoked pragmatic advantages of legally regulated assisted dying include: bringing into the open practices that were clandestine and solitary, allowing better peer and societal scrutiny and control; protection of caregivers against prosecution; boosting the development of palliative care insofar as universal access to palliative care is an ethical and political precondition for euthanasia, and; promoting reflection by members the public on what they want for their end of life.

Opponents (often called "Pro Life" thinkers) dismiss these views, arguing either that one ethical principle cannot dominate or dismiss another or that beneficence and nonmaleficence have primacy over autonomy (with regard to assisted dying) (Callahan 2008; Foster 2009). Proponents of the sanctity-of-life argument label the idea of death being beneficial or good as preposterous (when completely contrary to human nature). On a more general level, they argue that legal-assisted dying would denature medicine and corrupt society.

Apart from philosophical and theoretical-ethical arguments against the practice, international concerns of societal ratification of euthanasia focus on undesirable pragmatic developments, also referred to as the slippery slope. The various aspects of the slippery slope argument (or hypothesis as it is mostly composed of expectations and presuppositions) can be classified as follows:

1. *Effects for patients*, e.g., vulnerable patients such as the oldest old being pressured into requesting assisted dying (cf. "a duty to die?") (Lewis and Black 2013), patients not receiving adequate end-of-life or palliative care (Hudson et al. 2015), erosion of trust in their relationship with their physicians (Hall et al. 2005);
2. *Effects for physicians*, e.g., stress, burnout, and emotional problems or conversely desensitization from ending patients' lives (van Marwijk et al. 2007), confusion over deontological rules (Cohen-Almagor 2013), feeling pressured into granting assisted dying requests;
3. *Uncontrollable "runaway" practice*, e.g., nonadherence to legal requirements, hastening death without the patient's explicit request (Cohen-Almagor 2009; Pereira 2011), and expanding ("overstretching") interpretations of eligibility criteria (Shariff 2012).

4. *Effect for palliative care*, i.e., regulated euthanasia is also anticipated to undermine or overshadow the palliative care movement striving to improve quality of life for people with life-threatening conditions, particularly at the end of life (Materstvedt et al. 2003; Bernheim et al. 2008).

Many of these aspects have been subject to empirical research, mostly in the euthanasia-permissive Benelux countries and Oregon. Important to bear in mind here is that trends in time – as opposed to single-point-measurements – need to be studied in order to corroborate or assuage the concerns expressed in the slippery slope argument. To the extent that scientific research is able to examine this, the evidence shows that since legalization, overall, there have been no significant adverse "slippery-slope" effects (Battin et al. 2007; Chambaere et al. 2015; Chambaere and Bernheim 2015; van der Heide et al. 2017). However, given the fact that the practice is still fairly recent and evolving even in the Low Countries, developments need to be monitored closely.

All jurisdictions that have regulated assisted dying have installed safeguards, including both substantive and procedural requirements for assisted dying. While the safeguards slightly differ between the jurisdictions, there are commonalities (Emanuel et al. 2016). Substantive requirements include:

- A person's request must be voluntary, well-considered, and sustained/reiterated.
- That person must have a serious and incurable condition caused by either an illness or an accident (in Canada, Colombia, and Victoria [Australia] the person must also be expected to die soon).
- That person's suffering is unbearable and cannot be alleviated.
- There is no reasonable treatment alternative.
- That person must be informed about his/her health condition and prospects by the physician and both parties must together have come to the belief that no reasonable prospect of improvement can be expected.

Procedural requirements include:

- The treating physician must consult another independent physician before proceeding with the act of euthanasia.
- The physician must notify the case of euthanasia, a posteriori, for review by a multidisciplinary control and evaluation committee (with the exception of Colombia where this needs to happen a priori).

While the existing laws do not prescribe what substances should be used and, in principle, physicians can use several types of drugs to perform euthanasia, the recommended drugs in the jurisdictions where it is legal are usually a combination of benzodiazepine (optionally as a means to relax the patient), a high dose of a barbiturate such as thiobarbital (which usually suffices to cause the death) followed by a muscle relaxant, if required.

The concept of suffering lies at the heart of the assisted dying debate. The legal regulations and initiatives for legalization in various countries implicitly recognize that there can exist suffering that is both unbearable and irremediable. Opponents have attempted to point out flaws inherent in both aspects. First, unbearable suffering has been argued to be unobjectifiable and therefore precarious and untrustworthy when considering so grave and irreversible act as ending life. It is impossible to assess for a clinician in many cases, and best not left to the subjective judgment of the patient alone. Moreover, there might be underlying motives and fears (e.g., fear of abandonment, existential distress, solitude, perception of being a burden, socio-economic issues) that remain unsaid and unexplored. Second, opponents also argue that suffering is never irremediable, i.e., that there are always other ways to alleviate suffering than death, no matter how intolerable, with adequate palliative care and/or terminal sedation. This reasoning brings us back to the discussion of palliative futility (see above).

A final note relates to the relationship between palliative care and assisted dying: are these compatible practices or not? Arguments

negating their compatibility point to the authoritative WHO definition of palliative care which excludes assisted dying in the phrase ". . .intends neither to postpone nor hasten death." (World Health Organisation 2018). In fact, the foundation of palliative care (by Dame Cicely Saunders in the UK) was explicitly predicated on preventing assisted dying requests. As such, allowing assisted dying into palliative care practice would alter the mission and deontological code of palliative care altogether; in some scenarios palliative care would be tainted to the extent that it would become completely synonymous with ending life (Bernheim and Raus 2017). Adherents of the compatibility view on the other hand argue that a dismissal of assisted dying in palliative care departs from the palliative care tenets of patient centeredness, by prioritizing caregivers' values over patients' values, and of pluralism, by rejecting divergent but respectable views on decision-making at the end of life. Also, the canonical adherence to the WHO definition of palliative care is found to be objectionable in a number of respects. Lastly, there would be practical consequences to a separation in clinical practice in euthanasia-permissive countries (Bernheim and Raus 2017). In Belgium, the Flemish Federation for Palliative Care has explicitly assumed the position of "euthanasia embedded in palliative care" (Vanden Berghe et al. 2013) and was therein followed by the Brussels and Wallonia federations, based on considerations of continuity of care and empirical evidence in Flanders showing that euthanasia already was often provided in the context of palliative care (Vanden Berghe et al. 2013).

6.4 Active Hastening of Death Without Explicit Patient Request

Related to the subject of assisted dying but very distinct from it, drugs may also be used at the end of life explicitly to hasten death without the consent of the patient. Needless to say, this constitutes an extremely problematic practice in ethical and legal terms. It is considered illegal worldwide. It also violates many ethical principles, first and foremost the autonomy principle, signals the "malfunction" of rules as proportionality and double effect, and is not in accordance with the deontological code. This practice does occur, though it is rare; it has been observed in empirical studies in every country where it has been studied, including in countries where assisted dying is not legalized (van der Heide and Rietjens 2012). An in-depth analysis of empirically reported cases revealed that a somewhat nuanced view may be advisable: the drugs (mostly opioids and benzodiazepines) were administered with a focus on symptom control; a hastened death was highly unlikely; and/or the act was in accordance with the patient's previously expressed wishes (Chambaere et al. 2014). Nonetheless, having an explicit intention to hasten death without explicit consent from the patient is very difficult to justify as good clinical practice. The kinship with intensified pain treatment, palliative sedation, and euthanasia looks to be close, perhaps pointing to a considerable empirical "grey zone" between these archetypes of end-of-life practices. Ethical principles and considerations draw clear lines between them, but clinical cases cannot always be sharply categorized.

A distinction can be made between nonvoluntary and involuntary shortening of life (Materstvedt and Bosshard 2013). Nonvoluntary shortening of life refers to instances in which the patient lacks the ability to make decisions, e.g., children, the demented and unconscious patients. Involuntary shortening of life points to cases in which patients explicitly reject life-shortening acts. Though both forms still constitute unacceptable medical practice it is clear that the latter form aggravates any moral evaluation.

6.5 Voluntary Stopping Eating and Drinking (Self-Starvation)

Voluntary stopping of eating and drinking is a relatively recently addressed phenomenon that is gaining scholarly attention. It is mostly considered by older people with (an array of) serious but not terminal afflictions (polypathology) who

experience high symptom burden, in a context where assisted dying is illegal or not possible due to ineligibility of the patient or situational factors (Wax et al. 2018). As such, self-starvation is viewed as an alternative to assisted dying, and one that is ethically and legally less problematic given that there is no intervention from a physician to achieve death. Though strictly speaking it is not a "medical" end-of-life decision, it ideally does involve the supervision of an experienced clinician. To be sure, stopping the intake of nutrients entails an entirely new array of issues, not only physiological but also emotional and psychological in nature, which require the attention of medical professionals. It remains the clinician's task to keep the patient comfortable and address problems such as thirst, hunger, weakness, delirium, and restlessness. If a clinician does commit to medically accompanying the patient who decides to self-starve, and self-starvation amounts to suicide to some extent, then ethically speaking that medical accompaniment could be viewed by some to equate to assisted suicide (Jox et al. 2017). An ethical motivation in favor of assisting these patients, particularly used in countries where it is accepted practice, is taken from the nonabandonment principle. In any case, according to many observers, self-starvation is a less dignified way to die and therefore not a superior alternative to assisted dying.

7 Communication in the End-of-Life Decision-Making Process

To arrive at ethically sound end-of-life decisions, good information and communication are imperative. This section will briefly touch on a number of issues that deserve special attention in communication between the actors involved.

7.1 Truth-Telling

Correct, intelligible, and comprehensive information about diagnosis, prognosis, possible treatments and their pros and cons is a necessary condition for patients to be able to exercise their autonomy and to consent to or refuse treatment. This is what is signified in the "informed" in informed consent. Physicians should also provide ongoing accurate information about the patient's condition when appropriate (Emanuel and Johnson 2013). This may seem straightforward but research has found that information provided to patients is often lacking in clarity and comprehensiveness, and physicians are reluctant to disclose all information fully and timely to their dying patients for fear of taking away hope or eliciting requests of assisted dying and/or due to a lack of adequate communication skills (Sleeman 2013; Visser et al. 2014).

7.2 Shared Decision-Making

The principle of patient autonomy is often misunderstood as meaning that patients should make decisions on their own. Especially in end-of-life care, decision-making should rather be regarded as a process between partners, in which the actors each fulfil unique roles and have equally valuable perspectives in the face of the decisions that need to be made (Emanuel and Emanuel 1995; Makoul and Clayman 2006). Ideally, there is ongoing active and open dialogue between patient, family, physician(s), and care team, in order to come to a mutual understanding of the values and goals underlying treatment decisions. Clinicians can then provide recommendations and explain possible options based on their expertise, while the patient can use these recommendations as input to make an educated decision, taking into account the perspective of their family. This novel model of shared decision-making allows for the patient to exercise autonomy while at the same time retaining the positive aspects of paternalistic decision-making. Paternalism has been dismissed by research suggesting that physicians are bad at predicting their patients' wishes and tend to underestimate their quality of life (Uhlmann et al. 2004). It will only apply when the patient explicitly defers discussion and decision-making to the physicians, care team, and/or family. We suggest that such a patient chooses a filial position and mandates the doctor to be paternal (as distinct

from paternalistic, where it is the doctor, rather than the patient, who decides on the type of relationship).

7.3 Advance Care Planning and Advance Directives

The patient does not always have the ability to be directly involved in decision-making. In many cases patients nearing the end of life lose their (full) competences and/or their capacity to communicate clearly, let alone to make an informed decision about a given treatment course. Decision-making capacity relates to five distinguishable cognitive abilities: understanding the factors relevant to making a decision, appreciating the nature and importance of the decision, understanding the risks as well as the benefits of the decision, ability to communicate about the decision, and deliberation based on personal values. When one or more of these capabilities is compromised, the care team has to liaise with the family, who represent the default surrogate decision makers, to make end-of-life decisions together. (Note that this burden of deciding may lead to considerable emotional distress for the family.) To counter this suboptimal situation, guidelines, tools, and interventions are increasingly being developed to achieve what is termed "extended autonomy," encouraging patients to make advance decisions about their preferred care plan at the end of life, before they become incapacitated. This can be done via advance care planning initiatives, advance directives, and/or living wills.

Advance care plans and advance directives can designate the surrogate decision maker and/or set out the patient's values, goals, and treatment preferences. The advantages are evident: they allow for clear values and goals to abide by when an end-of-life decision needs to be made; they create trust between patient and physician; they prevent or at least reduce the risk of uncertainty and confusion, and they offer peace of mind to the patient and their family (Detering et al. 2010). However, some pitfalls exist to their use in end-of-life practice: patients often find it extremely difficult to predict their future preferences; advance care plans can lead to conflicts between patients and family and they may be difficult to locate or access when urgently needed.

7.4 Conflicts

Conflict between patient, family, and/or caregivers may occasionally occur (Mehter et al. 2015). When faced with such disagreement or conflict, it is important to thoroughly analyze the problem and involve the appropriate parties to resolve the issue. First, what is the nature of the conflict: ethical dilemma, legal uncertainty, or clinical uncertainty? When the conflict cannot be handled/resolved by the protagonists, additional parties to be involved would be, respectively, an ethics committee, a legal counsellor, and a clinical expert. Second, between which parties has the conflict arisen? Many conflict resolution techniques are available for the clinical setting, but the problem in an end-of-life setting is that the situation is often dire and in urgent need of resolution as the condition of the patient could change rapidly.

7.5 Cultural Issues in End-of-Life Communication

In our increasingly pluralistic and multicultural societies, the odds of patients and caregivers not sharing the same ethnic background or religious beliefs increase. This in turn increases the risk of conflicting views and perspectives. In all cases, mutual understanding of and respect for one another's views is of the utmost importance. Clinicians need to be sensitive to the intricacies of cultural and religious beliefs and how they influence attitudes toward end-of-life decision-making. Examples of this influence abound: patients may adhere to certain spiritual beliefs that disallow some avenues of treatment (e.g., blood transfusion for Jehovah's Witnesses); the family is highly influential in medical decision-making in some cultures, and bad news is to be conveyed to the family instead of the patient

("familism"); in other cultures there rests a considerable stigma on the use of opioids, even in the very last stages of life; etc.

Yet, valuing diversity and being sensitive to these and other culturally determined issues does not automatically imply a necessity to comply with them; certain beliefs may clash with the legal, ethical, and deontological norms that predominantly prevail in the healthcare context. In certain cases, clinicians walk a fine line between respecting culturally specific norms and adhering to local laws and regulations. Thorough and clear communication constitutes the best way to avoid and defuse conflicts. In this regard, physicians may do well to communicate on the patient's level and in their language (by involving an interpreter) and offer additional assistance for adequate decision-making (Kogan et al. 2002).

8 Summary and Conclusion

Nowadays, increase in life expectancy is considered as one of the highest achievements of humankind. However, despite the rising standards of medicine and living conditions, the prevalence of health problems and disability is not decreasing. On the contrary, whereas in the past most people died at a younger age and more unexpectedly of acute infectious and parasitic diseases, this and future generations are confronted with a diversity of chronic degenerative diseases at an older age. This happens at a time of a paradigmatic shift in human endeavors away from survival and procreation to quality of life.

Over the past decades, the medical culture has moved from medical paternalism (characterized by phyisicians' sovereignty in medical decision-making) to shared medical decision-making, balancing physicians' expert knowledge and values with patients' autonomous choice that best aligns with their own individual values. As a consequence, focus has shifted from striving for longer survival to striving for optimal quality of life. In the end-of-life context, these fundamental changes incite more and more people to reflect on end-of-life decisions that may curtail their life but also their suffering. With informed consent at the core of shared decision-making, more patients are in charge to decide, express, and specify what forms of medical treatment they would like to receive or refuse, ranging from all available medical interventions prolonging their life to hastening their death.

Providing a high standard of end-of-life care requires physicians to be well-informed of the legal framework in which a range of end-of-life decisions (from withdrawing and withholding treatment over palliative sedation to euthanasia) can be legally justifiable. It also requires sufficient interiorization of the basic four ethical principles in an end-of-life context (the principle of autonomy, beneficence, nonmaleficence, and justice). However, each of these principles is in its essence fundamental though not absolutely inviolable, as these principles can (seem to) conflict. In the assisted dying context, for example, the principle of nonmaleficence may be perceived as in conflict with respecting a patient's autonomous request to hasten death. In attempts to solve such conflicts, the double effect doctrine is often invoked, though it only provides partial justification and hence furthers continuing, unresolved discussions between proponents and opponents. Over and beyond these potentially competing ethical principles, there is also broad dissent on more specific principles. For example, there is a lack of consensus on the mere existence of medical futility: the situation in which there is no reasonable prospect that the intended therapeutic goals can be achieved in a reasonable period of time nor the patient's medical condition and/or quality of life can be sufficiently improved. Even a more incontrovertible principle as nonabandonment seems not always to be adequately translated in clinical practice, as scientific evidence shows too many patients still experience some degree of abandonment in their end-of-life context.

In order to acknowledge and coordinate these tenets, sharpening physicians' basic communication skills (based on truthful, accurate, intelligible assessment of what patients need and want to know in order to be able to make informed consent decisions) is quintessential; not only to avoid or solve ethical dilemmas but also to strengthen the patient-physician relationship.

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Palliative Sedation: A Medical-Ethical Exploration

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Jeroen Hasselaar

Contents

Abstract

Palliative sedation involves the intentional lowering of consciousness in the last phase of life to relieve refractory symptoms. Most ethical controversies concern the application of continuous deep palliative sedation. After an introduction about prevalence and terminology, the concept of a refractory symptom is discussed from an ethical viewpoint in particular with regard to existential suffering. After this, several ethical approaches to the topic of artificial hydration in relation to life expectancy are considered. This is followed by a reflection on decision-making for palliative sedation, in particular the role of informed consent and the possible emotional burden for family and professional caregivers. After this, the rule of double effect is discussed. Finally, the debate about palliative sedation and (hidden) euthanasia is introduced. Continuous deep palliative sedation as a last resort option for patients at the end of life operates at an

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_92

ethical fine line and should avoid both postponing and hastening of death. However, it is concluded that palliative sedation is rightly considered part of palliative care. Nevertheless ongoing concerns need further attention, for example, a need for up to date, ethically balanced, and well-implemented practice guidelines and a careful communication with patients and families.

1 Introduction

In the Western world, cancer and other chronic diseases have replaced infectious diseases as the major cause of death. Due to improved hygienic and medical interventions, people live longer than ever before. Medical interventions however allow people to live longer, but not always to live better lives. In the 1960s people Dame Cicely Saunders founded the hospice movement focusing on the care of the dying, initially in cancer. Since then, this movement has expanded to encompass a broader concept of palliative care, including symptom management for patients with advanced disease. One of the first studies that mentioned sedation in the context of palliative care is a prospective study from 1990 of Ventafridda et al. who investigated symptom prevalence in 120 terminal cancer patients and concluded that about half of them died with physical suffering that could only be relieved by palliative sedation (Ventafridda et al. 1990). During the past decade, surveys of physicians have shown that palliative sedation became a more common and accepted practice. However, ethical debate continues with concerns that palliative sedation contributes to the medicalization of death and dying.

1.1 Palliative Sedation: Not Only a Medical Debate

In 2013, Papavasiliou et al. showed that sedation has been discussed in many fields (for example, oncology, nursing, health sciences & services, neurology, ethics, and law). This shows that palliative sedation is not only a technical medical act but touches upon important ethical and societal values. When sedation for the dying was firstly debated, it was mostly referred to as terminal sedation. The word terminal refers to the terminal state of the patients who received sedation but it does not say much about what the procedure actually involves. Also, the adjective "terminal" was sometimes used to argue that sedation itself would imply the termination of life, because it has been considered, by some, as a slow euthanasia. Slow because during sedation, dosages of medication may be gradually increased to help the patient die sooner, quietly, and without suffering. Or slow because sedated patients are not able to take fluids anymore and may slowly die because of dehydration. These are important ethical considerations that will receive more attention in this chapter, but for now, it is important to see how much confusion the adjective "terminal" in "terminal sedation" has caused. And although still preferred by some, the majority of the scientific and medical community has departed from this term and turned to the term palliative sedation (Hasselaar et al. 2009a). Notwithstanding, there have been societal concerns that continuous deep palliative sedation may be used as a slow or hidden alternative for euthanasia. As an answer to these concerns, professional guidelines have been developed to define terms and frameworks for the appropriate application of palliative sedation.

The aim of this chapter is to give an overview of the ethical debate surrounding palliative sedation with a discussion of the most prominent dilemmas. This chapter, however, does not give a detailed overview of the medical aspects involved in palliative sedation, like drugs and dosages. The first part will consider the definition of palliative sedation and some practice characteristics. The second part will discuss ethical issues in the context of the clinical preconditions of palliative sedation. The third part will move into possible life shortening effects, the rule of double effect, and the debate surrounding palliative sedation and (hidden) euthanasia. Finally, the conclusion will discuss the role of the caring professions in relation to a need for societal trustworthiness.

2 Part I Terminology and Prevalence of Palliative Sedation

2.1 What Is Palliative Sedation?

Already in 2002, Morita et al. performed a literature review and formulated two core elements of palliative sedation, namely, (1) the presence of severe distress refractory to standard palliative treatment, and (2) the use of sedative medication with the primary aim of relieving distress by reduction of consciousness (Morita et al. 2002). However, they also noticed differences in the degree and duration of sedation, symptoms, and targeted patients which are currently still often found.

For palliative sedation, a distinction is often made between light or intermittent sedation and deep and/or continuous sedation. Light sedation means that a patient is still able to communicate, whereas during deep sedation this is no longer possible, at least not verbally. Intermittent sedation (also called respite sedation) can, for example, be applied during the night to provide a time-out. Continuous deep sedation involves sedation that is continued until the moment of death. Continuous deep sedation raised a lot of societal controversy because it was thought that it could be used to hasten the death of the patient. It has been proposed to distinguish several types of sedation: ordinary sedation, proportionate sedation, which is the minimum amount of sedation needed to relieve physical refractory symptoms, and sedation until unconsciousness with the intended endpoint of unconsciousness (Quill et al. 2009). Cellarius and Henry (2010), however, correctly noted that all sedations should be proportionate to the aim of relief of suffering. Sometimes this will involve intermittent or light sedation with lower dosages of sedatives; sometimes this may involve continuous and deep sedation with a higher and longer lasting administration of sedatives.

Currently, guidelines are available in several countries including Ireland, the USA, Belgium, Italy, Austria, Spain, Canada, the Netherlands, Norway, and Japan (Abarshi et al. 2017). The Dutch guideline for palliative sedation (2005, revised 2009) was one of the first clinical guidelines to define palliative sedation as *"the intentional lowering of consciousness in the last phase of life"* (KNMG 2009). In 2009, the EAPC recommended a framework for palliative sedation in which palliative sedation is considered as *"the monitored use of medications intended to induce a state of decreased or absent awareness in order to relieve the burden of otherwise intractable suffering, in a manner that is ethically acceptable to patient, family, and healthcare providers*" (Cherny et al. 2009). An overview of definitions can be found in a review of Schildmann and Schildmann (2014). Schildmann and Schildmann (2014) made an inventory of guidelines listing and comparing the topics that were addressed and noticed a considerable variation in recommendations with regard to artificial hydration and aspects of indication and decision-making. De Graef and Dean (2007) were among the first to list recommendations for palliative sedation. They concluded that most recommendations were based on expert opinion. Recently, Abarshi et al. (2017), in a review of sedation guidelines, concluded that most guidelines are conceptually similar, resembling the EAPC recommended framework, but that there are striking differences in the terminology used. Studies from the Netherlands (Hasselaar et al. 2009b; Swart et al. 2012) indicate practice improvements after the launch of a national guideline for palliative sedation, in particular with regard to the aims and goals of palliative sedation and the involvement of patients and their family in the decision-making process. However, in general, there is little known about the effect of guideline development and structured implementation is scarce.

The vast majority of literature and accompanying ethical discussions about palliative sedation concern continuous deep sedation until death, and the remaining part of this chapter about palliative sedation will be focused on this. However, from a clinical perspective, palliative sedation is often considered as a continuum from light to deep and from superficial to continuous sedation.

2.2 Prevalence and Cultural Acceptance of Palliative Sedation

The use of palliative sedation as a medical practice is considerable. In 2017, a Japanese survey among palliative care specialists showed that palliative sedation was used for symptom relief and decrease of consciousness level. About 4 out of 10 respondents aimed to preserve consciousness as much as possible, and 1 out of 10 also intended to shorten patient survival to some extent (Hamano et al. 2017). In a survey from the United States, 1 out of 10 physicians had applied palliative sedation the past 12 months with the aim to make the patient unconscious until death, while 8 out of 10 accepted unconsciousness as a side effect only (Putman et al. 2013). One study reported different perceptions between American and Dutch physicians regarding the use of sedation at the end of life and found more open and proactive discussion in the Netherlands (Rietjens et al. 2014). A vignette study with French speaking physicians in Quebec (Canada) and Switzerland showed that their attitudes towards palliative sedation were similar: not legal considerations but the perceived suffering and diagnosis of the patient were leading in decisions for sedation, although Canadian physicians seemed more open to take existential suffering into account (Dumont et al. 2015).

For Europe, a comparative death certificate study from Miccinesi et al. (2006) showed that the prevalence of continuous deep sedation until death as a percentage of the total number of deaths differed between Belgium (8.2%), Denmark (2.5%), Italy (8.5%), The Netherlands (5.7%), Sweden (3.2%), and Switzerland (4.8%). However, it is not unlikely that these figures need updating by now. Recent Dutch research showed significant increase in continuous deep sedation in the Netherlands from 8% of all deaths in 2005 to 18% of all deaths in 2015 (Van der Heide et al. 2017). Interestingly, the prevalence of continuous deep palliative sedation until death in Flanders decreased from 15% in 2007 to 12% in 2013 (Robijn et al. 2016). The prevalence of palliative sedation based on a physician survey was estimated at 19% in the UK in 2010 (Seale 2010). Looking at German speaking countries, a study among 2,414 patients from 23 Austrian palliative care units showed that 21% received sedation, which in 4 out of 5 concerned continuous deep sedation, with an average duration of 48 h (Schur et al. 2016). Research under 281 members of the German ethics academy with and without medical background showed 98% acceptance of palliative sedation for physical suffering in dying patients (Simon et al. 2007).

Fainsinger et al. (2003) starting from the observation that psycho-existential suffering has a much larger role in palliative sedation in Spain compared to Canada, studied differences in values of cognition and information disclosure between 100 Spanish and 100 Canadian patients and their families in hospital palliative care consultation settings. Canadian families put more emphasis on clear thinking towards the end of life and full disclosure compared to Spanish patients and families, who were also less agreeing with each other. Núñez Olarte and Guillen (2001) related the use of palliative sedation for psycho-existential suffering in Spain and Latin America to a so-called external locus of control influenced by a (Catholic) worldview, where life events and circumstances are highly regarded beyond one's own control. This is contrasted with Anglo-Saxon cultures including North-Western Europe with a so-called internal locus of control where life events and circumstances are highly considered as being influenced by one's own actions. Although relevant, this seems not the only demarcation line for the use of palliative sedation. Qualitative research from the Unbiased study in three Western European countries indicated that physicians in the United Kingdom use palliative sedation differently than physicians in Belgium and in The Netherlands. While in the UK this seems to involve titration of dosages with the aim to preserve consciousness as much as possible, in the Netherlands and Belgium continuous and deeper levels of sedation were more often considered and the start of palliative sedation was more often organized as a final farewell (Seale et al. 2015).

Although the abovementioned studies give an idea of the use of palliative sedation, one should be cautious to conclude that palliative sedation is more or less prevalent in one country compared

to the other because the methodology of the studies, the definitions and interpretations of palliative sedation, and the investigated target groups are diverse (from epidemiological to more clinical studies). Moreover, it needs to be considered that the increased media attention for palliative sedation may have increased the popularity of the practice over time but may have also lead to a more precise understanding of what it actually involves. Finally, cultural differences exist in how palliative sedation is approached and used.

3 Part II Ethical Issues in a Clinical Context

Nowadays, there is broad consensus that palliative sedation has two important preconditions, namely, that palliative sedation is restricted to patients who are severely suffering from refractory symptoms and to patients who are in the last phase of life. This paragraph will first discuss the concept of refractory symptoms and the ethical questions that are related to this. After this, the ethical discussion about artificial hydration, in particular, in the context of deep palliative sedation until death, will be discussed.

3.1 First Precondition for Palliative Sedation: Refractory Symptoms

Sometimes, symptoms cannot be treated without unacceptable side effects given the clinical situation of the patient or symptom relief cannot be expected in due time. In these cases, a symptom can become refractory, which means that it cannot be relieved by conventional medication or in due time (De Graef and Dean 2007). In a review by Maltoni et al. (2012), the most prevalent (refractory) symptoms were: delirium (54%), dyspnea (30%), psychological distress (19%), pain (17%), and vomiting (5%). Delirium is a prevalent symptom at the end of life. Especially agitated delirium can cause a lot of stress for patient and families and can become refractory (Bush et al. 2014). In such circumstances, before (continuous deep) palliative sedation is considered, regular symptom treatment needs to be evaluated thoroughly. Figure 1 introduces a stepwise approach to determine the refractoriness of a symptom. In addition, the Dutch guideline mentions a nonlinear combination of different dimensions of symptoms that can lead to unbearable suffering of the patient, like for example extreme dyspnea producing severe anxiety. The untreatable nature of symptoms must however be demonstrated beyond reasonable doubt (KNMG 2009).

Refractory suffering is not limited to somatic symptoms and therefore a multidimensional approach is needed in order for these to be fully assessed and managed. In this respect, especially the presence of existential suffering needs further attention.

It is challenging to define existential suffering. Most descriptions suggest a perceived loss of meaning, loss of perspective, or a perceived loss of dignity (Van Deijck et al. 2015). There are intercountry and cultural differences regarding the extent of existential suffering as an accepted

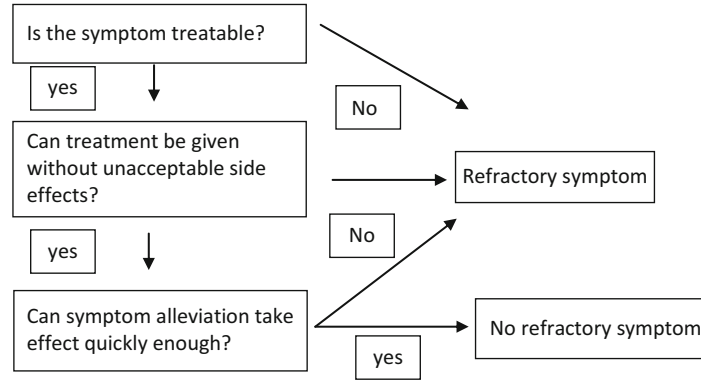

Fig. 1 Stepwise approach to identify refractory symptoms. (Dutch guideline for palliative sedation KNMG 2009)

reason for palliative sedation. Literature from Japan for example is hesitant at this point (Morita et al. 2005a). The majority of physicians from the United States also seems quite hesitant (Putnam et al. 2013), whereas Belgian and Dutch physicians seem to accept this to some extent as part of refractory suffering. When refractoriness is considered an aggregation of several symptoms, it can be imagined that some form of existential suffering will often be a part of this. Patients in the last phase of their lives can suffer when facing their own mortality. It can be considered a part of the normal dying phase that patients struggle or even wrestle with this. However, when existential suffering is the predominant reason to start palliative sedation, caution is needed because it can be questioned whether palliative sedation, in particular continuous deep sedation until death, is the right answer in this case. With continuous deep palliative sedation, patient awareness is suppressed, and, if applied for existential suffering only, important stages of loss and finishing life may be distorted. Hence, the first argument to be hesitant with palliative sedation in these cases comes from the perspective of providing good palliative care. A second argument is that patients who predominantly experience existential suffering are often not yet in the terminal stage of life, which would frustrate the second precondition for palliative sedation, namely the imminence of death.

Juth et al. (2010), in a critical reaction to the EAPC recommended framework for palliative sedation, argue that the concept of intolerable suffering needs more clarification. Suffering is a highly subjective experience and it can be difficult to distinguish existential or physical causes of suffering. Juth et al. point out that more clarification is needed about the perspective of patients and physicians in particular regarding concepts of intolerable distress and refractory symptoms, and how these relate in the context of identifying necessary and sufficient criteria for palliative sedation. This also echoes the viewpoint of Cassell and Rich (2010) who consider suffering to be a human and personal experience and warn that distinguishing causes of suffering may lead to an undesirable mind-body distinction. In a reply to this view, Jansen argued that philosophical mind-body distinctions are not needed to introduce a difference between neurocognitive and agent-narrative causes of suffering. She concludes that "Compared with neurocognitive suffering, it is exceedingly more difficult to establish that agent-narrative suffering is truly refractory" (Jansen 2010). A recent review of Rodrigues et al. (2018) identified several relevant concepts in the discussion surrounding existential suffering and palliative sedation, namely, mind-body dualism, existential suffering, refractoriness, terminal condition, and imminent death and concluded that more clarification in the ethical debate is needed at this point.

The last word has probably not been said about this issue. Therefore, in more complex cases of assessing refractory suffering, especially the application of deep and continuous sedation may call for multidisciplinary decision-making, which is also mentioned in the EAPC framework for palliative sedation.

3.2 Second Precondition for Palliative Sedation: A Limited Life Expectancy

During palliative sedation, a patient is not able to take fluids orally. The ethical concern has been that this could lead to a life shortening effect, in particular when deep sedation occurs over a prolonged period. In most guidelines therefore, it is stressed that continuous palliative sedation should be restricted to the last phase of life. Most guidelines also argue that the application of palliative sedation and the decision not to apply artificial hydration are two separate medical decisions that need separate evaluation. However, this "dual procedure" has raised critical remarks from an ethical viewpoint because both decisions are often implemented at the same time and especially in sedation trajectories with a longer duration, sedation without artificial hydration would prevent the patient from taking fluids which could result in life shortening due to dehydration (Den Hartogh 2016).

The work of Callahan (1992) assists in understanding this critique better. Callahan introduced

a thought "test" to distinguish "allowing to die," from killing. A central notion in this "test" is that an act of allowing to die only causes death in a very ill patient and not in a healthy person. Applied to palliative sedation, it can be argued that during continuous deep palliative sedation every person, whether healthy or ill, will eventually die from dehydration if continuously kept under sedation without (artificial) hydration. On the one hand it has been argued that during deep and continuous sedation, "often the patient dies of dehydration from the withholding of fluids, not of the underlying disease" (Quill et al. 1997). On the other hand, as mentioned before, continuous deep sedation is mainly applied in dying patients and maintained for a limited period of time (about 48 h). In these cases, the risk of dehydration due to sedation may be limited in practice. However, when the prolonged administration of sedatives frustrates the oral intake of the patient and eventually causes a life shortening effect due to dehydration, this may be morally problematic.

To avoid this problem and to clearly distinguish palliative sedation from hastening of death, guidelines restrict continuous deep sedation until the last phase of life, more precisely the last 1 or 2 weeks of life. A closer view learns that this last phase can be interpreted as the recognition of the approaching death like being bedbound, having cachexia, severe weakness, being disoriented, and limited or absent oral intake (KNMG 2009). In addition, some guidelines have used a reference to medical futility, by stating that the possible harmful effects of artificial hydration during sedation may outweigh the possible benefits. The Dutch guideline for example is hesitant about artificial hydration during continuous deep sedation, pointing to the possible negative effects of supplying artificial hydration in a dying patient like edema. Also the Belgian guideline is more hesitant at this point and stresses that it is a separate decision next to the decision to start sedation (Broeckaert 2012). The EAPC framework (Cherny et al. 2009) admits that practices vary and considers this as a separate decision which is left with the care teams and patients in their specific situations: for some it is a humane continuation of life support, for other it is superfluous and can be withdrawn because it does not contribute to goals of comfort care. If adverse effects however appear, withdrawal should be considered. This reflects an approach that artificial hydration can be withdrawn if it can be considered futile care.

Futility is a layered and much debated concept and agreed definitions are largely lacking (Macfadyen and Mcconnell 2016). One influential approach comes from Schneiderman et al. (1990), who argue that futility involves both a quantitative aspect, referring to the probability of success (5% or 10% etc.), and a qualitative aspect, related to the goals of care. In a later publication, they note that a patient is not merely a collection of organs or an individual with desires but a person who seeks healing (Schneiderman 2011). They remark that on the one hand physicians cannot be expected to deliver medical care with low probability of success, but on the other hand they should move beyond "pull the plug" and "nothing to offer" discussions. Truog (2018) agrees that futility often refers to the limits of medicine in the context of mortality, but he emphasizes that physicians as medical professionals should be hesitant to make judgments about essential human values. For this reason he criticizes the statement that treatment which merely preserves permanent unconscious life is as such futile care. According to Rinehart (2013), the diversity of our cultural values can make it difficult to agree on the goals of care. Therefore Rinehart proposes to adopt shared decision-making with a thorough inventory of a patient's values and life goals. In those cases however where agreement with patient and family is not possible, it may be wise to adopt a (narrow) concept of physiologic futility together with a careful procedural approach that takes into account values of patient, family, and society at large (Truog 2018).

In most clinical practices, with a short expected duration of palliative sedation, the discussion about artificial hydration may be considered less relevant because dehydration is not expected to happen in such a short timeframe or because the patient already stopped drinking as part of an approaching death. However, it is important

to be aware of the underlying ethical discussion. Although at first sight futility seems to refer to a rather technical decision aid, moral values are at stake. In the case of palliative sedation, a discussion about the medical futility of artificial hydration can involve the physiological effects of hydration, but it can also bring forth a discussion about whether it is ethically obliged to artificially prolong the life of otherwise dying patients. The well known WHO palliative care (WHO 2002) definition states that palliative care does not aim to prolong the dying process but also does not aim to shorten life. In decisions concerning palliative sedation, this can be a fine line, which requires medical and ethical sensitivity, preferably in a multidisciplinary deliberation, together with compassionate communication with patients and families.

3.3 Decision Making for Palliative Sedation and Emotional Distress

So far, the ethical issues in the context of the clinical preconditions of palliative sedation have been discussed. However, the EAPC framework for palliative sedation also mentions that palliative sedation needs to be ethically acceptable for patients, caregivers, and family members. This refers to the position and interaction of the several stakeholders involved in a palliative sedation process, to begin with the patient.

Informed consent is a procedure to obtain the written or oral consent of a patient for a medical treatment. It reflects respect for the patients' autonomy as a right to make his/her own decisions, including also the right to refuse medical treatment. Therefore, attaining informed consent of the patient for a medical treatment can be regarded as a general obligation for all caregivers, before the treatment starts. But this can become difficult when the patient has a reduced capacity for decision-making which is often the case for patients who are near to death. There are however several ways in which the application of medical treatment without the consent of the patient can be justified. If the patient is incompetent for decision-making, family members may act as proxies also called "surrogate decision-makers." A proxy should comply to the wishes, values, and perspectives of the patient as good as possible. To some extent, the physician might act as proxy, serving the best interests of the patient. In addition, advanced directives, whether oral or written, may be used, although these donot seem to play a major role in the context of palliative sedation. However, specific national laws may differ at this point.

Patient consent for palliative sedation has been addressed in several studies. A general concern has been that this consent is not always obtained, in particular with regard to continuous deep sedation. After the introduction of the Dutch guideline, patient involvement in decision-making increased from 72% to 82% (Hasselaar et al. 2009b). Interestingly, Morita et al. (2005b), in a Japanese prospective study, found that 67% of the patients expressed explicit wishes for sedation and families were involved in the other cases. This is an interesting outcome as research also showed that the general public is not always aware of terms related to palliative care and palliative sedation (Hirai et al. 2011; van der Kallen et al. 2013). Sometimes, patients can have different understandings about palliative sedation than their caregivers. It is an ethical duty of the physician to correctly inform patient and family about the available treatment options in a way that is understandable for him/her in order to make an informed decision. Often in palliative care, a shared decision-making process will be strived for.

In a survey about family experiences during palliative sedation (intermittent and continuous deep sedation) from Japan, 78% of 185 interviewees were satisfied with treatment but 25% expressed emotional distress (Morita et al. 2004a). In a review of Bruinsma et al. (2012), investigating 36 studies, family members appeared to be involved in the decision-making for continuous deep sedation in 69–100% of cases. Although in general, family members seem to be comfortable with palliative sedation, cases of distressed family members were also mentioned. Possible reasons for distress are that the patient still suffers, that the patient isn't able

to communicate, feeling a burden of decision-making, concerns about a possibly hastened death, a long duration of sedation, and ideas about more appropriate alternatives.

The Unbiased study, based on interviews with 78 nurses, 82 physicians, and 32 family members of deceased patients, has provided more insight in the everyday moral reasoning about palliative sedation in three Western European countries: UK, Belgium, and the Netherlands. Raus et al. (2014) found that dimensions of "closeness" to the patient determine the distress that caregivers experience with continuous palliative sedation until death. Firstly, in particular nurses, involved in the daily care for the patient experienced emotional closeness, especially when the patient is younger. Secondly, physical closeness was felt when caring for a patient. Thirdly, decisional closeness occurs when the interviewee was closer involved in the decision-making. And finally causal closeness occurred when administering sedatives can cause a feeling of distress in case the patient dies shortly thereafter. Feelings of distress were often associated with continuous palliative sedation, but could also be balanced with the relief it brings to a severely suffering patient.

In a large survey among nurses in hospitals and palliative care units, Morita et al. (2004b) found that a significant percentage (12%) of nurses felt serious emotional burden related to continuous deep sedation, for example, the experience of unclear patient wishes, insufficient time, belief that a diagnosis of refractor symptoms is difficult, and a perceived lack of skills. Feelings of burden were related to shorter clinical experience and younger age. Rietjens and colleagues (2007) published an interview study with 16 nurses about their memorable cases of palliative sedation, reporting that for many nurses being involved in palliative sedation is more than "just carrying out a medical order." Although palliative sedation is generally considered a good death, it is also a process that brings forth reflections about its appropriateness and conditions of adequate practices.

In sum, in many cases of palliative sedation patients and family members are involved in decision-making in some way. Reports from studies with bereaved family members show that many are satisfied with the care that has been received during a palliative sedation trajectory, although concerns and emotional distress remain in a considerable number of cases. Studies under nurses show that the application of palliative sedation is not considered a routine task and can be a burden. Data concerning medical doctors, however, was less easy to find. Care for the carer, in particular for younger professionals with less clinical experience, is needed. Care for the bereaved family members, in particular when unclarities remain, seems also important.

4 Part III Two Moral Dilemmas Surrounding Palliative Sedation

In the next paragraphs, two ethical problems surrounding palliative sedation will be discussed more in-depth. One has been around in the literature for a longer time, namely, the rule of double effect. And the other is an important but sometimes neglected topic, namely, the ethical value of consciousness.

4.1 The Rule of Double Effect

The past decade, the possible occurrence of life shortening effects during palliative sedation has been an important concern. The so-called rule of double effect has often been used for an ethical evaluation of palliative sedation, in particular continuous deep sedation.

The doctrine of double effect describes an act as having two effects, one positive and one negative. The good effect in palliative sedation can be defined as the relief of suffering. The negative effect is the possible shortening of life which may be foreseen but should not be intended. The rule is subdivided in four parts and reads as follows (Sulmasy and Pellegrino 1999):

1. The act is not in itself immoral.
2. The act is undertaken with the intention to achieve the good effect and without intention

to achieve the bad effect, even though the latter might be foreseen.
3. The act does not bring about the good effect by means of the bad effect (since that would imply that the bad effect is intended, too).
4. The act is undertaken for a grave and proportional reason.

In the literature, attempts have been made to apply this rule to palliative sedation in order to distinguish it from active euthanasia. The first criterion reads that the act should not be immoral in itself. The act, namely, the use of sedatives for the relief of suffering, is not immoral in itself. Relief of suffering is one of the basic tasks of medicine. Secondly life shortening effects, if present, may be foreseen but not intended. Therefore, according to this second criterion, the act of prescribing medication should be intended or titrated towards the effect of symptom relief, and not to the effect of shortening life. Drugs and dosages that are used for palliative sedation should reflect this intention by being proportional to the goal of symptom relief. The third criterion holds that the act of symptom relief is not achieved by means of life shortening. According to the rule of double effect, palliative sedation is cumbersome if it serves as a means to hasten death. In that case, the sedation is used to shorten life. According to the fourth criterion, proportionality and a grave indication for palliative sedation are needed to justify an act of palliative sedation. Proportionality means that there are no less harmful alternatives available to attain the good effect of symptom relief. This refers to the idea that palliative sedation is a last resort option, only to be applied in case of refractory symptoms when more conventional treatment is not (longer) available. Also it reflects the idea that intermittent or light sedation, if possible, is preferred above continuous palliative sedation.

Some authors have doubted the suitability of the rule of double effect for palliative sedation. Sykes and Thorns (2003), for example, argued that there are no life shortening effects reported for palliative sedation, and that, in fact, there is no life-shortening effect that needs to be morally justified. The actual occurrence of life shortening effects during continuous palliative sedation has been a topic of heavy debate. Maltoni et al. (2012) in a review about palliative sedation described 11 studies of which one reached statistical significance. This study, from Mercadante et al. (2009), reported that nonsedated patients had a shorter survival compared to sedated patients, measured in days from the moment of admission, with a mean sedation time of 22 h. One study of Kohara et al. (2005) reported a mean sedation duration of 3.4 days, with a statistically non-significant shorter survival after admission for sedated patients (28.9 vs. 39.5 days). However, they included mild to deep sedations which make their figures less comparable to studies that are limited to continuous deep sedation. One of the most robust studies so far about life shortening during palliative sedation involved a secondary analysis of a prospective research in 58 palliative care centers in Japan. In the sample of 1827 patients, 15% of the patients received continuous palliative sedation (Maeda et al. 2016). They did not evidence an increased risk of life shortening due to continuous deep palliative sedation. Based on this article, Caraceni (2016) called for more empirical data in this debate and less opinions.

The rule of double effect has been criticized because it relies heavily upon the distinction between intended and foreseen consequences. Surveys under caregivers from – among others – Belgium and Japan reported that palliative sedation is sometimes applied with a more or less explicit intention to hasten death (Hamano et al. 2017; Rys et al. 2014). According to the rule of double effect, this will be problematic in particular regarding the second criterion. However, intentions can be ambiguous. When confronted with a terminally ill patient, is it wrong to hope that suffering will soon be over and death will come soon? In addition, the methodological validity of asking after life shortening effects via surveys is not beyond doubt. Statements from general surveys should be interpreted with caution. On the one hand, intentions are important to consider in an ethical evaluation, but it does make a difference whether shortening of life is a matter of fact (or not). On the other hand, literature reporting that palliative sedation is used with the implicit

or explicit intention to shorten life, even when compassionate care is the main motive, cannot be neglected and deserves further ethical exploration.

Notwithstanding, the rule of double effect may be relevant to take into account in individual patients care. In terminal patients, symptom relief may require a delicate balance between the type of drugs, monitoring, dosage, and titration schedule chosen. In particular because the effects of medication in a terminal patient can vary due to, for example, renal problems and loss of weight. Hence, the precise effects may be difficult to estimate or predict beforehand. In 2005, Morita et al. reported a prospective research where serious complications occurred in 20% of sedated patients, with a respiratory or cardiac arrest in 4% of patients (Morita et al. 2005c). In such cases, if palliative sedation is applied as a proportional last resort of symptom relief, according to best possible standards of care, life shortening effects due to fatal complications may be accepted as an unintentional side effect of symptom relief.

4.2 The Ethical Value of Consciousness

The capacity to express oneself and to make one's own decision is considered important for human beings and a basic ethical value. At first sight it is clear that consciousness, also in the last phase of life, is important. For example, to say goodbye to loved ones, to make final arrangements, or simply to be consciously reacting to caregivers and family members. In principle, awareness is a basic requirement to express oneself in many ways. Although many patients who approach death suffer from a gradual decline of consciousness due to the natural course of terminal disease, to actively decline or suppress awareness until death by using medication is a serious intervention that calls for a convincing ethical justification. Considering that many persons experience periods of unawareness, for example, during anesthesia in a hospital, intermittent sedation for symptom control seems to be ethically justifiable at prima facie. When sedation occurs as a side effect of symptom treatment, symptom treatment will be the primary goal and sedation will be the foreseen but unintended side effect. But if sedation is the direct aim or intention, in particular in the case of continuous deep sedation until death, it is less obvious how the rule of double effect can be applied. Concerning the first criterion, for example, continuous suppression of consciousness may not be morally desirable as a general ethical value. However, it may be acceptable in some cases like patients near to death who suffer unbearably. It is not totally clear how the rule of double effect can fully account for such context related elements. In any case, the continuous suppression of consciousness needs a thorough medical and ethical justification.

In particular for deep and continuous sedation, fundamental ethical values are at stake. It is therefore important that continuous deep palliative sedation is used as a last resort only, to be justified only by grave reasons like refractory symptoms and excruciating suffering, and to be considered in a continuum of palliative care at the end of life.

5 Part IV the Debate About (Hidden) Euthanasia

The relation between euthanasia and continuous deep palliative sedation (then called "terminal" sedation) was firstly questioned during the discussion about the US Supreme court cases Vacco v. Quill and Washington v. Glucksberg. Here, the Supreme Court rejected a constitutional right to physician assisted suicide and insisted on the distinction between – accepted – withdrawal of life sustaining treatment and – prohibited – assisted suicide or euthanasia. Representatives of the medical profession wrote to the court that even the most intolerable pain can eventually be resolved by so-called terminal sedation. Orentlicher (1997), in an article heading that the court rejects assisted suicide but embraces euthanasia, argued that with terminal sedation, the unconscious state of the patient is initiated deliberately by the physician and as a consequence a process of dehydration is initiated by the same intentional decision for sedation of the physician (see our discussion of this topic earlier). Moreover, as terminal sedation

may also be applied without the explicit permission of the patient, its application may be more vulnerable to abuse than euthanasia (see also Quill et al. 1997 for similar concerns).

Raus et al. (2011), analyzed these court decisions and concluded that continuous sedation is not to be considered a morally preferable alternative to assisted suicide. Their article raised many reactions, of which we highlight only one. Broeckaert (2011), in a critical reply, outlined the differences between palliative sedation and euthanasia in (a) their intent, (b) their procedure, and (c) their consequence. For palliative sedation, physicians in general do not aim to kill the patient, the drugs and dosages differ, and the result of palliative sedation is that the patient dies as a result of the illness and not because of lethal medication. However, to accept palliative sedation in principle as a part of palliative care does not imply that possible concerns about the practice should be neglected. For example , in November 2017, the Belgian minister of healthcare has raised concerns about palliative sedation being applied as a hidden euthanasia and pleaded for a legal procedure (newspaper de Standaard 2017). In the recent third evaluation report of the Dutch law on termination of life, concerns were raised about a possible grey area between euthanasia and intensified symptom treatment, with a call for more research into the practice of continuous deep palliative sedation (Onwuteaka-Philipsen et al. 2017).

How to continue with ongoing concerns surrounding palliative sedation? Perhaps we should look at the trustworthiness of medical practice as a whole. It can be argued that autonomy is often exercised in a relational context with family members and professional caregivers. Therefore, the first and most important safeguard regarding palliative sedation should be grounded in the patient-physician relationship. This is not primarily to be considered a contractual relationship between two contract partners, but an ethical relationship based upon mutual respect, sharing values, and shared decision-making (see also Emanuel and Emanuel 1992). Virtues like integrity and courage are needed in combination with excellent skills for communication and symptom management in a context of advance care planning to early detect preferences and possibilities in the palliative phase. In addition, the caring professions have a role here. When palliative sedation is principally regarded a part of palliative care, the medical and nursing professions have the primary responsibility to establish and support adequate practices, together with other multidisciplinary professions. They should address societal concerns about palliative sedation by ensuring well-established practice standards, with an adequate implementation, monitoring of current practices, and where needed medical disciplinary law. Its policies and practices should be directed at improving quality and trustworthiness for patients, families, and society at large.

6 Conclusion

David Clark (2002) argued that palliative care may have contributed to a certain medicalization of death and dying in their efforts to provide better symptom relief. In line with this observation, he does not recommend to totally avoid medical interventions at the end of life but to “reconcile high expectations of technical expertise with calls for a humanistic and ethical orientation.” The ongoing debate about palliative sedation emphasizes the importance of such a reconciliation. In principle, palliative sedation including deep and continuous sedation can be considered part of palliative care. Probably the often debated problem of artificial hydration is not the most pertinent problem currently, given that sedations at the end of life last about 48 hours on average and current guidelines restrict continuous deep sedation to the last days of life. In the context of longer during sedations, for example, in case of existential suffering, caution is needed and this remains controversial in the literature. More research is needed to investigate palliative sedation to further answer medical and ethical questions, for example, about how to establish refractory symptoms and what this exactly involves.

Considering palliative sedation as a palliative care intervention, the question as to whether more safeguards are needed needs to be primarily answered within the palliative care and medical

community. Regular updating and further implementation of ethically and medically balanced clinical guidelines are recommended together with ongoing education of care professionals and patients to avoid confusion about terms and conditions in daily practice. When it comes about concerns for hidden euthanasia however, societal values at large also come into play.

The task to provide humane care till the end is an important "raison d'etre" for palliative care. For patients with refractory symptoms, palliative sedation can bring comfort as a last resort. To exclude palliative sedation as a palliative care intervention would be highly problematic for the comfort care of many terminally ill patients. From an ethical viewpoint, palliative sedation can be acceptable in principle, but it remains important to (a) avoid both undertreatment leading to discomfort and overtreatment leading to unnecessary medicalization of death and dying, and (b) avoid both postponing and hastening of death. In finding the right middle, practical wisdom, the right skills and expertise, and a careful interaction with patient and family are pivotal.

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Nutrition and Hydration in Palliative Care and Their Diverse Meanings

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Jean B. Clark and Lesley S. Batten

Contents

Abstract

Essential for life, food and fluids are regarded as basic care, professionally, ethically, and legally. This chapter seeks to contextualize and explore the significance and meaning of compromised nutrition and hydration in contemporary adult palliative care. The internationalization of Western medicine, Western bioethics, and palliative care generates new perspectives and can challenge established practices. It is important that evidence of the relevance, efficacy, and appropriateness of

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_117

artificially intervening in the natural course of terminal illnesses is developed; however, that knowledge will not necessarily resolve the issues associated with the reality that food and fluids mean different things to those involved.

Universally, food and fluid, its preparation, use, symbolism, and value are inherently meaningful. Discussions, opinions and decisions vary regarding supporting oral intake, and clinically assisted nutrition and hydration, particularly towards the end of life. Inevitably, the perspectives of the ill person, their companions, and informal and professional caregivers are not necessarily consistent or static.

Endeavors to address declining oral intake must be individualized, congruent with care goals, and cognizant of cultural values, religious, and personal beliefs. It is an aspect of care (and dying) that should not be taken for granted nor considered problematic. Rather, it is inevitable for many people and no lasting resolution should be anticipated or desired. Professional knowledge and curiosity towards the multiple meanings surrounding eating, food, nutrition, and hydration, and their meaning is the proposed aspiration.

1 Key Points

- Declining oral intake is meaningful for patients, family members and clinicians.
- Perceptions that food and fluid intakes influence lifetime are essentially well founded.
- Refractory cachexia in people with a progressive life-limiting illness is not ameliorated by clinically assisted nutrition and hydration.
- There is a paucity of evidence to provide unequivocal guidance for clinicians regarding artificial nutrition and hydration, although facts alone are unlikely to change clinical practice and patients' and families' expectations.
- Clinicians hold diverse views regarding forgoing, providing, and withdrawing clinically assisted nutrition and hydration.
- The goals of care regarding nutrition and hydration require on-going review with informed and meaningful dialogue between patients, family members, and clinicians.

2 Introduction

> **Vignette one**: A close family member of a person recently diagnosed with a terminal illness and with probably months to live focuses on the "not eating": "He doesn't seem to want to eat, if I make it for him he does, but I don't think he is bothering to eat anything except pudding if I am not there. Should I get him some [supplement] or something? But then, does it matter? I know it is illogical to worry about that at this time, but I do."

As is identified in this vignette, food and fluids, eating and not eating are everyday challenges and also key flags of actual or impending change for the person, their family and friends when someone has a life-limiting condition. This chapter explores this complex issue, reviews the goals of care in palliative and end of life care, and contextualizes the meaning of food and fluid and **clinically assisted nutrition and hydration (CANH)** in life-limiting illness. Basic care includes food and fluids, while CANH is regarded as a medical intervention (Druml et al. 2016). The ethical principles drawn on in palliative and end-of-life care, including autonomy, beneficence, non-maleficence, and justice are applicable to the provision of food and fluids and decisions to forgo, utilize, or withdraw CANH (Druml et al. 2016). Exploring and contextualizing the diverse meanings of oral food and fluids and CANH in the adult palliative care population in relation to bioethics requires consideration of many interconnected elements (Fig. 1).

In this chapter, small vignettes have been developed from the authors' combined clinical practice and research experience to illustrate and explore the most pertinent issues. There are consistent elements:

- A person's life is ending.
- Food and fluids are meaningful and essential for life.

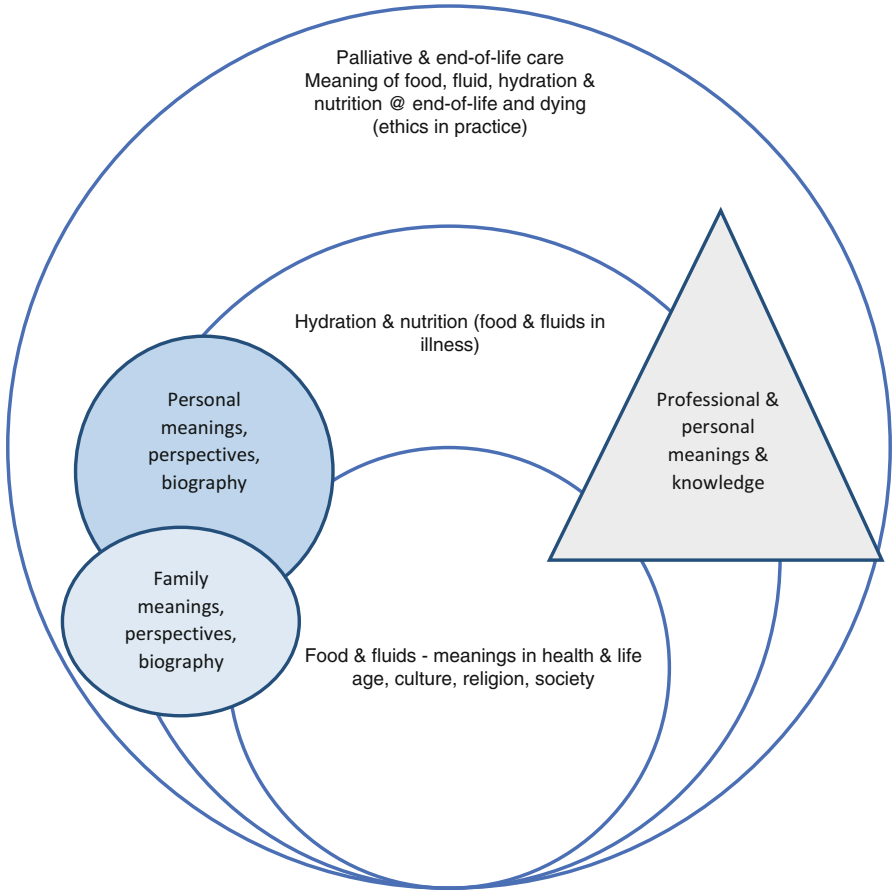

Fig. 1 The multiple contexts of food and fluids in palliative care

- The dying process results in the loss of oral intake.
- CANH is available but does not reverse the dying process.
- Suffering should be mitigated.

Ethical discussions regarding dilemmas associated with food and fluids and CANH are inevitable in palliative and end-of-life care, because nutrition and hydration are requisites for life. Factual clinical data related to this topic, while important, is unlikely to significantly ameliorate this challenging and complex aspect of clinical practice because all parties experience hydration and nutrition as meaningful. The intention of this chapter is to inform, support dialogue, and encourage professional reflection and acceptance of the inevitable ambiguity and complexity for patients, families, and their companions, so providers of palliative care are enabled to meet their dynamic needs ethically.

3 Oral Food, Fluids and Clinically Assisted Nutrition and Hydration in Palliative Care

Addressing the unmet needs of people dying from malignant conditions in acute care was the main catalyst for the modern hospice movement, established in London in 1967 (Fallon and Smyth 2008). Subsequently extensive efforts to promote and mainstream palliative care have occurred. This has influenced where palliative care is delivered (acute hospital settings, home, aged care facilities), expanded the population

focus to include people with progressive nonmalignant illnesses (e.g., congestive heart failure, chronic obstructive pulmonary disease, or neurological conditions), and the integration of palliative care earlier in the disease trajectory (Fallon and Smyth 2008; World Health Organization 2002). Additionally, previously well people who experience acute life-threatening events may require and benefit from palliative care. In this latter cohort interventions like CANH may be in place while the person is fully assessed and the likely outcome determined. Sudden changes in physical condition, devoid of anticipated and witnessed deterioration can make decisions regarding CANH more fraught for all parties.

The majority of people with progressive disease from malignant and nonmalignant causes experience declining oral intake and will eventually struggle to take food and fluid safely (Royal College of Physicians and British Society of Gastroenterology 2010; Watson et al. 2009). These changes are often associated with weight loss, altered physical appearance, declining function, and increasing fatigue (Watson et al. 2009). The person, family members, companions, and clinicians all bear witness to these changes. All parties may have differing perceptions of the need, purpose, and benefits of food and fluids and CANH (del Rio et al. 2011). Additionally, perceptions of the benefits and burdens of oral food and fluids and CANH may not be congruent amongst clinicians and the recipients of care. Indeed the differences in the utilization of CANH identified in literature reviews indicates that clinical practice (del Rio et al. 2011; Raijmakers et al. 2011; Torres-Vigil et al. 2012), as well as family members' and patients' perceptions of food and fluid and CAHN are influenced by multiple factors, not just knowledge (del Rio et al. 2011).

In diverse societies globally, food and fluid are meaningful in life, health, culture, religion, and society. They have roles and functions other than the avoidance of dehydration and starvation. Food and fluids are often central to social interactions, be this within daily family life, among friends, for celebrations and as gifts (Raijmakers et al. 2013; Rozin 2005; Wallin et al. 2015). The importance of food and fluid is not confined to the factual, calorific, and measurable because in most, if not all societies, food and fluids have meanings that extend beyond nutritional values (Rozin 2005). Therefore, it is understandable that questions will arise regarding what is adequate and appropriate, and how food and fluids will, could, or should be obtained or provided in palliative care.

In their simplest and most poignant, the issues that underpin the complexity of food and fluids and CANH in palliative and end-of-life care can be seen as a battle between an illness ending a life and perceptions of being deprived of the essentials for life. Mal Morgan (1999), an Australian poet living and dying with terminal lung cancer, captured this dichotomy in the following extract from one of his poems (p. 56).

> . . . I look at the stick-man
> In my bathroom mirror
> every morning.
> There he is.
> Cancer can do this.
> Ethnic cleansing
> can do this. . . .

Morgan's (1999) poem illustrates cancer cachexia and inflicted starvation as highly visible threats to a person's embodied existence.

The perception that lack of food and fluids leads to death is well founded. When nutrition is withheld in a previously well person, death may take weeks (up to 10); however, in the absence of fluids, it is estimated to be between 3 and 14 days and is more rapid in the unwell (Royal College of Physicians and British Society of Gastroenterology 2010). "If water is given in the absence of food, survival is long enough for death from nutritional deprivation to occur. Whilst giving hydration seems a humane act, it may prolong dying" (Royal College of Physicians and British Society of Gastroenterology 2010, p. 16). The latter point is important in the context of progressive life-threatening illness and in acute catastrophic events where recovery is not expected. Usually the ethical doctrine of double effect, whereby an action is justified if the intention is good, is related to the use of opioid analgesics in palliative care. The action itself should not be the direct cause of death. If a person's death is not foreseen,

withholding CANH may be a direct cause of death. In those people close to death, the doctrine of double effect can however be applied to the use of CANH, as "...withholding feeding may foreseeably end the life of the patient. This effect is not aimed at death but is aimed at avoiding the suffering or burdens associated with (artificial) feeding therapies, relative to their possible benefits" (Royal College of Physicians and British Society of Gastroenterology 2010, p. 42).

Changes in the patient population, diagnoses, place of care, and the point in the illness trajectory when palliative care may be appropriate have not altered the central tenets of palliative care. Alleviating suffering, the relief of symptoms, quality of life, neither hastening nor postponing death, the unit of care (patient and family), and a holistic approach (World Health Organization 2002) remain and are pertinent in relation to CANH.

Proponents for and against CANH in the context of palliative and end-of-life care are committed to negating suffering and harm. Nevertheless, perceptions differ regarding what is more likely to be harmful. Families, in particular, perceive the person as suffering in the absence of fluids (Bear et al. 2017). Conversely, advocates of palliative care often accept changes in oral intake as part of the natural dying process and focus on ameliorating symptoms such as a dry mouth (Watson et al. 2009). The continuation or initiation of CANH when it is apparent a person is dying is usually regarded as clinically futile, harmful rather than beneficial, prolonging dying, and diverging from focusing on quality of life. Questions related to CANH can occur along the palliative care continuum and across all diagnoses; however, it often arises when oral intake declines, becomes more arduous, and when the oral route is no longer possible. The intended palliative care goals to neither hasten nor postpone death (World Health Organization 2002) is not a neatly delineated dichotomy. Decisions regarding forgoing, administering, or withdrawing of CANH may contribute to hastening or postponing death. Intervening when oral feeding difficulties arise has a long history, and new developments bring complex challenges about their appropriate utilization.

4 Ancient and New: Interventions That Have Been, Are, and Could Be Utilized

People have been attempting to redress or overcome difficulties and deficiencies related to oral food and fluids for millennia. The history of enteral nutrition "... dates back as far as 3500 bc to the ancient Egyptians, Indians, and Chinese. Their medical practices were the first reports of enteral feeding therapy, provided via the rectum with enemas of wine, milk whey, wheat and barley" (Vassilyadi et al. 2013, p. 209). Relatively, more recent experimentation related to the parenteral route occurred in the twelfth century (Vassilyadi et al. 2013), and in the twentieth century, substantial advances were made with improvements in equipment, techniques, nutritional knowledge, and developments in formula to meet specific nutritional requirements (Royal College of Physicians and British Society of Gastroenterology 2010; Vassilyadi et al. 2013).

The goals of enteral feeding have become increasingly complex, moving towards aiding recovery, healing, improving immunity, the treatment of illness and injury, and the ability to provide a person's full nutritional requirements (Royal College of Physicians and British Society of Gastroenterology 2010; Vassilyadi et al. 2013). Hence many therapeutic options are available to clinicians when declining oral intake occurs; however, the challenge is not solely related to the capacity to intervene. In this vein, Barrocas refers to the troubling trichotomy – the "... conflicts between can (technology), should (ethics) and must (law) as they apply to nutrition support" (2016, p. 295). The challenge is often not the therapies themselves, rather that there are other underlying considerations like an unresolvable illness that continues to progress (Royal College of Physicians and British Society of Gastroenterology 2010; Truog 2014). Indeed, the intentions of CANH, to maintain a person's nutritional and hydration status by securing alternative routes to meet their ongoing metabolic needs, may be at odds with a palliative care approach, particularly at the end of life (Orrevall 2015; Royal College of

Physicians and British Society of Gastroenterology 2010).

The European Society for Parenteral and Enteral Nutrition's (ESPEN) definition of artificial nutrition includes oral nutritional supplements, which are not usually controversial, as well as enteral (nasogastric and nasogastrojejunal percutaneous tubes and endoscopic gastrostomy) and parenteral nutrition (peripheral intravenous, central venous line) (Druml et al. 2016). Artificial hydration includes fluid for hydration delivered by means other than the oral route (Druml et al. 2016). Contemporary developments regarding the ability to provide CANH gives rise to questions about whether CANH should (ethically) be provided and if indeed CANH must (legally) be provided (Barrocas 2016).

The ethical principles of beneficence, nonmaleficence, and the provision of care that reflects the principles of justice inform health care generally and are applicable in relation CANH in palliative and end-of-life care (Barrocas 2016; Bear et al. 2017; Druml et al. 2016; Royal College of Physicians and British Society of Gastroenterology 2010; Watson et al. 2009). Alongside obligations to treat, cure (when possible), and relieve symptoms, is the relief of suffering and the provision of comfort (Royal College of Physicians and British Society of Gastroenterology 2010). Clinicians have a duty of care to meet people's needs and to act in their best interests. However, there is a paucity of unequivocal evidence regarding CANH to guide clinicians providing palliative and end-of-life care (del Rio et al. 2011; Ganzini 2006; Good et al. 2014; Kozeniecki et al. 2017; Royal College of Physicians and British Society of Gastroenterology 2010). This includes the care of cancer patients in the last week of life (Raijmakers et al. 2011). No clear benefit of one route of CANH administration over another has been identified among cancer patients, although there was a greater risk of infection with parenteral nutrition over enteral nutrition and neither improved survival (Chow et al. 2016). Parenteral nutrition was also noted to be twice as expensive (Chow et al. 2016), providing a resource argument to support the preferred use of enteral nutrition along with the benefits to gastrointestinal health and function. Route may also influence the place of care, leading to resource implications alongside social and cultural considerations.

A recent review of the literature (Bear et al. 2017) identified a number of arguments for and against the provision of clinically assisted hydration (CAH) at the end of life with both potentially enhancing comfort. Arguments in support included that the provision of fluid is a basic human need, preventing complications of other treatments and relieving thirst (Bear et al. 2017). Arguments against CAH at the end of life include its provision impeding the acceptance of the terminal situation, prolonging a person's suffering and dying, and contributing to uncomfortable symptoms like edema and ascites. These authors also cite the argument that the accumulation of metabolic by-products in dehydration may reduce pain perception and improve comfort (Bear et al. 2017). The potential benefits and burdens of different methods of CANH (enteral and parenteral) have also been tabulated (Kozeniecki et al. 2017). While all may provide a sense of relief for patients and families, all have significant risks and no clear outcomes to guide clinicians have been identified (Bear et al. 2017; Good et al. 2014; Kozeniecki et al. 2017; Raijmakers et al. 2011). Importantly, significant limitations in the evidence available was noted, with authors suggesting there may be a subset of this population who may derive some benefit (Kozeniecki et al. 2017). Research to obtain evidence is challenging when the population may be significantly debilitated, cognitively impaired or actively dying. Alongside these challenges are the risk of injustices occurring, specifically among vulnerable population groups, when evidence is lacking resulting in inequitable care (Bear et al. 2017). The absence unequivocal evidence makes ethical decision-making more challenging.

Justice is one of the ethical principles relevant to the provision of appropriate care which does no harm and is beneficial for the recipient. Fairness, treating people equally and the equitable distribution of resources, is also inherent in the ethical principle of justice (Bear et al. 2017; Royal College of Physicians and British Society of Gastroenterology 2010; Watson et al. 2009).

ESPEN offers guidance for clinicians regarding ethical aspects of CANH, proposing the following three prerequisites be considered, with the key priorities to do no harm, to do good and respect autonomy (Druml et al. 2016, p. 546).

1. An indication for a medical treatment
2. The definition of a therapeutic goal to be achieved
3. The will of the patient and his or her informed consent

Indications for CANH (or not) will vary significantly over the course of a life-limiting illness and in acute events, as will the goals, preferences, and perceptions of its purpose. Utilizing CANH may be indicated and uncontroversial early in an illness to ameliorate the side effects of therapies, to treat concurrent or incidental illness, improve a person's health status, and to enable therapeutic treatment to be given. The difficulties encountered require consideration of reversible causes and the natural progression of an illness alongside the goals of care.

5 Natural Progression Versus Reversible Causes

Screening for malnourishment, identifying those underweight, and enquiring about unintended weight loss so reversible causes may be redressed is common in health care (O'Hara 2017). Prior to the more imminently terminal phase, the goal is to enable and support oral intake by assisting with feeding, providing appropriate food and fluid, oral care, and a providing a conducive environment. The primary goal regarding "nutrition in palliative care is to maximise food enjoyment and minimise food discomfort" (O'Hara 2017, p. 24). To facilitate this, identifying and addressing symptoms, reversing reversible causes, and accessing and providing appropriate nutritional advice or support is central to maximizing quality of life and is basic care. Oral intake can be adversely impacted by candida infections of the mouth and upper gastrointestinal tract, the side effects of medications or treatments, dry mouth, taste changes, nausea, indigestion, malodourous wounds, dyspnea, fatigue, early satiety, and bowel obstruction (Royal College of Physicians and British Society of Gastroenterology 2010; Watson et al. 2009). Unfortunately, the effects of an illness and the changes wrought are not always reversible.

Cachexia is the consequence of a number of progressive life-limiting illnesses and general cachexia, unrelated to malignancy, has been defined as (Evans et al. 2008, p. 794):

> . . . a complex metabolic syndrome associated with underlying illness and characterized by loss of muscle with or without loss of fat mass. The prominent clinical feature of cachexia is weight loss in adults (corrected for fluid retention) or growth failure in children (excluding endocrine disorders). Anorexia, inflammation, insulin resistance and increased muscle protein breakdown are frequently associated with cachexia. Cachexia is distinct from starvation, age-related loss of muscle mass, primary depression, malabsorption and hyperthyroidism and is associated with increased morbidity.

Subsequently, an international consensus defined cancer cachexia as (Fearon et al. 2011, p. 499):

> . . . a multifactorial syndrome characterised by an on-going loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment. The pathophysiology is characterised by a negative protein and energy balance driven by a variable combination of reduced food intake and abnormal metabolism.

The important distinguishing characteristic of cachexia (all causes) is that unlike malnutrition, which may be concurrent, or starvation, it cannot be adequately redressed by nutrition (Evans et al. 2008; Fearon et al. 2011; Royal College of Physicians and British Society of Gastroenterology 2010; Watson et al. 2009). Commonalities are evident between the general and cancer cachexia definitions, with both acknowledging metabolic changes, changes to the body composition, and the impact on the person. In defining cancer cachexia, guidance is offered for staging, covering a spectrum which includes precachexia, cachexia and refractory cachexia (Fearon et al. 2011). Malignancies differ in terms of their cachexic

impact and an individual's progress across the spectrum to refractory cachexia before death is uncertain. Cancer cachexia, which remains poorly understood, affects approximately 80% of this population and is usually accompanied by other symptoms (Fearon et al. 2011; Watson et al. 2009). These changes, acknowledged in the staging of cancer cachexia, include anorexia, loss of appetite, weight loss, metabolic changes, inflammatory changes, changes in performance status, and expected survival (Fearon et al. 2011). For both cancer and non-cancer related cachexia, clinicians are reliant on the clinical context, a history of unplanned weight loss, body mass index, anorexia, declining oral intake, performance status, inflammatory, and other biomarkers (Evans et al. 2008; Fearon et al. 2011). Confronted by difficulties in eating and drinking in advanced illness, patients, families, and some clinicians may consider CANH.

The metabolic changes occurring with cachexia can inform clinical decisions to forgo or utilize CANH. Orrevall (2015, p. 615) suggests trying to "estimate if the cancer spread allows the patient a survival longer than 3 months. No benefit can theoretically be expected by an active nutritional support if a starving patient is going to die of tumour progression within that time interval." Starving is an emotive word that is frequently used, especially by family members. However, patients' and family members' perceptions of and attention to mitigating starvation may obscure the real issue; the person is not dying because of nutrient deprivation (Kozeniecki et al. 2017).

Importantly CANH is unable to reverse refractory cachexia in advanced illness and it is not a source of pleasure (Cohen et al. 2012; Orrevall et al. 2005). Indeed CANH may become a source of discomfort and can be contrary to the nutritional goals of palliative and end of life care (O'Hara 2017; Orrevall 2015). Unfortunately, the pleasure of oral intake is often lost, adversely affected by taste changes, difficulty eating and drinking, and associated with anxiety, worry, and physical discomfort (Watson et al. 2009). Refusing oral intake to hasten death is an alternative to navigating the uncertainty of disease progression.

6 Choosing to Stop Eating and Drinking

Voluntarily choosing to stop eating and drinking (VSED) is the action of a competent and capable person to deliberately forgo oral intake. The "primary intention [is] to hasten death because unacceptable suffering persists" (Ivanović et al. 2014, p. 1). They exchange what is unacceptable suffering for them for the suffering often perceived by families and companions when the oral route is lost in advanced illness. VSED leads to death within days to two weeks, depending on the person's preceding health status (Ivanović et al. 2014; Wax et al. 2018). Reasons for choosing to VSED include being ready to die, believing continuing to live is futile, perceiving their quality of life as poor, and a desire to control the circumstances and method of their death (Ganzini et al. 2003; Ivanović et al. 2014). VSED is considered a more accessible and less bureaucratic option than seeking euthanasia or physician-assisted suicide, and it can occur in the absence of a terminal diagnosis and without requiring medical input (Wax et al. 2018). Ethically and legally, given certain requirements, VSED is defendable (Ivanović et al. 2014; Wax et al. 2018). The following criteria are proposed for physician-supported VSED (Wax et al. 2018). Firstly, there is a "terminal or serious debilitating illness with intolerable suffering which remains after access to high-quality palliative care evaluation and support" (Wax et al. 2018, p. 443). Additionally, it is necessary to establish that the person has capacity, is informed of the risks, benefits, and possible alternatives. It also requires ascertaining that the choice is voluntary and verifying that mental illness or cognitive impairment are not factors. Support by the person's main caregivers is considered important, as is confirming VSED is consistent with the values of the person (Wax et al. 2018).

Understanding the often multidimensional suffering associated with choosing VSED to hasten death and responding appropriately is crucial (Ivanović et al. 2014; Wax et al. 2018). Included is the impeccable management of symptoms and psychosocial and existential support (Ivanović et al. 2014; Wax et al. 2018). All competent people

can change their mind regarding the plan of care. However, carers and clinicians may be morally and ethically challenged when a person's cognitive state is impaired in the dying process and they express a wish for fluids or food which may prolong their dying, contrary to their previously expressed wishes (Wax et al. 2018).

Choosing VSED results in end of life symptoms that are described as similar to those experienced by the withdrawal of CANH. Thirst, dry mouth, hunger, dysuria, weakness, delirium, and somnolence are anticipated and require management (Wax et al. 2018). Hospice nurses in Oregon, who responded to a survey (72%), perceived patients choosing VSED "... as suffering less and being more at peace in the last two weeks of life" than those who chose physician assisted suicide (Ganzini et al. 2003, p. 362). They noted that 85% of deaths occurred within 15 days, the stand-down period required for physician-assisted suicide in Oregon (Ganzini et al. 2003). VSED appeared to be accepted by the nurses and not a source of moral distress or ethical concern for them, although this is not explicitly explored. The perceived lack of suffering may be comforting for the nurses and reflects European findings that decisions to withdraw or forgo CANH did not lead to suffering based on the comparative use of end-of-life medications for symptom management (Buiting et al. 2007).

Authors (Ivanović et al. 2014) argue that VSED has received marginal attention within palliative care. Although commentary is emerging, there is a paucity of systematic approaches to assess people choosing to VSED and to provide guidance to clinicians (Wax et al. 2018).

7 Oral Intake: Focusing on Eating and Not Eating

The introduction to this chapter began with a vignette illustrating the relatively common challenge of declining appetite and oral intake and the endeavors of those who care for them to prepare and offer tempting and nutritional food and fluids. As a clinical and ethical issue, it may be overlooked by clinicians and overshadowed by debates regarding the appropriateness or otherwise of CANH when illness is advanced and the end of life near. In addressing oral feeding difficulties and dilemmas, it is proposed that three questions are considered (Royal College of Physicians and British Society of Gastroenterology 2010, p. 9–10):

1. What is the underlying diagnosis?
2. What is the mechanism of the oral feeding problem?
3. Can the person eat and drink and if so, at what risk?

These are critical questions in relation to oral intake in palliative care and can inform thoughtful consideration and appropriate responses. Knowledge of the underlying diagnosis is important as is the extent of the disease and prognosis. As discussed earlier, clinicians have a responsibility to identify and address potentially reversible causes for declining or poor oral intake (Royal College of Physicians and British Society of Gastroenterology 2010; Watson et al. 2009). Eating and drinking when there is a risk of aspiration, coughing, and the potential for choking may or may not be acceptable to the person and ultimately, they should be able to exercise their autonomy whenever possible. Indeed, the pleasure of eating may override difficulties, including the unpleasantness of vomiting (Orrevall et al. 2005).

Declining oral intake in the presence of life threatening illness is full of meaning for patients (Wallin et al. 2015) and family members (Amano et al. 2016; Hopkinson 2016; Raijmakers et al. 2013; Reid et al. 2009a, b; Reid et al. 2010). For patients, changes in oral intake have been described as "... existentially loaded markers of impending death" (Wallin et al. 2015, p. 123). Declining oral intake and appetite is also meaningful for clinicians in terms of prognosis (Royal College of Physicians and British Society of Gastroenterology 2010; Watson et al. 2009) and is one of the ten phenomena identified by palliative care experts as indicating approaching death (Benedetti et al. 2013).

For relatives, food can symbolize love, concern, and compassion and result in significant

efforts to tempt and provide favorite foods (Raijmakers et al. 2013; Reid et al. 2009b). Food and fluid also represent nourishment, preserving life, enjoyment, special memories, social activities, providing a routine to daily life, a way to care, express love, and meet the ill person's wishes (Raijmakers et al. 2013). Relatives' responses to declining oral intake include laboring to prepare special food, tempting them to eat and drink, and endeavoring to maintain routines and ordinariness in their daily lives (Raijmakers et al. 2013; Wallin et al. 2013). Awareness of the life-threatening context informs relatives' responses and they often expend significant thought and effort. Internationally researchers have noted tensions between family members and the ill person regarding declining oral intake (Amano et al. 2016; Raijmakers et al. 2013; Reid et al. 2009b, 2010; Wallin et al. 2015).

Tensions can arise when a person who is debilitated, fatigued, and experiencing loss of appetite endeavors to eat to please, is no longer able to eat as expected, or at all (Raijmakers et al. 2013; Reid et al. 2009b). Conflict as a result of declining oral intake can result in patients feeling "... like they were constantly in an environment focused on food from which they could not escape"(Reid et al. 2009b, p. 441). Relatives could become embroiled in what they described as a "vicious circle" (Raijmakers et al. 2013, p. 670) whereby they and their ill relative were trying to please each other to avoid worry and conflict, which was recalled vividly when it had occurred. Some relatives accepted changes as part of the process of dying, while others perceived this change, in part, as the person's choice (Raijmakers et al. 2013).

These experiences and their complex meanings are not exclusive to European societies. Amano et al. (2016) found Japanese relatives also pressured ill family members to eat in the belief that this would be beneficial and they went to significant effort to entice and encourage oral intake. Conflict could occur. Their findings inferred there was a higher risk of bereavement depression for relatives who felt they had forced oral intake and who believed they had inadequate information about weight loss, cachexia, and nutrition (Amano et al. 2016).

The desires of patients and relatives for more information and greater understanding is well documented (Amano et al. 2016; Raijmakers et al. 2013; Reid et al. 2009b, 2010; Wallin et al. 2015, 2013). Openly discussing the changes occurring (when this is what the patient and relatives want) may appear obvious yet it may not occur. Communication regarding food and fluids, hydration and nutrition is acknowledged as difficult even for palliative care clinicians (Clark et al. 2017; Millar et al. 2013). Interestingly, bereaved relatives recalled little information being conveyed to them by health professionals regarding declining oral intake (Raijmakers et al. 2013), yet health professionals in the same service richly described how they respond, inform, and guide relatives, although they tended to wait for cues and opportunities. A mismatch in experience and perceptions was revealed (Clark et al. 2017).

The lack of open acknowledgement of weight loss by health professionals, even when apparent, concerned relatives and patients alike (Reid et al. 2010). They wanted their weight loss acknowledged, information and a response regarding appropriate interventions; however, health professionals' lack of engagement damaged patients' and families' confidence in them (Reid et al. 2010). Awareness of the significance of cachexia and tacit acceptance of its inevitability have been identified as potential contributors to clinicians' avoidance (Millar et al. 2013). The authors (Millar et al. 2013) believed palliative care staff avoided the issue less than nonpalliative care staff and were more holistic in their approach. The relative silence regarding weight loss and cachexia encountered by patients and family members from health professionals may be related to the paucity of therapeutically effective interventions (Reid et al. 2010). Inaccurate knowledge can result in nurses and doctors relying on a nutritional response, even when they knew it would not be effective (Millar et al. 2013). In addition to knowledge, dialogue needs to be effective and the active integration of patients, families, and nurses into clinical decision-making is recommendation (del Rio et al. 2011).

Issues associated with declining oral intake are likely to arise over a longer timeframe than

dilemmas associated with CANH. A degree of burden and potential harm for both the ill person and their family members is evident in relation to declining oral intake, as are the challenges of exercising autonomy when unwell. The concept of autonomy, that a person has the right to accept, refuse or decline care and treatments is widely accepted in Western bioethics (Bear et al. 2017; Royal College of Physicians and British Society of Gastroenterology 2010; Watson et al. 2009). Nevertheless, few people act or make choices about health care completely independently of other influences. Included may be the wishes of others, hopes, prior knowledge or experience, cultural influences, and religious beliefs. Having the capacity to act autonomously does not necessarily translate into one's personal choice being fulfilled.

Failing to meet the needs of both relatives and patients reveals a significant burden, a potential source of harm, and the possibility of undermining autonomy. All have implications for justice in care delivery. The ethical principle of justice also relates to how health professionals engage with those they care for and includes honesty in terms of not imposing one's own wishes, values, and preferences (Truog et al. 2015). Clinicians should be cognizant of this when they are enveloped in and perhaps invested in not only the philosophy of palliative care but also what is routine and standard practice. Acceptance of the status quo or professional comfort may adversely impact on care. In the presence of declining or compromised oral intake, patients, families, and clinicians may consider the use of CANH.

8 Clinically Assisted Nutrition and Hydration: Forgoing, Providing, and Withdrawing

> **Vignette two**: Nasogastric feeding commenced amidst rapid deterioration from an undiagnosed illness. In the family meeting, the irreversible cause could finally be explained to the patient's family, with death anticipated very soon. The partner requested feeding continue. A sibling recalled the person's preceding loss of appetite and interest in food, another noted how unsightly the feeding tube was on their now severely debilitated and barely responding brother. Tearfully the partner responded, "I can't bear the thought of him starving to death. I don't want him to think we have given up and I have abandoned him."

Family members are not alone in perceiving the forgoing or withdrawal of CANH as harmful and a sign of care being abandoned. Ethically, the focus in palliative care is often on CANH, its appropriate and timely provision and decisions to withdrawal or forgo it (Royal College of Physicians and British Society of Gastroenterology 2010; Truog 2014).

Clinicians often feel more comfortable withholding (acts of omission) rather than withdrawing (acts of commission) therapies such as CANH, although the two are often regarded as ethically the same (Royal College of Physicians and British Society of Gastroenterology 2010; Truog 2014). Withdrawing CANH is a decision to stop a therapy after commencement, while withholding or forgoing CANH is the decision not to start. All decisions around CAHN require careful consideration, including if it is appropriate in the last weeks to days of life (Royal College of Physicians and British Society of Gastroenterology 2010). Differing views are held by individual practitioners and professional groups, including physicians (Chambaere et al. 2014; Morita et al. 2002; Torres-Vigil et al. 2012) and nurses (Stiles 2013) regardless of professional and ethical frameworks. Those most affected by these decisions are patients and family members.

9 Patients and Families

Many people receiving palliative care experience declining oral intake over the course of their illness. In the terminally ill, causes of declining oral intake are often multifactorial and include swallowing difficulties, loss of appetite, nausea and vomiting, and physical obstruction (Raijmakers et al. 2011). In the presence of weight loss, and difficulties with oral feeding, it is common for standard care concerning food and fluid to be questioned, leading to discussions on how best to redress perceived needs for nutrition and hydration. Although there is an obligation to use ordinary means to support

food and fluids, there is no firm obligation to use extraordinary measures, which require consideration of both the benefit and burdens of medical therapies, CANH included (Druml et al. 2016; Royal College of Physicians and British Society of Gastroenterology 2010). Despite this clear description of CANH as a medical therapy rather than ordinary care, it is more complex in practice. Artificial hydration and nutrition can be a controversial topic in specialist palliative care yet it is often, but not always, perceived positively by patients and families. Table 1 illustrates some of the meanings and perceptions of patients and family members.

The attentiveness, loss of shared mealtimes, and social isolation experienced when supporting a person receiving CANH are similar to challenges described by family members in relation to declining oral intake (Raijmakers et al. 2013; Wallin et al. 2013). Significantly, CANH does not redress these aspects of daily life. The perceived benefits and burdens of CANH should not obscure the necessity to engage in efforts to consider the less tangible elements which influence the experiences of care giving and receiving, like ethics, culture, and emotions (del Rio et al. 2011).

Potential benefits, clinical risks, and burdens can be and are tabulated (del Rio et al. 2011; Kozeniecki et al. 2017; Royal College of Physicians and British Society of Gastroenterology 2010). However, there is a paucity of clinical evidence to guide and inform (Good et al. 2014; Royal College of Physicians and British Society of Gastroenterology 2010). A review of the literature regarding the emotional impact, perceptions, and decision-making among patients, families, and clinicians associated with CANH identified that insufficient information and misunderstandings prevailed (del Rio et al. 2011).

Patients and family members have expressed similar preferences in relation to CANH at the end of life and patients were usually very clear about their preferences (Bükki et al. 2014). However, relatives tended to be more conservative when deciding for others rather than themselves. Older age was associated with deciding to decline CANH by relatives and patients, with relatives more concerned about the physical impact of withdrawing CANH than patients. Importantly, more than one third of the participants (patients and relatives) would forgo CANH and the authors (Bükki et al. 2014) noted this differed from other qualitative studies.

Vignette two illustrates complex yet familiar challenges in palliative care. Routine intravenous fluids had commenced when the severity of the patient's illness was unclear and the patient could exercise autonomy. He consented to the nasogastric tube (NGT) when swallowing became difficult but his wishes if the prognosis was poor were not explored. Opportunities for advanced care planning were missed, compromising his autonomy. When the prognosis became clear, the patient's verbal and written communication abilities had been lost. The siblings, alarmed at the partner's determination to maintain CANH, recalled his anorexia. They did not perceive him as hungry nor the feeding as beneficial and believed he would not want his life prolonged in this context. The partner acknowledged their concerns but could not reconcile feeding withdrawal with her sense of abandoning him. A compromise was reached; the IV fluids would be reduced and stopped when the line occluded. Feeding would be reduced and the NGT removed when he became unconscious.

Continuing CANH could be conceived as poor resource use, and contrary to the principle of justice. Endeavors were made to minimize staff time and optimize resources with reduced IV fluids and feeding volumes. Negotiating a compromise minimized risks of unnecessary current and future suffering for the patient, partner, and siblings. The clinicians endeavored to care for the patient and family unit and to do so holistically. The ethical challenges resulted from an initially unknown prognosis, the absence of clear communication, and recording of the patient's wishes combined with differing family perspectives, and the lack of robust scientific evidence regarding the benefits and burdens of CANH at the end of life. Although utilization of CANH as a resource could not be justified due to the poor prognosis (Orrevall 2015; Royal College of Physicians and British Society of Gastroenterology 2010), it could be argued that it was in their psychological best

Table 1 The meaning of CANH for patients and families

Population	Key points	Authors
Positive perspectives for patients and families		
The meaning of CAH for hospice patients and family carers (USA)	Hope Of prolonging life Supporting dignity Improved quality of life through reducing symptoms Provided comfort By reducing pain Enhancing the efficacy of analgesics Nourishing holistically	Cohen et al. (2012)
Patients' and relatives' perceptions of CAH (Italy)	IV fluids perceived as highly effective Nourishing Positive psychologically (>90%) IV fluids were perceived as more effective and not burdensome IV fluids were preferred over SC fluids even at home	Mercadante et al. (2005)
Patients' and relatives' perceptions of home parenteral nutrition (Sweden)	Relief and security that nutritional needs were being met Positive effect on QOL, weight, energy, strength and activity Relieved the pressure to eat Shared burden with the home visiting clinicians (distinguished between enteral and parenteral routes),	Orrevall et al. (2005)
Family members experiences of caring for patients receiving tube feeding (Canada)	Negotiating a new "normal" Supported their priority to provide adequate hydration and nutrition Reduced family tension over intake	Penner et al. (2012)
Limitations or burdens for patients and families		
The meaning of CAH for hospice patients and family carers of (USA)	They knew it wouldn't cure, nor replace eating	Cohen et al. (2012)
Patients' and relatives' perceptions CAH (Italy)	SC route not as effective nor less troublesome	Mercadante et al. (2005)
Patients' and relatives' perceptions of home parenteral nutrition (Sweden)	Restricted family and social life Checking on overnight administration – "free" and not free evenings Only partially solves issues by delivering nutrition (social aspects of eating not redressed)	Orrevall et al. (2005)
Family members' experiences of caring for patients receiving tube feeding (Canada)	Negotiating a new "normal" Changed roles Little choice and redefined from spouse to caregiver Challenge of multiple roles (old and new) responsibility of new skills, providing feeds, responding to symptoms Physical toll, disturbed sleep, and psychological burden Altered lifestyle Lack of freedom, less personal time, fitting life in between feeding, being tied down in their caregiving role and diminished social contact Changes to their oral intake (guilt and to reduce food odors)	Penner et al. (2012)

interests (Royal College of Physicians and British Society of Gastroenterology 2010). In clinical discussions, the issue of prolonging dying by providing fluids in the absence of nutrition should be addressed (Royal College of Physicians and British Society of Gastroenterology 2010).

10 Clinicians

Vignette three: Lucy, diagnosed with metastatic bowel cancer, presented to the hospital emergency department overnight with intractable vomiting. An abdominal x-ray revealed a high bowel obstruction. Treatment commenced with an NGT and IV fluids, and a scan planned for the morning. Lucy declined the scan and surgical review and requested hospice transfer for terminal care. This was arranged on the understanding that IV fluids would stop. At the morning clinical meeting, hospice staff discussed Lucy's impending transfer and plan of care. Lucy's goals and wishes had previously been documented by a hospice community nurse. Included were her intention to decline further surgery if a bowel obstruction occurred and her wish to die in the hospice. A doctor questioned Lucy's decision because she was not significantly cachexic when seen the previous week and chose to explore Lucy's decision. Lucy described her previous complicated postoperative journey, becoming increasingly distressed and eventually angry that her decisions were revisited. Her husband remained beside her, tense and silent. The doctor looked to the husband who eventually spoke. He did not want Lucy to die but he could not stop it happening. He explained he would never ask her to experience again what she had already endured. Silence followed. Eventually, the nurse asked Lucy what her wishes and priorities were now. She wanted to be comfortable, supported to live, if possible, until her daughter and grandchildren arrived. Then she wanted the clinical team to stop anything that might prolong her life. A plan was agreed, including a NGT on free drainage, oral intake as desired, trialling medical management of the obstruction, medications subcutaneously, and subcutaneous fluids overnight until the family arrived.

Endeavors to ensure ethical principles and professional obligations are appropriately met can result in tensions between the triad of patients, family members and clinicians, and within families and among clinicians. Peoples' hopes and expectations, including those of clinicians, are often not uniform and static. Palliative care nurses hold heterogeneous attitudes towards CANH, including whether it was a medical treatment or a minimum standard of care (Stiles 2013). Their views varied in recognition of the complex interaction of multiple influences including legal, ethical, social, clinical, and professional elements. Others, including patients, family members, doctors, and nursing colleagues influenced them. Although significant variation across the six research studies reviewed (Byron et al. 2008; L. Ke et al. 2008a; L. S. Ke et al. 2008b; Konishi et al. 2002; Miyashita et al. 2008; van der Riet et al. 2008) was identified and the influence of culture noted, nurses perceived the patient's autonomy as most important. In four studies from Asia, family rather than individual decision-making was identified as predominant although in all publications CANH was a significant issue and nurses experienced moral distress when family wishes prevailed over patient autonomy (Stiles 2013).

Physicians, like nurses, have differing attitudes regarding whether CANH is a medical treatment or a minimum standard of care (Morita et al. 2002), including those in specialist palliative care (Torres-Vigil et al. 2012). Internationally, practices regarding physicians' decisions to forgo or withdraw CANH for patients at the end of life differ (Buiting et al. 2007; Morita et al. 2002; Raijmakers et al. 2011; Torres-Vigil et al. 2012). In the care of patients with cancer in the last week of life, the utilization of CANH can vary widely with CAN administration varying from 3% to 53% while the utilization of CAH ranged from 12% to 88%. (Raijmakers et al. 2011). Mixed results were identified from this literature review, with some studies reporting positive effects and others negative and no studies focused solely on CAN. Utilization of CANH was less common in specialist palliative settings where death may be more likely to be predicted. While focused on the last week of life, reviewers noted the paucity of evidence regarding CANH's efficacy, and the positive perception of it by family members and patients (Raijmakers et al. 2011). The prevalence of studies from Asia, particularly in relation to CAH was noted and ongoing enquiry concerning CANH from the Asia Pacific region has continued (Bükki et al. 2014).

Decisions regarding withdrawing or forgoing life-prolonging treatments also differed across six Western European countries (Belgium [Flanders], Denmark, Italy, The Netherlands, Sweden, and Switzerland) (Buiting et al. 2007). Forgoing CAH occurred least in Italy (2.6%) and most frequently in the Netherlands (10.9%). Withholding CANH was more common than withdrawing and occurred more often for older people

(≥80 yrs), females, a malignant diagnosis and diseases of the nervous system. It was least common in hospitals, except for Sweden (Buiting et al. 2007). A more recent survey of physicians in Flanders, Belgium, found "... a decision to forego ANH occurred in 6.6% of all deaths (4.2% withheld, 3.0% withdrawn)" (Chambaere et al. 2014, p. 501). Patient characteristics were similar to the earlier study (Buiting et al. 2007). Variation in prescribing practices also occurs outside Europe and among palliative care physicians.

Prescribing practices of palliative care physicians (n = 238) in a Latin American study were not congruent with usual palliative care practices where CANH is more likely to be forgone at the end of life (Torres-Vigil et al. 2012). Over half (60%) prescribed CAH for their patients in the last week of life and beliefs that it was beneficial clinically and psychologically were the main reasons. The physicians were more likely to disagree with the premise that withholding CAH was beneficial for symptom management. They believed CAH met minimum standards of care and the SC route was preferred. Hospital in-patients were more likely to receive parenteral hydration (57%) and receive it IV (59%) than patients at home (45%) who were more likely to receive fluids SC (68%). Practical issues inhibited in-home CAH.

Physicians do believe CANH impacts on life time, with European physicians reporting decisions related to CANH and other measures as foreshortening life, most often by less than a week, although it could be longer (Buiting et al. 2007). Interestingly, with the exception of Belgium, when CANH was forgone fewer medications were given for symptom management than for other patients, leading the authors to conclude this did not add to symptom burden and suffering (Buiting et al. 2007). Physicians in Belgium (Chambaere et al. 2014) estimated that in 77% of cases the decision had some influence in foreshortening life. "An explicit intention of hastening death was present in a quarter of cases where ANH was withheld and in half where it was withdrawn" (Chambaere et al. 2014, p. 502). This needs to be considered in the legislative context of patients' rights, euthanasia, and palliative care in Belgium. Including patients in discussions may not have been possible because of their cognitive status, and in Belgium, physicians can autonomously withdraw futile treatment (Chambaere et al. 2014).

Clinician experience is one of many influences on clinical practice. A 2002 study of Japanese physicians (n = 584, a response rate of 53%) identified that comfort and experience with end-of-life care influenced their perceptions of the appropriateness of IV hydration in terminally ill cancer patients (Morita et al. 2002). Those less involved in end of life gave greater volumes of fluid and believed there were greater benefits than harm. While 96% agreed with patients' right to decline CAH, declining oral intake in the terminal stage was not seen as part of the natural dying process for 53% of respondents. Nearly one-third (32%) agreed that it was not ethically permissible to allow patients to die dehydrated, while 40% believed IV fluid was the minimum standard of care rather than a medical treatment. Once again a tension is revealed between the professional position that CANH is a medical treatment, established palliative care practice, acceptance of the dying process as natural and individual physician's practices. Diverse perceptions and decision-making regarding the influence of CANH in postponing or hastening death adds to the complexity of the palliative care goals to do neither.

The need for early discussions with patients to identify their preferences has been noted, as was the need for clinicians to be well informed due to their significant influence on decision-making regarding CANH (Mercadante et al. 2005). Knowledge is crucial to dispel myths and engage confidently with patients and families (Bükki et al. 2014). Nevertheless, education alone may not be sufficient. An education program in Taiwan focusing on CANH did not override the influences of the food and family culture to change clinical behavior (L. Ke et al. 2008a).

Returning to vignette three, the clinical staff had a responsibility to ensure Lucy was making an informed decision and understood possible benefits and burdens. Justice was evident in offering a surgical review and an acceptable level of care negotiated. Importantly, with death anticipated,

clinical staff rechecked if Lucy's wishes had changed. Unfortunately, this was distressing for her. The appropriate utilization of resources, with the offer to explore surgical options, could be questioned (Royal College of Physicians and British Society of Gastroenterology 2010). However, as it transpired, the resources to support her wishes were modest and met the psychosocial needs of the patient and family and were congruent with palliative care goals of care (World Health Organization 2002). This vignette illustrates the complexity of autonomy, the uncertainty of what may be a benefit or a burden and the importance of having courage in difficult conversations. It also reinforces the importance of knowledge, quality communication, advanced care planning, and appreciating the diverse meanings of food and fluids and CAHN for all parties.

11 Summary and Conclusion

Clinicians draw on clinical evidence, ethical frameworks, protocols, guidelines, and established practice, but these do not eliminate emotional responses, anxiety, cultural and religious influences, and misunderstandings. They are embedded in their own life biographies, a milieu of spiritual, societal, and cultural influences including ethnic, workplace, and professional cultures. Equally, the people they care for are also embedded in their life experience and influenced by their spiritual belief system, society, culture, family culture, and relationships. These factors in the context of living and dying, food and fluids, experiences with and the meaning of food and fluid creates a complex dynamic. With such diversity, freely exercising autonomy and perceptions of benefit and burden and fairness are unlikely to be congruent. Disparity and the need for early, repeated, collaborative, and ethical dialogue is inevitable and should be anticipated and accepted.

Clinician communication is a recurring theme in relation to the meaning of food and fluids, CANH and the perceptions of patients, families. The potential to moderate the focus on food and fluids which can be constraining and oppressive is an important clinical and ethical issue. The changes that occur in advanced illness and dying require open acknowledgement and early engagement whenever possible. These discussions should include the goals of care in relation to the use of CANH, its benefits, burdens, role in symptom management, the patient's and family's wishes, their values, beliefs, and cultural practices. Communication is clearly important although it alone is unlikely to assuage all concerns.

The development and refinement of CANH continues to be discussed, questioned, and researched regarding its place in the context and provision of palliative care. Perceptions of basic care and medical treatment in relation to CANH is not homogenous within professions. Additionally, the established palliative care approach of accepting declining in oral intake and dehydration as natural at the end of life is not universally accepted. The diversity identified and challenges faced, including those by palliative care clinicians, raises issues not addressed here regarding how to best support the mainstreaming of palliative care practices, and the growing international specialty in managing these ethical issues.

The commonality is a desire to alleviate suffering. However, the lack of certainty regarding the type and amount of suffering underpins the need to keep knowledge current and personalize care. Clinicians will have encountered conversations where the desire to give food and fluids prevails in the absence of a patient narrative that indicates they desire it or feel they are suffering in its absence.

Clear evidence of the acceptable benefits of CANH would probably be more readily accepted and acceptable than clear evidence of unacceptable burdens. Importantly, not all benefits related to CAHN are nutritional. A definitive answer appropriate for people with malignant and non-malignant conditions with advanced progressive illness at the end of life is unlikely. Therefore, in the absence of certainty, current knowledge, effective appropriate dialogue, clinical case-by-case consideration and negotiated compromise are appropriate. Individualized care for patients and their companions that is respectful of their

biographies, varied rather than homogenous, and founded on curiosity rather than a prescribed dialogue is indicated. Food and fluids and CANH are likely to remain enduring ethical challenges in palliative and end-of-life care; however, when these issues arise and decisions are made in partnership, there are important opportunities to improve care at the end of life.

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Attending to the Suffering Other: A Case Study of Teleconsultation in Palliative Care at Home

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_119

Abstract

Although this chapter has its origins in the Dutch practice of palliative care at home, its message is relevant to all countries in which a considerable percentage of the population prefers to die at home. These people usually depend to a great extent on general practitioners to realize such a death at home. Although there are exceptions, many generalists lack experience with and/or knowledge of palliative care. These limitations show themselves most in complex cases and often result in the patient being hospitalized. This chapter provides a perspective on a potential (part of the) solution to integrate generalist and specialist palliative care at the patient's home: teleconsultation. It describes how to empirically and ethically study such a complex, technological intervention within a particular care practice, with a focus on the fit of the technology. Teleconsultation technology should be considered non-neutral. It mediates the relationships between patients and their accompanying professionals, while also coshaping experiences of virtual proximity and real-time autonomy. It can also be a constant reminder of an approaching death. Teleconsultation appears to provide opportunities for professionals to experience responsibility for a patient's suffering and to address it adequately, although its scripts do not fill the need for meaningful moments of silence. In the end, this chapter claims that teleconsultation can be of value to the practice of palliative homecare, if special consideration has been given to its careful use by professionals. Teleconsultation requires an open and humble attitude toward both patients and colleagues, as well as sensitivity for privacy issues.

1 Introduction

> Ms. K., in her mid-60s, suffers from recurrent bladder cancer. During her last visit at the hospital, it appeared that the disease was already in an advanced stage and metastasized into the liver, the lungs, and the bones. Her oncologist recently told her that recovery was very unlikely and that she would advise her to opt for a palliative care approach. Such an approach would focus on preserving her quality of life as long as possible by trying to prevent and relieve pain, other physical discomfort, as well as psychosocial and spiritual problems. She agreed with her oncologist and discussed her future care and treatment plan with the hospital-based palliative care specialists. During this discussion the question arose where Ms. K. would like to spend the last phase of her life. She immediately responded that home is where her heart is. Her husband is there, as well as her little dog. Moreover, her home contains 30 years of personal history. She hopes she can stay at home until she dies, but she fears that dying at home might be impossible due to all the complex problems that will probably come with her physical decline. How can treatment and care be organized in such a way that Ms. K. is able to pass away peacefully in her own home?

Each year, a lot of people like Ms. K. are in need of palliative care. The continuously increasing aging of Western populations will induce an increase of chronic diseases, such as cancer, heart failure, and dementia, leading to a steep rise of non-sudden deaths in the nearby future Statistics Netherlands (2017). This chapter focuses on a potentially important shift in healthcare policy, namely, to provide adequate care for most of these chronically ill people in *their own homes*. This includes providing adequate palliative and end-of-life care at home. One of the challenges is to make expert palliative care available for those home-based palliative care patients who develop

complex problems and needs and for whom the general palliative care delivered by primary care physicians is no longer sufficient. Such expert palliative care is supposed to prevent burdensome transitions to specialist palliative care facilities and/or hospitals in the last phase of life. Communication technologies supplying synchronous audiovisual contact are considered potential solutions for the transfer of expert palliative care, but the fit of these technologies in existing palliative care practices is only limitedly explained (e.g., Pols 2012). This chapter aims to show and explain the fit of teleconsultation in the practice of palliative care at home, with particular attention to the ethical dimensions of palliative telecare.

2 Ethics: Will Palliative Telecare Contribute to Attending to a Patient's Suffering?

Literature of patient narratives demonstrates that suffering quite often is an alienating experience for (palliative care) patients (Cassell 1991; Frank 2001). When patients are suffering, their wounded body or mind preoccupies them, hindering subjectivity, intentionality, and involvement in everyday life (Charmaz 1983; Van Hooft 2003). Healthcare professionals only have limited practical tools to heal these wounds and are often confronted with patients who continue to be socially and aesthetically out of sync with healthy others around them, as well as with their own previous lives (Frank 2001). Those who suffer as a result of life-threatening illnesses often no longer have the "enchantment of a future," (Cassell 1991) and they have often also lost what "they valued and enjoyed in the past" (Charmaz 1983).

2.1 Introducing the Perspective of Levinas

Healthcare professionals get acquainted with a patient's suffering through what Levinas refers to as the *Face* (Box 1).

Box 1
Why the ideas of Emmanuel Levinas (France, 1906–1995) are relevant to current medical practice?

- Levinas' life's work concerned hospitality, intersubjectivity, and lived immediacy.
- Levinas has written on what precedes (medical) ethics, about the responsibility to our patients before we even begin to think about it.
- Levinas offers a unique phenomenological description of the intersubjective relation between, for example, a patient and a healthcare professional before they start trying to categorize one another in work and words.
- Levinas challenges us to become aware that every conversation, every type of communication always demands a response: a responding to another. The patient who is in the immediacy of healthcare professionals already summons these professionals, even before a de facto command is uttered.
- Levinas' work about the face-to-face encounter, which is essential in patient-professional communication, forms a solid base to think over the mediation of patient-professional communication by modern communication technologies.

Levinas' Face can be understood as all those elements of a suffering being that express a pre-reflexive, ethical, demanding appeal: crying, bodily gestures, becoming rigid, the skin, et cetera (Burggraeve 1986). The capital "F" emphasizes the pureness of the suffering – its nakedness as a consequence of an extreme vulnerability – that appeals to other human beings through its uncoveredness and finitude. A patient's Face is disruptive; it commands humility while not representing something else but itself (Peperzak 1991; Levinas 1996, 2005).

The Face communicates suffering as an intangible and untranslatable part of the human being. It defines the patient as an Other, as one who is appealing beyond the reach of common comprehension and rational analysis (Pinchevsky 2005). Healthcare professionals may experience standing face-to-face with their suffering patients: a patient's suffering urges healthcare professionals to surpass their professional ability to appropriate and objectify the patient and his/her suffering in words (medical diagnosis) and work (treatment) (Levinas 2011). The Face commands caregivers to openly and unconditionally engage *with* the patient, to greet and "welcome" the patient as a fellow human being before anything else can be communicated or done.

2.2 "Welcoming" a Patient: Proximity in Technology-Mediated Communication

A patient's suffering forces healthcare professionals to maintain the wondrous orientation, the welcoming, that precedes all (communicative) action. It offers the opportunity to open up to the patient without knowing for sure how he/she will be able to be involved in actual communication and further action (Levinas 2011). Such a humble communicative stance precedes any procedural frameworks of physician competences and activities. It implies an awareness of the "communicating of communication," wherein previous images and concepts are still irrelevant and patients are unconditionally welcomed. For the patient, such an original and silent invitation of the healthcare professional creates a way out of the isolation into which the suffering has forced him. A humble attitude enables proximity and, figuratively, an engaged wandering in patients' stories that will redefine the healthcare professional's personal, medical role. This being said, how could this idea about welcoming a suffering human being be related to teleconsultation technologies? These Internet-based communication technologies, at least, call into question (a) the appearance of suffering (the Face) within these communication technologies, (b) the pre-communicative orientation toward a suffering patient, and (c) proximity.

2.3 The Need for Empirical-Ethical Research

The innovative application of teleconsultation to the practice of palliative homecare should be considered "a complex practice still under construction" (Pols 2012). A long-term, naturalistic approach is considered essential to study such complex practices still under construction in which patients, informal caregivers, and healthcare professionals continuously try to reshape and refine teleconsultation in palliative care at home. A qualitative, naturalistic approach helps to uncover the interactional patterns, participants' continuous adaptations to teleconsultation, as well as unanticipated results. The knowledge resulting from a long-term and naturalistic investigation could determine how teleconsultation changed the existing palliative homecare, if at all (Corbin and Strauss 2008; Pols 2012). Teleconsultations can be considered crossings where various perspectives and actions meet, bringing about new perspectives and actions in the home of patients, in the primary care practice, and in the hospital (Ihde 1990). Such an approach implies the use of several qualitative methods, such as observations, interviews, and group interviews, to follow participants over time to learn about their experiences, stories, and practical knowledge (Pols 2012). Analyses should then lead to a conceptual understanding of the practice of teleconsultation in palliative homecare based on participant perspectives and experiences, which would enable discussions and negotiations between different professionals (Charmaz 2009).

Don Ihde's *postphenomenology* functions as a conceptual base for empirical research on teleconsultation in palliative care. The postphenomenological approach indicates, in line with pragmatism, that people continuously interact with their physical and social environment (Ihde 2009). By adding teleconsultation to the environments of patients, family caregivers, and healthcare professionals, participants' interactions

with both these environments and the persons being engaged in them are likely to change. How teleconsultation technology is presented to its participants is highly dependent on how the technology "fits" into daily practice: will the technology magnify its users' worlds without being too noticeable? Will physicians, for example, be able to assess a patient's physical status without being too restrained by the use of real-time, audiovisual communication technologies? The question of fit is not solely restricted to these particular embodiment relations, but extends itself to the question of the "fit" of the teleconsultation technology within existing and historically emerged care practices. Ihde and others propose a "concrete empirical study of technologies in the plural," just like this study of teleconsultation technologies (Ihde 2009; Pols 2012). How does teleconsultation technology, in the course of a palliative care process, appear in and impact relationships between home-based palliative care patients and healthcare professional(s), between different professionals embedded in different care cultures, and between all participants and their personal and/or professional environments?

Central to both postphenomenology and the applied ethics of technology is Ihde's notion that technology is "non-neutral." Technology changes our perceptions of the surrounding world, thereby forcing people, however subtle, to think and act differently. Technologies mediate human (inter)actions (Ihde 1990; Swierstra and Waelbers 2012). Teleconsultation technologies redefine the original situation (e.g., all of a sudden, a hospital-based healthcare professional is virtually present in the living room of a seriously ill patient) and mediate the practical options (e.g., a distance diagnosis is made easier due to the addition of vision, but a private room to make these diagnoses is no longer available). Such a magnification/reduction scheme that is inherent to a technology calls for ethical reflection: if one knows how technology mediates the situation and the practical options, what then "ought to be done"? This question gains relevance when it is translated to questions on stakeholders, on consequences, and on considerations of the good life.

Research projects on telehealth solutions in palliative care practices should be designed to explore and describe the normative issues that arise with telehealth in the practice of palliative care, to reflect on them with "common moral vocabularies," and to study how these issues are resolved in practice. The normative issues and their practical solutions need to be critically evaluated in order to control the normative power of the factual. This chapter will further focus on what teleconsultation in palliative care means to the caring relationships between a suffering patient and healthcare professionals, which are considered to be at the heart of palliative care. In addition, a description and analysis of normative issues as a consequence of teleconsultation-induced changes in interprofessional relationships will be given.

3 Context to the Research Project on Teleconsultation

A cross-national study on preferred place of death in Europe shows that "at least two thirds of people prefer a home death in all but one country studied [Portugal]" when confronted with advanced cancer (Gomes et al. 2012). Deaths occurring at home, however, are not common practice in Europe (Cohen et al. 2010) and vary largely based on country-specific cultural, social, and healthcare factors. One can thus conclude that a considerable amount of patients with advanced cancer do not and/or cannot realize their wish to die at home. Moreover, the chances of dying at home steadily decrease for chronically ill patients from the age of 70 years and beyond (Van der Velden et al. 2009).

Let us start with the presumption that access to expert palliative care supports home-based patients in receiving high-quality palliative care and also, therefore, in dying at home. In the Dutch case, primary care physicians, the professionals responsible for palliative care at home, report having mainly general knowledge of treatment options but limited knowledge and competencies (through lack of education and experience) with respect to applying specific medical-technical

treatments required for complex palliative care (Groot et al. 2007). Such data imply that primary care in general would benefit from some form of specialized support and/or education to provide adequate palliative care to patients suffering from complex problems. Therefore specific collaborations between primary care and expert palliative care, in which treatment and care are continuously attuned to the individual patient's problems and needs, have to be explored.

3.1 Early Steps in the Generalist and Specialist Palliative Care Integration Process

Home-based palliative care patients are ideally adequately cared for by their primary care physicians. However, patients who suffer from complex problems require more integrated generalist and expert palliative care at home (Quill and Abernethy 2013; Den Herder-van der Eerden et al. 2017). The integration of different professional palliative care services in Europe is still in an incipient stage (Wright et al. 2014; Den Herder-van der Eerden et al. 2018).

Still being an inceptive form of interprofessional integration, "primary care physicians-expert palliative care" consultations already showed some essential barriers to a far-reaching integration of services. Primary care physicians, for example, mostly consult expert palliative care services at their patients' (very) end of life, thereby strongly focusing on medical-technical aspects (Desmedt and Michel 2002; Abarshi et al. 2011). Interprofessional consultations do not automatically evoke an early integration of multidimensional palliative care at home. Despite this narrow use of interprofessional consultation, different collaboration initiatives positively impacted patient outcomes such as dyspnea and sleep, anxiety, and spiritual problems and needs (Marshall et al. 2008; Rabow et al. 2004), while also improving advance care planning and reducing urgent care visits. The collaborations examined, however, were less favorable to extensive information sharing, joint decision-making, and interdisciplinary teamwork in a homecare culture. Apart from some promising results, current consultations (usually by phone) demonstrate shortcomings. Therefore, new services and technologies are needed that support continuous care and sharing responsibilities (professional integration), while at the same time guaranteeing a patient and informal caregiver focused perspective (clinical integration) (Valentijn et al. 2013).

3.2 Patient and Informal Caregiver Participation in Integrated Palliative Care?

Palliative (home)care asks caregivers to be open to various contexts and care practices and to different patient values and experiences in order to guarantee a patient-centered, flexible palliative care process. This care is about being attentive to the individual patient and to give room to the patient as a person and as an agent (Randall and Downie 2006). Most patients would like to have a relationship with their doctors and nurses that provides them with the opportunity to decide on treatment and care in line with personal goals and values. Integration in palliative (home)care, from a patient perspective, means being able to work flexibly with a "pool of professionals" (Randall and Downie 1999) who are all well-informed, mutually attuned, and focused on common aims but have different ways and expertise to solve a variety of problems.

3.3 Innovative Use of Synchronous, Audiovisual Teleconsultation to Align Home-Based Patients' Interests with Generalist and Expert Palliative Care

As shown by the paragraphs above, the integration of generalist and expert palliative care to serve home-based patients is mainly based on communication. Inspired, among others, by the Michigan telehospice project (Whitten et al. 2004) and Canadian research on telehomecare supporting hospital-home transitions of severely ill children (Young et al. 2006), the Radboud

University Medical Center developed and researched an innovative integrated palliative care service, centered around synchronous audio-visual teleconsultations between home-based palliative care patients, primary care physicians, and a hospital-based specialist palliative care team. Those earlier projects showed that patients appreciated the direct contact with the hospice or healthcare organization, especially when they were living in rural areas. Telehospice proved to reassure patients and family caregivers, to enable physical and pain assessment, and to provide information and support (Whitten et al. 2004). The study of Gagnon et al. (2006) showed that, as a consequence of telehomecare, intensified relationships between patients and homecare nurses came about. Continuity and closer follow-up care were believed to contribute to a better quality of care, with healthcare professionals experiencing an improved trust in relationships with colleagues. Patients did not consider the lack of physical presence to be a major issue. However, part of the healthcare professionals did experience a loss of the "personal touch and hands-on care tailored for each individual" (Whitten et al. 2005). This loss of physical presence combined with a diminished flexibility of the working agenda and doubts about the perceived convenience for vulnerable patients led providers to reject telehospice more often, compared to patients.

3.4 The Nijmegen Palliative Care Teleconsultation Service and Its Devices

The Dutch Radboud UMC is a university medical center serving a big area in which approximately two million people reside. In contrast with the Northern American projects, the aim of the teleconsultation service central to the Radboud University Medical Center research project was to include both interprofessional communication ("telemedicine") and patient-professional communication ("telecare") (Pols 2012) in order to create a high-quality, interdisciplinary palliative care service that would include patients. This teleconsultation service aimed to digitally connect home-based patients, their primary care physicians, and a hospital-based specialist palliative care team (Fig. 1). During the research period, the teleconsultation technology was employed for (bi-)weekly videoconferencing interactions between a hospital-based specialist palliative care team and palliative care patients living at home. Primary care physicians were invited to attend the teleconsultations at the patient's home so as to construct the triangular consultation between patient, primary care physician, and specialist palliative care team. Easy to use software that adequately supported *digital* triangular consultations at reasonable costs was unfortunately not available at the start of the study. In the Netherlands, approximately 95% of the households have access to the Internet, making it a fruitful environment for telecare and interprofessional teleconsultation. At the start of this project's implementation process in 2010, just under 60% of the Dutch people aged between 65 and 75 used the Internet, compared to 75% in 2012. In 2012, the generation that will most often require palliative care in the foreseeable future, those between the ages of 50 and 65, used the Internet. Due to technological progress during our research project, two teleconsultation devices were subsequently utilized in this study: (1) a simplified desktop computer called a "Bidibox" and (2) an iPad2. Encryption of the digital teleconsultations guaranteed the privacy of health information.

4 How Teleconsultation Fits Palliative Care at Home: The Relationship Between Patient and Professional

The following paragraphs will show teleconsultation technologies' "multistability" (Ihde 1990): the technologies present themselves in different forms and functions in the palliative care practice, and they mediate different relationships. In these paragraphs the focus is on the relationship (a) between patient and professional and (b) between research participants – patients, informal carers, and healthcare professionals – and their

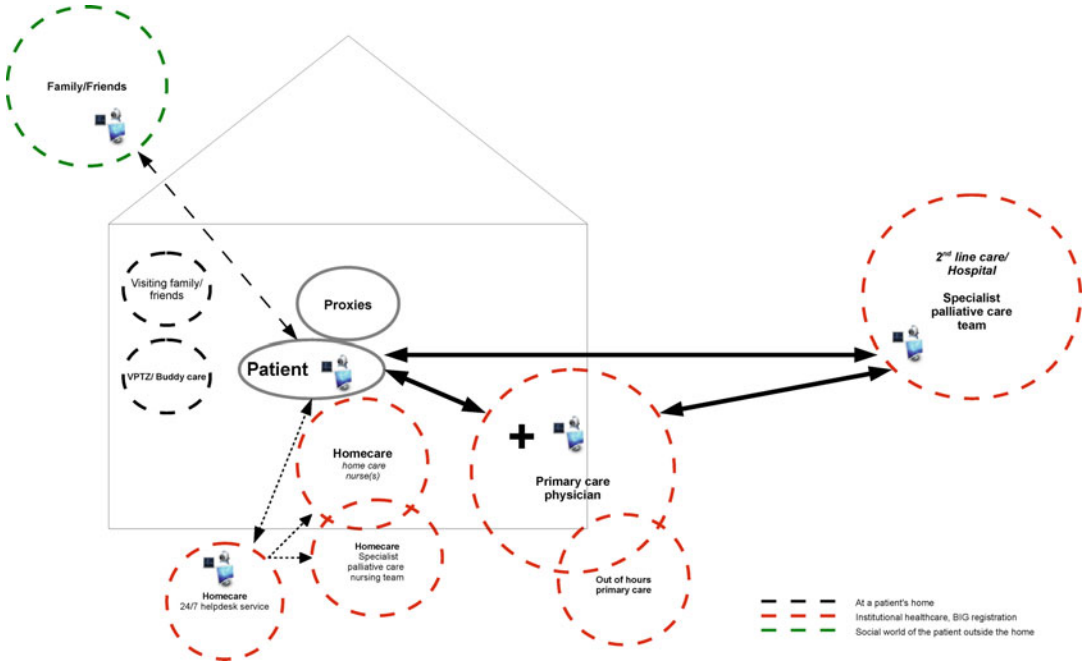

Fig. 1 A Dutch home-based palliative care patient is usually supported by her proxies, her primary care physician, and various homecare nurses. Teleconsultation offers possibilities to digitally connect the patient with a specialist palliative care team, primary care physician, the homecare help desk, and relatives living further away. A triangular connection also seems possible

practical environments, i.e., home and hospital. The full results of the empirical-ethical study with 18 home-based palliative care patients (16 suffering from cancer, 2 from COPD; age range 24–85 years old), their family/friends, 12 hospital-based specialist palliative care team clinicians, and 17 primary care physicians are published elsewhere (Van Gurp et al. 2015, 2016). Central to this study were serial observations of teleconsultations in home and hospital contexts, as well as serial interviews with everyone involved (patients, family members, palliative care specialists, and primary care physicians).

4.1 Physical Proximity and Diagnosis

Palliative care professionals, and healthcare professionals in general, consider face-to-face communication and physical proximity with their vulnerable and dying patients prerequisites for good clinical practice. These clinical contacts usually lead to an adequate clinical touch and solid clinical knowledge. In this study, the palliative care specialists' need for clinical contact resulted in a strong demand to see the patient in the hospital at least once before teleconsultation could start. In practice, however, these first, physical visits did not always take place, a fact that turned out not to hinder the development of long-term and meaningful digital relationships with patients and their primary care physicians. Without wanting to disregard the value of clinical contacts with patients, the research shows on more occasions that physical proximity between healthcare professionals and patients is not always necessary, and sometimes even undesirable, to address many forms of patients' suffering.

> Specialist palliative care team nurse 1: "[right after a teleconsultation] sigh… that was intense [and cries]. You just notice that you're far away […]. This man will deteriorate rapidly from now on […]. I would really prefer to sit next to him now. A bit more personal. However, that's how it is."

> Patient 1: "I cried during the conversation. [I: Yes, and afterwards. . .] I'm calm again. Relieved too [. . .] You just have the opportunity to pour your heart out."

With respect to monitoring a patient's physical state, the professionals' need for physical proximity appears justified most of the time. Teleconsultation technologies (a combination of hardware, software, and the Internet) not only exclude sensory information such as smell and touch, but the technologies' information encoding-decoding schemes are so opaque that palliative care professionals cannot be certain of the accuracy of the translation of a patient's color and physical details into an image. Instead, professionals can only rely on the general information that these images provide, such as physical progression or regression and the most prominent nonverbal cues. During teleconsultations, this less detailed information can still be used in an extensive clinical reasoning process wherein the visual is but one source of information for clinical reasoning. An extensive clinical reasoning process also includes stories of patients, observations, and accounts of informal caregivers and primary care physicians. To gather these pieces of information from other (non-)professionals, to qualify them, and to relate them to other stories requires palliative care expertise and advanced interviewing skills. Palliative care specialists need to learn how to incorporate teleconsultation's images in their clinical reasoning in order to draw reliable conclusions.

> Specialist palliative care team clinician 4: "And the image, it's additional and supportive. You see someone's status [. . .], which makes the picture complete."

4.2 Patient-Centered Care by Means of Teleconsultation

The lack of physical proximity caused by teleconsultation did not hamper patient-centered care and knowing the patient as a person per se (in contrast to Demiris et al. 2006). For patients, a teleconsultation meant that they did not have to make a sometimes burdensome journey to their palliative care specialists. In addition, being at home and not in a hospital also left patients feeling less of an ill and/or dying person, as well as feeling more in control of treatment, care, and conversation. The physical distance caused by teleconsultation technology can contribute to patients experiencing more autonomy, as they are less hindered by the physical presence of a hospital and/or healthcare professionals. To allow patients to remain at home as long as possible, palliative care specialists can use teleconsultation to build trusting relationships with the patient and his/her social system, as well as with their primary care physician. Teleconsultation offers palliative care specialists an opportunity to build and commit to long-term relationships with patients who reside at home. With continuous digital care and/or contact, professionals can prevent patients from experiencing abandonment in the last phase of life.

> Informal caregiver: ". . . at that moment, she was no longer capable of going to the hospital. And contact with the specialist palliative care team, through the video screen, came in handy then. Because if she had to go to the hospital every time, she would have been just too tired for that."

4.3 Virtual Proximity Counterbalances Rationalization

A common response to the use of technologies in the medical domain (such as Internet-based communication technologies) is that of a fear for "cold care" (Bauer 2001; Pols 2012). Especially in palliative care, intensive use of technology is often associated with dehumanization and rationalization, turning the suffering patient into an object and medicalizing the intimate sphere of dying (Randall and Downie 2006). Research, however, shows that although Internet-based communication technologies sometimes dehumanize or rationalize parts of palliative care, they can also enable empathic care and intimate relationships at a distance. Teleconsultation technologies supply intimate views of patients' daily lives, offer room for

personal stories, and provide contact with important informal caregivers.

Teleconsultation technologies proved to center their users' attention, thereby fostering a hyper-focus on the conversation partner's face. In addition to Pols' observations of "topologically reversed telepresence," where participants experience visiting one another in the physical space of the other (e.g., the experience of "sharing a cup of coffee" at the patient's home/in the hospital), this study recorded moments of actual telepresence, the shared experience of meeting one another in a virtual space, during discussions of intimate topics related to illness and dying (Savenstedt and Knudsen in Pols 2011). This actual telepresence is characterized by a physical orientation toward the other (e.g., bending over to the screen; "serious" facial expressions) as well as becoming totally absorbed in the virtual encounter. Virtual proximity is simply about two faces and two minds directed toward each other via the screen.

4.4 Teleconsultation Penetrating into the Daily Lives of Patients

The value of the different devices utilized for this study in the daily life of patients is best illustrated with two observations: (1) the large and immobile desktop device that was first used in this study was too visually dominant. It was usually installed in the living room. The devices were often placed close to the patients' beds or places of comfort due to the limited mobility of both patients and devices. The device remained constantly in sight, reminding the patient and informal caregivers of their inability to get rid of the device when desired, their precarious situations, as well as the approaching death of the patient. Some could not stand the sight of the devices anymore and handed them back. This observation came closest to the presumption that "medical" technology intrudes into and disrupts the home as a peaceful place (Sandman 2005).

> Patient: "[a teleconsultation device] is not something you have at home when you're in full glory... It reminds you of going toward an ending."

(2) The tablet computers were better suited to the patients. Tablet computers could be easily taken up and put away when needed. They functioned as handheld portals to a different world where patients could find medical expertise, attention, and comfort. One patient even called his tablet computer affectionately "his little painting," a strong reference to the characteristic of a two-dimensional painting that evokes different and distant worlds. Tablet computers fitted well into the daily, often impaired, lives of the patients. Interestingly however, the use of tablet computers in the hospital practice paved the way for privacy infringement, as these mobile devices were more often used in public rooms and in between other activities.

5 How Teleconsultation Fits Palliative Care at Home: The Mediation of Professional Relationships

During our research, two teleconsultation models emerged. In the first model of teleconsultation-induced team care, which occurred most frequently during our study, palliative care specialists and primary care physicians decided to work as a multidisciplinary team. This means that both primary care physicians and specialists engage in private conversations with the patient. The latter engages with the patient by means of teleconsultation technology, and the former usually by physically visiting the patient. In addition, the palliative care specialists and the primary care physicians use interprofessional backstage conversations to share their insights about the patient and attune treatment and care.

This form of collaboration strongly requires standardization of backstage communication in order to prevent the occurrence of ambiguous and/or parallel care and medical treatment (Gardiner et al. 2012). This backstage communication relies on the commitment and discipline of all professionals involved to promptly and accurately inform one another when the patient's situation changes. Furthermore, multidisciplinary teams require prudence from all members in order

to appear to the patient as a complementary team with an attuned perspective and treatment plan. In multidisciplinary team care, there is less room for primary care physicians to work solo. Specialist palliative care teams also have to exercise restraint in their teleconsultation approach to the patient in order to sustain a central coordinating position of the primary care physician in homecare. One of the most striking examples of such a competence is primary care physicians providing hands-on end-of-life care for patients at home. A pitfall of multidisciplinary team care, with and without teleconsultation, is for professionals to communicate with one another via the patient. In the research, this occasionally resulted in patients feeling insecure, being confronted with opposing care perspectives.

If team members can maintain a prudent attitude, teleconsultation can lead to a long-term "personal liaison" between the healthcare professionals involved. Such liaisons will result in a sharing of the burden of the palliative care provision at home, mutual understanding of each others' professional practices, profound and patient-centered decision-making and advance care planning, and finally mutual trust.

In the second teleconsultation model, a real-time tripartite, and therefore interdisciplinary consultation, is organized. This collaboration model occurred in our research in only one instance. As the teleconsultation technology used only allowed for high-quality *bilateral* videoconferencing by connecting no more than two locations, one healthcare provider had to be prepared to travel to join the patient (or the other professionals) in order to set up interdisciplinary treatment and care conversations. Most primary care physicians mentioned that difficulties in attuning the different professional agendas were the main reason for not being able to engage in this type of interdisciplinary care (Gardiner et al. 2012).

In *tripartite* teleconsultations the negotiation of responsibilities between professionals became more obvious due to the instant reciprocity between patient, primary care physician, and specialist palliative care team clinician(s). This reciprocity demands a modest and open attitude from professionals: they need to have the ability to deal with criticisms and comments in front of the patient as well as an open mind to new perspectives (Esterle and Mathieu-Fritz 2013). Tripartite teleconsultation requires relinquishing personal control over communication, planning, treatment, and care. Interdisciplinary dialogues make medical-technical jargon inappropriate, as not every conversation partner will be able to understand it. Instead, professionals need to find a common language with an appropriate level of complexity in tripartite teleconsultations.

5.1 Teleconsultation in Palliative Care at Home Requires Careful Use of Technology

Instead of dehumanizing and rationalizing the intimate sphere of suffering and dying, as is suggested by the literature (Seymour 1999; Randall and Downie 2006), recurring teleconsultations by means of synchronous audiovisual contact showed the potential to install a valuable patient-professional ritual in which the mutually focused gaze and mutual chatter can form the prelude to a proximity in which the suffering patient appears as a Face: an original, provoking Other that demands responsiveness. In their response, healthcare professionals have to surpass the usual, medical-technical imperative ordering: the wondrous orientation on the suffering human being can only be revived when the healthcare professional is prepared to offer a digital welcome to home-based patients. Thus, palliative care specialists do not have to fear losing their ability to "touch upon a patient's personality" in teleconsultation. They rather have to fear their own inability to adopt a humble attitude that facilitates an open space in which the patient can appear (DasGupta 2008). Palliative care specialists' reluctance to discuss sensitive topics in teleconsultation due to an experienced lack of control about what happens on the other side easily closes the door to virtual proximity.

During the teleconversation, the tablet computer used for the teleconsultations is held at arm's length, thereby shaping and showing a rather detailed portrait of the other person. The

tablet computer magnifies (the importance of) the human face and, as a consequence, can stimulate an intense hyper-focus toward this face. This technology-led orientation allows the suffering patient to emerge as someone who asks his/her healthcare professionals to leave the realm of medical discourse, in which the patient is easily transformed into a "distinctive manifestation." However, the occurrence of such an open and welcoming orientation is not obvious, as the technology's ambivalent nature equally enables the reduction of another's face into a smaller, two-dimensional *object* that can be placed next to other objects in the physical viewing environment (Pols 2012). Professionals therefore have to make a conscious effort to avoid the objectification of the patient.

Easing the suffering of a patient does not require physical proximity per se: the distance created by technology can also support an openness with new dimensions. The original thinking of Levinas that proximity is independent from space seems to be reflected in some of the results from our qualitative study. The virtual proximity observed in this teleconsultation study, however, implies two problematic situations.

First, moments of virtual proximity usually ended in moments of silence, but teleconsultation technologies' scripts continuously invite participants to verbally interact with one another (Akrich 1992; Verbeek 2006). In other words, the hyper-focus demanded by audiovisual communication technologies requires participants to speak as soon as the image of one's conversation partner appears. Underlying the technology-instilled chatter, however, remains what Levinas calls Saying (Levinas 2011): an inclination toward a mutual, open orientation between interactants in which one may suddenly touch upon the ineffable presence of suffering. In our empirical study, we captured the story of an apparently superficial teleconversation starting with a healthcare professional asking a simple opening question "How are you doing today?" The ensuing talk gradually transformed into a conversation about the existential topic of an approaching death. The early conversation already seemed to contain an implicit, joint wandering (the Saying) that slowly but surely laid the foundation for a proximity wherein the patient eventually felt free enough to approach the healthcare professional with his deepest thoughts about not having much time left and the intense sorrow that accompanied these thoughts. Technology supports patients in creating their stories as a bricolage (Ihde 1990; Radley 2004): patients can use their facial and some of their bodily expressions, their physical positions, and their words to communicate a composed personal aesthetic (Chouliaraki 2006). Patients use these technologized aesthetics mostly for downplaying their suffering. They put on a brave face and avoid giving free reign to their inner feelings. However, the Saying within such aesthetic chatter can create moments in which the aesthetic façade is taken off and the patient shows her-/himself at her/his most vulnerable. However, such intense communicative moments are accompanied by the conversation partners falling silent, as there is nothing left to say. Interestingly, these silences did *not* fit with the technology's continuous invitation for hyper-focus and chatter. The silence feels awkward and out of place, whereas sitting with someone in silence is considered essential in the approach of suffering human beings (Randall and Downie 1999). In this study, participants did not yet find appropriate ways to insert moments of silence in teleconsultations. Instead, long silences led to conversation partners ending the teleconsultations.

Second, the digital hyper-focus and virtual proximity are vulnerable to disturbing elements from the home or the hospital that pierce their fragile exclusiveness. Intrusions of unannounced others – nurses, colleague physicians, or informal caregivers – bring about immediate disruptions of exclusive conversations. As a consequence of these disruptions, conversation partners feel caught, their intimacy betrayed, and their privacy infringed. The intimate connectedness that is needed to converse truthfully about a patient's situation, hope, and/or suffering does not allow for the presence of unknown others.

The empirical study also exposed healthcare professionals' (natural) inclination to act upon patient suffering. Observations showed that *after* teleconsultations, notwithstanding the discussion

of private and/or emotional topics, patients usually expressed a feeling of relief and/or gratitude and a desire to continue with their daily lives. In contrast, the observed healthcare professionals were regularly left with a strong desire to be physically close to their suffering and vulnerable patients after such consultations. This desire for physical closeness does not only stem from a need to reinforce proximity through a comforting touch or a caress but also from a need to regain valuable senses such as smell and touch with which healthcare professionals attempt to master their patients' suffering. This strong desire to work on the patient's suffering, however, is hampered by technology. In this way, the technology seems to be able to guard the privacy of the home against the inclination of healthcare professionals to physically control patients and their contexts. By possibly making the physical presence of healthcare professionals superfluous, teleconsultation technology breaks open the traditional, asymmetric relationship between professional and patient. Interestingly, proximity, which Levinas already thought of as being independent from space, is now maintained by the distance created by the technology: palliative care teleconsultations show that physical presence and face-to-face communication are not prerequisites per se for proximity and meaningful communication.

6 Conclusion

Through Internet-based communication technologies that provide synchronous audiovisual contact, healthcare professionals can offer their patients short moments of reconnection with a social albeit medical world that, if professionals display open and attentive communication, can be receptive to their patients' suffering. However, this chapter also shows that teleconsultation technology is in itself non-neutral and has to be used carefully by professionals in order to contain the rationalizing and dehumanizing scripts that are also present in these technologies. What follows are some concluding statements accompanied by suggestions for careful use:

1. Communication technologies supporting synchronous audiovisual communication tempt healthcare professionals to make the visual element dominant in teleconsultations. During teleconsultations, however, the visual should always be compared with the medical history and stories/information provided by proxies and primary care physicians in an extensive clinical reasoning process, so as to triangulate information and come to reliable conclusions. In this way, technology's limited transparency and opaque encoding-decoding schemes can be overcome.
   1a. Palliative care specialists should learn about how the teleconsultation technology encodes and decodes visual information. In other words, they have to learn about the quality of the images as well as about the appropriate probing questions for checking the images. Expert palliative care teleconsultations thus require (a) excellent interviewing skills with which they can, via *teleconsultation, elicit truthful stories from patients and proxies, (b) professionals capable of interacting with people on different levels and different topics (patients, proxies, physicians), and (c) professionals capable of "connecting the dots" between all these information to gain credible clinical knowledge.*
2. Teleconsultation technology enables continuous and long-term commitment to a patient, regardless of physical distance. Teleconsultation thereby neutralizes a patient's fear of abandonment. Patients experience a sense of relief and safety, knowing that expert palliative care is available at home and believing that this will prevent distressing hospital visits to occur due to the combination of generalist and specialist palliative care.
   2a. Palliative care patients can find comfort and relief in staying at home, where they feel less of a dying person and more in control with respect to their own care. With this in mind, teleconsultation should be offered to (a) patients who require a gradual transfer from high-technological care settings to the home and who will suffer from feelings of

abandonment as a result of these transfers, (b) patients who desire to maintain their personal autonomy and control, and (c) patients at home who are in need of specialist palliative care treatment and support.

3. Patients do not necessarily experience a sense of medicalization of the home with teleconsultation. In fact, they may experience more comfort and autonomy in their homes, which will help them to better express themselves and to feel more in control with respect to decisions on treatment and care. The physical distance created by teleconsultation can contribute to the experience of autonomy as it complicates physical apprehension by healthcare professionals and/or healthcare settings.
   3a. In order to prevent patients from being constantly reminded of a medical system that monitors their last phase of life, the devices used for teleconsultation in palliative care settings should be as "transparent" as possible. They have to be mobile (WiFi) and light. Moreover, they have to blend in with the households in order not to become a continuous reminder of an approaching death.
4. If well applied, teleconsultation can foster a hyper-focus on the conversation partner that induces the acknowledgment of the patient as an original human being and true contact.
5. Teleconsultation technology invites conversation partners to involve in chatter, which can serve as a breeding ground for creating *virtual* proximity with the patient as a person.
6. Both the hyper-focus and the small talk bear implicit elements of being oriented toward the patient as an Other person and as such are preludes to moments of intimate yet technology-mediated contact in which truthful dialogues can come about.
7. Such intimate, humane contact through teleconsultation gives room for the suffering of a patient to appear, but appropriate endings for these intimate contacts on suffering have not yet been found: it appears difficult to sit with a patient in silence as the teleconsultation technologies continuously invite participants to verbally interact.
   7a. As patients (and proxies) experience feelings of intimacy and relief as a consequence of virtual proximity, palliative care specialists should adapt a humble and open attitude so as to establish the virtual proximity in which the patient can fully appear as another person. Through an open orientation and closely listening to the patient, palliative care specialists "welcome" the patients and their stories. The innocent small talk has to be cherished as, especially in teleconsultation, one reaches virtual proximity only through sharing of and building on stories.
   The disruption of the fragile virtual proximity by the intrusion of unannounced others led to patients experiencing being looked at, betrayed, and deprived of their privacy. To prevent such experiences from occurring, private teleconsultation rooms should be used.
8. Patients desire to be able to flexibly work with a "pool of professionals" (Randall and Downie 1999) who nevertheless appear as a cohesive team with a shared perspective on treatment and support. Interprofessional collaborations as a consequence of teleconsultation are, therefore, best supported by a modest and prudent attitude of the practitioners. Professionals should explore each other's strengths and weaknesses and deploy this knowledge for the provision of maximum complimentary team care.
   8a. Long-term engagement of palliative care specialists by means of teleconsultation results in solid knowledge of the patient's situation and an interprofessional trust based on thorough knowledge of palliative care specialists' and primary care physicians' medical practices.
9. Professionals should make a deliberate choice between working from a multidisciplinary and interdisciplinary team care perspective. With multidisciplinary team care, professionals should commit to and invest in intensive backstage communication to make this kind of team care work. With interdisciplinary team care, professionals and patients should work on a form of communication

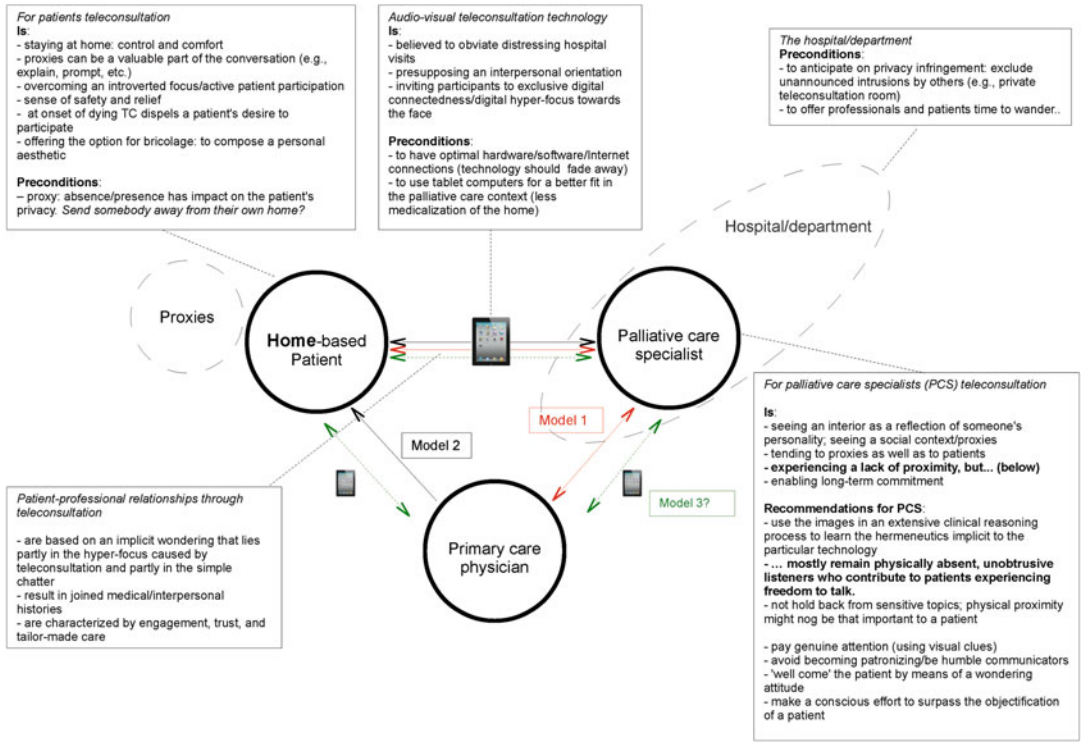

Fig. 2 Transmural palliative care by means of teleconsultation

in which all participants, but especially the patient, feel free to express their thoughts.

9a. Teleconsultation in a palliative homecare setting requires an active and continuous tuning and division of responsibilities. In multidisciplinary team collaborations, professional freedom seems more guaranteed. In contrast, in tripartite, interdisciplinary team collaborations, the direct digital contact between patient, primary care physician, and palliative care specialists results in a more concentrated responsiveness and mutual control.

10. Multidisciplinary and interdisciplinary team care both require backstage work. For that reason, standardization of and technological support (e.g., sharing patient files, opportunities for e-mail) for this backstage work are required. Solid backstage work is a high priority as it prevents patients from getting caught between two or more different perspectives on their treatment and care.
11. Especially interdisciplinary care requires strict agenda management to bring professionals, proxies, and the patient together at the same time.

In Fig. 2 this study's most important findings have been translated into an informative map.

Disclaimer This chapter is an adaptation of three unpublished chapters from the PhD dissertation "Teleconsultation: enhancing personalized palliative care at home. An empirical-ethical analysis." A PDF of this PhD dissertation is hosted at the Radboud Repository of the Radboud University Nijmegen.

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Request for Assisted Suicide

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Rachel E. Diamond, Puneeta Khurana, and Timothy E. Quill

Contents

Abstract

Physician-assisted dying (PAD) is receiving increasing media and academic attention, and legalization is expanding internationally. The potential legitimization of this practice is laden with medical, legal, and ethical considerations. Regardless of legality or willingness to participate, clinicians must be able to respond to enquiries about this topic, whether the patient's aim is information gathering or a formal request to end his or her life.

1 Introduction

The goal of this chapter is to use a real clinical case to outline the process by which clinicians might counsel a patient requesting help to end his or her life. This includes the process by which to assess the clinical context of the request, as well as the associated legal and ethical considerations.

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_90

Case Presentation: Over the past year, you have been in conversation with a patient with a brain tumor about what options he might have if he develops severe intractable headaches or if he begins to lose capacity to make his own decisions. He was particularly afraid of being "out of his mind" at the very end, a condition he felt would be "worse than death." He had read about Brittany Maynard and wondered if this option might be open to him in New York and was disappointed that it was not. He wanted to hear about the possibilities for a controlled death that might be available either legally or illegally. He was not ready to act now, but potential situations in the future that appeared far worse than death loomed large in his imagination.

Over the last few decades, the concept of PAD has made its way into both the medical and public worldview through various academic and media outlets. Some of these stories have captured the public's imagination in compelling ways, like Brittany Maynard, and others have been more problematic and polarizing like some of Jack Kevorkian's actions (It's over, Debbie 1988; Quill 1991). All these cases seem to strike a chord in our society and raise serious discussions about possibilities and practices in our communities. At the heart of the issue lies the boundaries and options for how clinicians and society should respond to genuine human suffering and/or to the fear of future suffering, associated with a debilitating illness.

Given the increased public exposure PAD is receiving, as well as an increasing trend toward legalization in the developed world, it is important that clinicians are well versed in these issues. Although physicians are directly involved in PAD, all healthcare professionals should understand the medicolegal and ethical arguments involved. Responses should be considered in advance of receiving a request for PAD, keeping in mind whether it is legal or not in the states or countries in which the clinician practices. It is also important to know what other tools are available to practitioners, when treating seemingly intractable physical and psychological suffering in patients with a life-limiting condition.

2 Defining Terminology and Practice

2.1 Physician-Assisted Dying

PAD is defined as the process through which a physician provides the means (a lethal drug potentially taken orally by the patient him or herself) to a competent patient fitting certain criteria, at the patient's request, to end his or her life voluntarily and independently (Fins and Bacchetta 1995). This practice has been referred to as "physician-assisted suicide" mainly by opponents of the practice, but, given negative connotations of the word "suicide," "physician-assisted dying" or "physician aid-in-dying" is often preferred when discussing the issue with patients. The criteria that a patient has to meet to be considered for PAD are different around the world. In parts of the USA where the practice is legal, a patient must be terminally ill and fully capable of decision-making and of self-administration. In the USA, after the patient meets agreed criteria, which usually includes a 2-week waiting period, a physician writes a prescription for a specific drug. Most often a barbiturate is prescribed, which the patient will then obtain at a pharmacy and take at the time he or she decides is most appropriate (Quill and Battin 2017a).

2.2 Voluntary Active Euthanasia

Voluntary active euthanasia (VAE) is a practice in which a clinician both provides and then administers the means to directly cause death for a patient, who has voluntarily requested to die and otherwise meets agreed criteria (Fins and Bacchetta 1995). This is typically done with lethal drugs delivered intravenously by the patient's physician. In Belgium, the Netherlands, and Colombia, this is the preferred practice because it is more reliably effective and because it does not depend on the ability of a very sick patient to self-administer. In these countries, there is also more emphasis on the presence of intolerable suffering that is refractory to treatment, deemed unacceptable by the patient without the patient necessarily being imminently terminal (Quill and Battin 2017a).

3 Additional Alternatives to PAD

When a patient requests PAD or VAE as an option, either in the present or future, it is critically important for him or her to know alternatives that could also help alleviate suffering. A palliative care consultation should always be pursued if possible and should ideally include access to an interdisciplinary team, including but not limited to a physician, nurse and/or nurse practitioner, social worker, pharmacist, chaplain, and massage and music therapists. In addition to providing expertise on managing challenging symptoms, the palliative care consultation can provide holistic care and counseling around end of life. The goal is to understand the basis of the request for PAD or VAE and address underlying suffering as effectively as possible. Hospice services (specifically referring to the U.S. model of an insurance benefit supporting comfort-oriented care at the end of life), potentially in the setting of an acute inpatient setting if symptoms are severe, should be instituted to maximize expert symptom management and also enhance social supports. Not only might the seemingly intolerable symptoms be addressed in these circumstances, but such consultations can also be a source of support for the patient and his or her family, potentially extending into the bereavement period after the patient dies. A systematic approach to this process is outlined in Fig. 1 below and will be discussed in the following sections.

Patients should have access to more formalized psychological/psychiatric services, especially if there is a concern that the request is associated with or stemming from an underlying mental health illness such as depression. Such a step may also be built in to criteria or steps required for a formal PAD request in places where it is offered as a legal option.

3.1 Intensification of Symptom Management

The first step in addressing requests for PAD is to ensure that the request is not a direct result of inadequate symptom control. If symptoms are being inadequately addressed, it is appropriate to proportionally escalate palliative treatments. Sometimes the doctrine of double effect will come into play in the process of intensification of symptom management (Quill et al. 1997a). According to this ethical principle, effects that would normally be seen as unethical if performed intentionally are permissible as long as they are foreseen but unintended. In this situation, administering larger doses of medications to proportionately relieve intractable suffering in a terminal illness may have the unintended, but

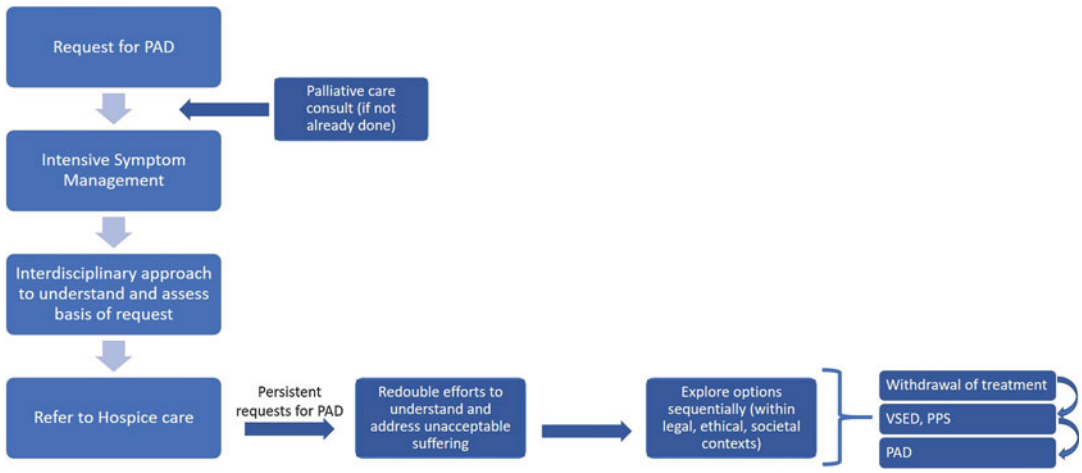

Fig. 1 Practical approach to requests for PAD

potentially foreseen effect of sedating the patient and even hastening/causing death. Because the appropriate medications are dosed strictly in *proportion* to, and with the intent to relieve the patient's *physical* suffering and not to cause death, the act is ethically permissible under this rule or principle. In the vast majority of cases, expert symptom management does not shorten life (and may sometimes even lengthen it) and certainly enhances the quality of the patient's life.

3.2 Withdrawing Life-Sustaining Therapy

In keeping with the ethical concept of personal autonomy, patients are given authority over their own bodily integrity (i.e., the patient must give informed consent to receive any medical treatment). Similarly, it is widely accepted that a patient can chose to refuse (i.e., either withhold or withdraw) any medical therapy even if the patient's intent is to die more quickly. This may include more invasive therapies such as a ventilator or dialysis or less invasive therapies such as oral diuretics, insulin for type 1 diabetes, or steroids for brain cancer. Despite the generalized legality, the motives for why a patient is choosing to make a treatment withdrawal decision at a particular point in time must still be thoroughly explored and understood.

3.3 Palliative Sedation and Voluntary Stopping Eating and Drinking

Both palliative sedation (PS) and voluntary stopping eating and drinking (VSED) are considered interventions of "last resort," meaning that they are available to patients experiencing extreme suffering at the end of life who do not respond to standard palliative treatment (Quill et al. 1997b).

Palliative sedation (PS) is defined as deliberately decreasing a patient's level of consciousness, to relieve severe and refractory symptoms that cannot be otherwise addressed despite other intensive palliative efforts (KNMG Guideline for Palliative Sedation 2009). This is generally achieved by giving medications specifically designed to reduce consciousness as a means of escaping suffering, but can also occur as an unintended side effect of symptom-targeted therapy (Quill et al. 1997b).

PS is generally considered when death is imminent from the patient's underlying disease and is administered continuously from initiation until the time of death. Proportionate palliative sedation (PPS) means that the lowest amount of sedation is used that can adequately relieve the patients suffering. If a relatively small dose of the sedating medication can relieve the adverse symptoms and still preserve some level of awareness, the dose would be held at that level. Sometimes sedation must be taken all the way to unconsciousness in progressive steps (e.g., severe agitated delirium), but this is done relatively gradually and would stop at the least level of sedation that would achieve the desired goal. On rare occasions, a patient may also be sedated all the way to unconsciousness in one step ("palliative sedation to unconsciousness" or PSU), usually for more severe, acute, catastrophic medical events (e.g., bleeding out from a carotid artery perforation from cancer) (Schildmann et al. 2015). One of the prerequisites for PSU is that the patient's death is expected to occur within a few weeks at most. While it has been suggested that PPS or PSU hastens the dying process directly or indirectly, the clinician's primary intention of this treatment is not to shorten life, but rather to relieve otherwise intractable symptoms and decrease suffering.

PS is most commonly used for refractory symptoms such as pain, dyspnea, and delirium or a combination of symptoms. The working definition of "refractory" is that existing palliative interventions cannot provide relief in an acceptable period of time. The clearest indication for PS would be to treat otherwise refractory, predominantly physical suffering, but the specifics may vary for each patient and family depending on their concepts of suffering, dignity, and symptom relief.

Another option that can be considered in cases of unacceptable suffering at end of life is

voluntary stopping eating and drinking (VSED). VSED is an action of a legally competent person, who is still physically able to eat and drink, but who voluntarily decides to completely stop eating and drinking with the primary intention to hasten death to escape unacceptable suffering (Quill and Byock 2000).

The main ethical argument in favor of supporting VSED is based on the principle of autonomy. A competent patient with a terminal illness has the legal right to decline life-sustaining measures, including forms of artificial nutrition, even if his desire is to achieve an earlier death. Choosing to stop eating and drinking can similarly be considered a waiver of life-sustaining measures to not further prolong suffering, but it differs from forgoing medical treatment (such as *artificial* hydration and nutrition) in that it involves a conscious choice to stop taking ordinary food and liquids, despite being physically able to partake (Quill et al. 1997b).

4 Putting the Request into Context

4.1 Clinical Context

In exploring the demographic data from Oregon and the Netherlands where PAD is legal, it is possible to gain some understanding of the characteristics of patients that request PAD. They are mostly of higher socioeconomic class, married, insured, and almost all Caucasian. Male to female ratio is about equal, and most are in their sixties and seventies. The most common diagnoses are cancer and ALS (Battin et al. 2007).

Regardless of legality, many patients wish to explore PAD as an option in response to real-time or fear of future physical and/or emotional suffering, as well as real or threatened loss of autonomy and dignity. If the request is to gain information and reassurance from the clinician about what options the patient might have in the future, the clinician should be honest about which "last resort" options he can, and which he cannot, support if it comes to that in the future. If the request is for consideration of PAD *right now*, the clinician has to explore what is happening with the patient at this point in time to trigger such a request. The first step should be a detailed assessment of current symptom management, including anxiety and depression, and redoubling of efforts to adequately address those symptoms. This can be done through a primary care physician or subspecialist (often oncologist) but should also include an expert in palliative care medicine if possible. If a patient is nearing the end of life, it would be appropriate to discuss the benefits of hospice care in supporting the patient and family as well as aiding in symptom management.

The most common inquiry about PAD is not reactive to immediate suffering, rather it is from the proactive planning standpoint (Quill et al. 2016). Often the motives driving the enquiry are fears of losing control of the circumstances surrounding death and perhaps wanting to die at home rather than a facility of some kind. Most patients who make such enquiries fear loss of dignity, independence, quality of life, and self-care ability (Ganzini et al. 2007). Whether living in an area where PAD is legal or not, the request deserves exploration by and understanding from the clinicians involved. In addition, regardless of the clinician's stance on directly assisting with PAD, they should reassure the patient that he or she will not be abandoned in a time of need. Physicians should discuss with patients what options are legally available in their place of residence and also which of those options the clinicians can personally support. In addition to exploring the full range of "last resort" options outlined above, this discussion should also include reviewing advance care directives and filling out a MOLST (medical order for life-sustaining treatment) or equivalent form. It is important to understand the patient's views and values via these documents and also rationalize and adjust their medications based on their current situation and goals.

Another important aspect to explore with patients is whether they might like to know what the very terminal stages of their disease may look like. This discussion would ideally begin with the patient describing the kinds of deaths they have witnessed among their own families or friends.

Knowing how such deaths might be approached by the clinician or hospice team might be very reassuring depending on the patient's main concerns (i.e., if someone that the patient knew died in severe pain, because the doctor was afraid to prescribe opioids in proper doses, the doctor can reassure them that they would be very aggressive if needed with future pain management). Sometimes this exploration may alleviate some of the patient's fears about the future; however it may also exacerbate anxieties, depending on the patient's experiences, views, and values.

As with any patient interaction, these discussions should be focused on responsiveness to the particulars of the patient and her values, as well as respect for her autonomy. Reviewing the legal status of PAD in the patient's particular jurisdiction, in conjunction with the interdisciplinary team's approach and commitment to the patient, develops a crucial, ongoing, and committed partnership to address her suffering. Both patient and physician will need to establish and voice their own goals and limits, amidst the legal milieu in which they live.

4.2 Legal Context

The legal status of PAD across the USA is varied and rapidly changing. As of April 2017, there are six states in the USA that have legalized PAD (Oregon, Vermont, Washington State, California, Colorado, and the District of Columbia) (Quill and Battin 2017b).

State	Law
Oregon	Oregon Death with Dignity Act Passed by simple majority of voters in November 1994 Law enacted in October 1997 Upheld by the U.S. Supreme Court in January 2006
Washington	Washington Death with Dignity Act Passed by Washington State voters in 2008 Came into effect March 2009
Vermont	Patient Choice and Control at End of Life Act Signed by Vermont Governor in May 2013
California	End of Life Option Act Signed in October 2015 Came into effect June 2016
Colorado	End of Life Options Act Passed by Colorado voters in November 2016 Came into effect December 2016
District of Columbia	Death with Dignity Act Signed in January 2017 Came into effect February 2017

In the state of Montana, the Supreme Court ruled that state law currently does not prohibit a physician from participating in PAD, but there is no legislation or regulatory framework guiding the process, so it is in a legal "gray zone."

Outside of the USA, there are a number of countries that have legalized PAD and/or voluntary active euthanasia (VAE): the Netherlands, Belgium, Luxembourg, Colombia, and Switzerland (Quill and Battin 2017b).

In February 2015, the Supreme Court of Canada ruled in Carter v. Canada that certain sections of the Criminal Code are unconstitutional in that they prohibit competent adults who are not terminally ill from having access to PAD and VAE (Government of Canada 2017). The ruling mandated that assisted dying should be available to all adults with a "grievous and irremediable medical condition that causes enduring suffering that is intolerable to the individual in the circumstances of his or her condition (Quill and Battin 2017b)." In June of 2016, the Canadian Parliament passed a bill to legalize and regulate assisted dying in Canada, although there has been continuing debate about the degree to which the bill limits the Supreme Court's directive. To avoid "suicide tourism," only individuals eligible for health services funded by the Canadian government can be eligible for assisted dying in Canada (Government of Canada website 2017).

The Australian state of Victoria passed a bill in November 2017 making it the first state to pass PAD legislation, since the Northern Territory's "Rights of the Terminally Ill Act (1995)" was overturned in 1997. There are certain criteria that will be put into place, such as residency in the state of Victoria for at least 12 months before a

request can be made. The bill is planned to be implemented into law in June 2019 (Victoria 2018).

As in the USA, laws around PAD and VAE are changing in the developed world, so it is important that clinicians are aware of the laws in the regions in which they are practicing.

4.3 Moral/Ethical Context

There are a number of arguments that have been made for and against the practices of PAD and VAE.

Part of the debate centers around patient autonomy. Autonomy in medicine means that a competent patient is able to make decisions for him or herself, based on adequate information and free from controlling interference from others (Varelius 2006). Proponents argue that patient autonomy dictates that they have the right to determine what kind of life is worth living, and this includes being able to choose when and how to die. Critics of this argument say that patient autonomy cannot include the ending of one's own life, because such an act would mean ending the possibility of further exercising autonomy (Fromme and Smith 2017). There are also societal factors to consider. Every individual who is living as a part of a civilized society accepts that there are limitations placed on their autonomy in order to properly function in that society. Hence in considering PAD, the autonomy of the individual should be considered alongside the effects upon the rest of the society, according to the ethical principle of justice for all.

The principles of beneficence and nonmaleficence also apply in context of PAD and VAE. If a patient is experiencing physical or psychological suffering that is not alleviated by palliative care, an assisted death may be perceived to be the only way to adequately relieve that suffering. Critics argue that eliminating the suffering by eliminating the sufferer cannot possibly be beneficial and that the number of patients that continue to experience pain and suffering, after providing adequate palliative care, is too small to justify permitting the use of PAD or VAE. They argue further that medicine cannot relieve all suffering and that society should focus in improving access to quality palliative care for a much broader group of patients who might otherwise "choose" this path.

Proponents also argue that PAD or VAE can be considered an extension of withdrawal of life-sustaining treatment, which is generally agreed to be ethically acceptable. They argue that in both cases, patients consent and accept death, the physician participates in the action that results in patient's death, and the final result of the intervention is death for the patient. Critics argue that intention plays an important role here. In withdrawal of life-sustaining treatment, the physician's intent is not to cause death, but rather to remove or avoid treatments that are futile or adversely impact quality of life. They argue that in PAD or VAE, the intent is to specifically end the patient's life, and this potentially sets it apart and cannot be ethically justified in the way withdrawal of life-sustaining treatment can. The end result of the patient dying is also not consistent between the two scenarios. There have been numerous cases, such as that of Karen Ann Quinlan, where the patient lived for an extended period of time after withdrawal of treatment. Finally, the need for life supports to sustain life restricts the practice by definition to seriously ill patients, whereas PAD and VAE could potentially achieve death for patients with no discernable illness (Fromme and Smith 2017).

5 Clinician Limitations

In situations where patients and/or families are considering PAD or VAE, there may still be barriers that exist beyond the legal context. Clinicians may have personal values that prohibit them from participating in PAD or VAE even where it is legal, and these values should be honored regardless of other circumstances. The interdisciplinary team involved with these patients should meet at the onset of care and periodically thereafter to explore such limits, debrief, and make sure everyone is "on the same page." Professional caregivers should be

encouraged to be clear about their own limitations, avoiding ambiguous or false promises about their ability to participate. Referral to another clinician who would be prepared to take over this aspect of the patient's care should be considered as early as possible, should the patient desire such a change. Before that occurs, the clinician should be honest about what kinds of assistance he or she can, or cannot, provide, always looking for some kind of common ground to satisfactorily meet the patient's needs.

It is important for the clinician to take time to evaluate possible psychosocial consequences for him or herself in participating in PAD, or any other last resort options, even in environments where the practice is legal. It can be helpful to confer with another clinician who has palliative care experience and who could provide clinical consultation as well as support. In the USA, one such service is Doc2Doc, hosted by the advocacy organization Compassion & Choices, which provides information for clinicians about numerous end-of-life practices including PAD (Fromme and Smith 2017). In the final analysis, after an assiduous attempt to find a mutually acceptable way to respond to the patient's situation, clinicians must be able to live with their decisions and personal principles. Consultation and conversation with trusted colleagues is essential.

6 Approach to the Patient Who Refuses Palliative Care Involvement

There may be patients along the way who express interest in PAS or VAE however refuse any alternatives, including a palliative care consultation. While every patient has the right to refuse treatment, it is imperative to unpack the reasoning behind the patient's refusal. It may be a misunderstanding of the role of palliative care or a previous personal experience that has affected his or her opinion. Some patients may feel uncomfortable voicing their requests to additional practitioners – they may even feel betrayed that a trusted primary care provider or specialist is suggesting the involvement of another party into such a deeply personal conversation. Reassuring the patient that their current trusted care team remains actively involved and that palliative care is involved to make sure they have considered all options to potentially improve his or her quality of life before making such a final decision.

Identifying a main medical provider that the patient trusts and has a trusted relationship with the patient in such situations is crucial. This may be a PCP, an oncologist, or others. If it seems like roadblocks are being encountered in exploring and evaluating a patient's request for PAD, involving such a provider may help move the conversation forward.

Involvement of social work can also sometimes be very helpful. They can help assess for psychosocial, financial, and other stressors, potentially putting services and supports in place.

Pastoral care may also be beneficial depending on the patient's underlying views and values. Components of a patient's underlying suffering may be spiritual or religious in nature. Having the opportunity to meet with a chaplain or other spiritual guide and voice this suffering may bring some peace and understanding of the full nature of their suffering.

Patients clearly have a right to refuse palliative care consultation or consultation of any kind. Yet physicians have the right not to participate in PAD even where it is legal, especially if they do not feel all alternatives have been thoroughly explored (or if they don't feel they can live with the consequences of participation). As always, every effort should be made to find common ground without violating fundamental values on all sides.

Case Resolution: In discussing future options, the patient was informed that PAD was illegal in New York State and that while his doctor was not personally opposed to the practice, he did not feel comfortable prescribing the medication under this circumstance. He was told his symptoms related to headache, seizures, or confusion would be aggressively managed with standard hospice care. If his symptoms in those domains were

severe, he would get proportionate doses of sedating medication, even if it required heavily sedating him to escape the unacceptable suffering. He was also told that he could stop his steroids at a time of his choosing if his desire was to die more quickly and that any associated headache and confusion would be aggressively managed. He could also stop eating and drinking if he chose to do so, though this would probably not be necessary if he were to stop his steroids. He was made aware that there are groups such as Compassion & Choices who advise patients who want additional options which may be illegal such as PAD in the state of New York.

The patient and doctor agreed that at some point in the future stopping the steroids along with aggressive symptom management would probably be the best of the available options. About a month later, the patient began to develop more severe pain that was harder to treat with opioids along with higher dose steroids. He and his doctor began a conversation about whether it was time to initiate the plan to stop his steroids and aggressively palliate when the patient developed headache, confusion, and/or a seizure. Before he made any potentially death hastening decision, the patient had a grand mal seizure, and when he awoke in the hospital on the palliative care floor, he was quite frightened, but was very clear that he felt the time to withdraw treatment and begin more aggressive symptom management was now. The primary doctor, the palliative care specialist, the patient, and family all agreed, and a plan was made to stop his steroids and provide proportionate sedation with benzodiazepines and analgesia with a continuous opioid infusion. The benzodiazepine and opioid required considerable upward adjustment over the first 24 h until the patient appeared peacefully sedated after which it was maintained at that level. He died 48 h later in the presence of family. While all agreed he would have preferred PAD had it been legal and available to him, they were appreciative that the clinical team found a way to allow him an escape his suffering.

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Part IX

Research in Palliative Care

Public Health and Epidemiological Research in Palliative Care

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Lara Pivodic and Joachim Cohen

Contents

Abstract

Palliative care has been declared an important topic for public health. In turn, concepts of public health such as health promotion are highly relevant for populations in need of palliative care. In recent decades, public health and epidemiological research methods have been applied to study the circumstances of dying, including palliative care provision, in large communities or populations. This chapter starts by outlining several characteristics that distinguish public health from clinical research in palliative care. It subsequently gives an illustrative, rather than exhaustive, overview of several different methodological approaches that have been used in public health research in palliative care, as well as their advantages and limitations. The focus is on quantitative, epidemiological methods, which reflects the current dominant approach in public health research. These include population-based survey research and specifically the mortality follow-back design, the use of death certificate data to study place of death, studies of routinely collected administrative data on the population-level, and the use of existing epidemiological monitoring tools. Finally, the chapter describes the importance and contributions of qualitative and mixed methods public health research in palliative care. It does so by describing examples of community-centered

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_106

palliative care initiatives and research in less visible populations. Acknowledging that no single of these methods can answer all relevant questions about a topic, this chapter argues that it is the combination of a diverse set of research methodologies that will lead to the best possible view on and understanding of the circumstances of dying and provision of palliative care in populations.

1 Palliative Care as Public Health

Public health has been defined as the combination of sciences, skills, and beliefs directed toward the protection, promotion, and restoration of people's health through organized collective or social actions (Sallnow et al. 2016a). "Protection, promotion, and restoration" of health does not imply an exclusively curative approach to illness. It is to be interpreted in the context of the commonly accepted definition of health that has been put forward by the founders of the World Health Organization (WHO). According to this, "health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"(World Health Organization 2018). This definition detaches health from categories of disease or mortality and places it in a broader context of human well-being and includes mental and social, next to physical, well-being. Consequently, health promotion, as a crucial component of public health practice, encompasses, next to curative and restorative approaches, attention to well-being in a broader sense, including personal and social resources and physical capacities (Sallnow et al. 2016a).

This conceptualization of public health and health promotion makes apparent that both are highly relevant for people affected by life-threatening illness, dying, death, and bereavement. Indeed, the central ideas of public health and health promotion – attention to mental, social, and physical well-being – are reflected in the WHO definition of palliative care, which includes attention to physical, psychosocial, and spiritual problems (WHO 2002). Public health approaches to palliative care focus on maintaining and improving well-being of dying people and those affected by dying, death, and bereavement (Sallnow et al. 2016a). The reference to "collective or social actions" in the definition of public health suggests that it is a collective counterpart to individual patient care in a patient-professional relationship. As a result, public health practice and research in palliative care look at total populations – local, regional, national, or global – rather than limiting its focus to the health of individual patients and families or persons at risk or those receiving certain health services (Cohen and Deliens 2011).

Not only are the aims of palliative care and public health compatible, palliative care has in fact the typical characteristics of a public health priority: the need for palliative care places great burden on societies given the large number of people who die from diseases for which it is indicated (Murtagh et al. 2013); it has a major impact with respect to health consequences for populations and costs for individuals as well as the public; and it harbors potential for prevention and harm reduction (Glasgow et al. 1999). Addressing the challenge of providing high-quality palliative care in populations therefore requires applying public health methods to palliative care research.

While there are some paradigmatic differences between "classical" and "new" public health approaches, both approaches to public health research in palliative care have several important characteristics that distinguish them from clinical and health services research:

1. Focus on communities rather than on individuals who are at risk of developing a specific health problem or who are receiving a particular health service or treatment
2. Inclusion of social science alongside medical research methods
3. Recognition of the importance of non-professional actors (e.g., family, friends, wider networks) in palliative care alongside professional services
4. Attention to social and economic determinants of health as opposed to a focus solely on the immediate health services or interventions under study

5. Recognition of community involvement and empowerment as essential to maintaining and improving well-being toward the end of life
6. Evaluation of the impact of policy changes and societal debate on palliative care on a larger scale and less strong focus on impact of isolated interventions

Public health research in palliative care uses a variation of research methods, ranging from experimental and quasi-experimental studies, through classic epidemiological research methods, to methods from qualitative and action research. It would vastly exceed the scope and possibilities of this chapter to provide an exhaustive overview of possible methods to use in public health research on palliative care. The aim of this chapter is rather to highlight the potential of public health research in this field by giving an illustrative overview of several different methodological approaches that have been used, as well as their advantages and limitations. We describe population-based survey research and specifically the mortality follow-back design, the use of death certificate data to study place of death, studies of routinely collected administrative data on the population level, the use of existing epidemiological monitoring tools, and studies using qualitative and mixed methods in less visible populations.

The selection of research methods included in this chapter was guided by the aim to present different methods that can be applied to study palliative care either in full populations or in population-based samples. In the tradition of classic public health research methods, all of these methods are quantitative. Additionally, we included a section explaining the importance and advantages of including qualitative public health research alongside quantitative population-based methods. The specific studies that are used to illustrate the different methods were chosen based on the research that the authors of this chapter are experienced in. In our selection of studies presented, and where possible, we paid particular attention to include cross-national comparative studies. In doing so, we aimed to highlight the particular advantage that public health research offers in studying the same phenomena in different countries using standardized and comparable research methods. This approach was shown to be very useful for generating hypotheses regarding the impact of public policy on palliative and end-of-life care.

2 Population-Based Survey Research and the Mortality Follow-Back Design

Population-based surveys are conducted in representative samples of populations or communities. Most surveys have in common that they ask people questions and then analyze these responses quantitatively, using statistics (Addington-Hall 2007). The quantitative data are collected (i.e., the questions are being asked) in a standardized way in order to obtain comparable results across the sample. Once the results are summarized and analyzed, inferences are drawn from the sample to the entire population about which one aims to make conclusions. Surveys may be used to describe attributes, attitudes, opinions, knowledge or beliefs, as well as intended and/or actual behavior regarding a population at a given time point.

As the central purpose of a population-based survey is to draw reliable, valid, and unbiased inferences about the population, and not just about the sample, it is crucial to ensure that the sample is representative of the population. Therefore, particular attention needs to be paid to the sampling frame. The sampling frame is a list of all the units in the population of interest who are eligible to be sampled. It is important to ensure that the sampling frame is well chosen, because a sample can only be representative of the sampling frame. An incomplete sampling frame is therefore a threat to the representativeness and generalizability of a survey (Addington-Hall 2007).

A core feature of population-based surveys in palliative and end-of-life care is their aim to provide information that is generalizable to whole (national) populations or communities. They offer important insights about the health problems of entire populations of dying individuals and other people affected (e.g., family carers). The sampling frames of population-based studies in

palliative and end-of-life care have included, for instance, all registered deaths in a country (as identified on death certificates) or all deaths among patients of representative samples of general practitioners (see studies in Boxes 1 and 4). Drawing population-based samples prevents bias that would be introduced by other sampling methods that systematically, explicitly or implicitly, exclude certain subpopulations. For instance, a sample of older cancer patients attended by a palliative care service excludes those dying without receiving this service. Hence, based on this sample, no general conclusions can be made about the full population of older people who are dying from cancer.

A very frequently applied design in population-based surveys in palliative and end-of-life care is the mortality follow-back design. It allows for the identification of individual deaths and thus creates a clear population-based sampling frame that is relevant to studying the end of life. Researchers conducting surveys in palliative care that use a mortality follow-back design typically select a random population-based sample of deaths and subsequently ask relevant respondents to retrospectively describe or evaluate the care the deceased person received shortly before death (i.e., the final hours, days, or weeks of life). The sampling frame for these studies is often death certificates, although other methods, such as deaths identified by GPs belonging to epidemiological surveillance networks, have also been applied (see Box 4). The respondents typically are groups who have relevant knowledge on the deceased person's end of life such as bereaved relatives (see VOICES study in Box 1), the treating physician (see ELD study in Box 1), or care home nurses (see PACE study in Box 1).

The frequent use of retrospective designs in population-based studies is largely due to difficulties in prospectively obtaining information from representative samples of dying people. This would entail following large numbers of persons for extended periods of time, in numerous care settings, and thus would be hardly feasible (Chambaere et al. 2008; Earle and Ayanian 2006). Furthermore, those who are most ill would have a high risk of being underrepresented due to their likely non-response, attrition, or decisions by researchers, healthcare staff or family not to overburden them. Additionally, it is difficult to prospectively identify who is dying. Research has indicated that clinicians perform poorly at predicting expected survival and usually overestimate it (Tavares et al. 2018). Retrospective studies offer a realistic possibility to researchers to study population-based samples of people nearing the end of life rather than nonrandomly selected subsets of patients defined by a disease characteristic (e.g., diagnosis of metastatic cancer), care setting (e.g., enrolled in a palliative care service), or specific event that identifies them as dying (e.g., assignment of a formal "palliative status" linked to reimbursement of healthcare costs) and thus provides a more inclusive approach (Earle and Ayanian 2006). They provide a clear denominator or sampling frame for the population under study (e.g., all non-sudden deaths in the ELD study and Euro-Sentimelc study; see Boxes 1 and 4) and allow limiting the analyses to a clearly defined time period, such as the last 3 months of a person's life. This is particularly important when examining aspects of care that are a function of time, such as the time of initiation of palliative care prior to death or frequency of palliative care service use.

Mortality follow-back studies also carry several challenges. Firstly, selecting the most adequate respondent to report on the care received by a deceased person requires careful consideration. The treating physician, nurses, and relatives are suitable respondents for different kinds of research questions. For instance, a physician or nurse may better report on medications administered and their dosages than a family carer. However, both the physician and the family carer can report on symptoms experienced by the patient (Klinkenberg et al. 2003). Secondly, there is a risk of recall bias because periods before death need to be cognitively reconstructed by the respondent. Therefore, the period on which respondents are asked to report is usually limited (e.g., the last 3 days or the last 3 months of life), and respondents are not asked to report on deaths that occurred more than a few months ago (Pivodic et al. 2016a). This also means that this

method is particularly useful for studying the circumstances of the imminent dying phase rather than the longer course of disease until death. Thirdly, an important challenge is obtaining good response rates in mortality follow-back surveys. While there are studies where this is less of a problem (e.g., registrations by epidemiological surveillance networks; Pivodic et al. 2016b), it has been particularly difficult to get high response rates from bereaved relatives (Pivodic et al. 2016a).

Box 1 describes three examples of mortality follow-back studies: VOICES, the End-of-Life Decisions study, and the epidemiological study of the PACE project. They were chosen to represent different topics surveyed, populations, sampling frames, and respondents.

Box 1 Three Examples of Mortality Follow-Back Studies

National Survey of Bereaved People (VOICES)

The first large-scale population-based mortality follow-back survey was the National Survey of Bereaved People (VOICES), in England. The first VOICES study examined the quality of care in the last year of life given to patients aged 15 years or over who died from a range of conditions (e.g., cancer, stroke, chronic obstructive pulmonary disease) and in different locations. The authors conducted structured interviews with bereaved relatives and asked about their perceptions of the care given to recently deceased persons (Addington-Hall and McCarthy 1995). The Office for National Statistics (ONS) identified from death registrations deaths eligible for inclusion in the study and, for each death, the person who had notified authorities of the death. This was usually a relative or friend of the deceased. In later editions of the VOICES study, instead of conducting interviews, structured questionnaires were mailed to respondents by the ONS (Burt et al. 2010). The respondents then mailed the completed questionnaires directly to the research team. Furthermore, the period before death studied changed from 1 year to 3 months. The VOICES questionnaire covers the following topics: details about the deceased (sociodemographic and clinical characteristics including cause of death, care settings where she/he had received care), perceptions of the quality of care delivered in each setting (e.g., home, hospital, hospice), coordination of care, quality of care in the last 2 days of life, decision-making toward the end of life, preferences for place of death, respondents' views on the ultimate place of death, and support provided to family/friends in the last 3 months of life and after the death. Numerous research articles have resulted from this study, including analyses of these topics for specific groups according to cause of death, place of death, or age (Burt et al. 2010; Young et al. 2009; Hunt et al. 2014).

Following the publication of the End-of-Life Care Strategy in the United Kingdom, the Department of Health commissioned a modified VOICES study to monitor key aspects of the quality of care identified in the strategy. The National Survey of Bereaved People was conducted by the Office for National Statistics on behalf of NHS England for the first time in 2011 and has been repeated annually thereafter. For this purpose, the original VOICES questionnaire was redesigned to meet the requirements of the End-of-Life Care Strategy (Hunt et al. 2017). This government-funded monitoring program of the quality of end-of-life care has continued until today and is regularly collecting survey data and publishing findings through government reports.

End-of-Life Decisions (ELD) study

The End-of-Life Decisions (ELD) study is a mortality follow-back survey carried

(*continued*)

Box 1 (continued)
out in Belgium (Flanders), the Netherlands, Switzerland, Italy, Denmark, and Sweden (van der Heide et al. 2003). Its aim was to obtain reliable and valid incidence estimates of ELDs and their characteristics as well as data on the decision-making process prior to ELDs and the treatments and care provided to people at the end of life. The ELD study design is based on a method first developed in the Netherlands in 1990 (Van Der Maas et al. 1991).

The sampling frame consisted of individual deaths. A sample of death certificates was taken, corresponding to almost 25% of deaths in a 6-month period. The sample was stratified proportionally for month of death (and, where applicable, province) and disproportionately for cause of death, as ELDs are known to vary by these factors (Chambaere et al. 2008). Both minors and adult deaths were included, using separate questionnaires for both groups, and they were analyzed separately. From the sampled death certificates, the research team identified the physician who certified the death and who was the information unit for the study. Physicians received the study questionnaire by regular mail. If the certifying physician was not the patient's treating physician, they were advised to forward the questionnaire to the treating physician (or to discard the questionnaire, if the treating physician's identity was unknown) and to inform the research team of this. The respondents returned the completed questionnaires to a trusted third party (TTP; e.g., a lawyer in Belgium) whose task it was to safeguard anonymity by removing any possible identifying information from the questionnaires. The TTP also linked the returned questionnaires to anonymized sociodemographic and morbidity information they received from national death certificate processing agencies for each identified deceased person. The TTP then

Box 1 (continued)
transmitted the anonymized and linked data to the research team.

The physician was asked at the beginning of the questionnaire to indicate whether the death was sudden and completely unexpected. Only if this was not the case, i.e., if the death was non-sudden and expected, were they instructed to complete the further sections. This was done to ensure that only those deceased people were included for whom ELDs had been a realistic option. The questionnaire concerned the last weeks of life of the deceased person and included sections on the types of ELDs made and decision-making process, characteristics of care and involvement of palliative care services, as well as several questions on palliative sedation. Next to providing important insights into end-of-life decisions and the decision-making process in several European countries (Chambaere et al. 2015a; Cohen et al. 2007a), the ELD study has been an important monitoring tool of the incidence of euthanasia which has been legalized in Belgium in May 2002 (Dierickx et al. 2018; Chambaere et al. 2015b).

Palliative Care for Older People (PACE) study: mortality follow-back study in nursing homes

The international Palliative Care for Older People (PACE) study included a cross-sectional epidemiological study of deceased residents in nursing homes in Belgium, Italy, Finland, the Netherlands, Poland, and England (Van den Block et al. 2016). It is an example of a mortality follow-back survey in a specific care setting (i.e., nursing homes). Its overall aim is to generate international data regarding the quality and costs of palliative care in several types of nursing homes in different countries across Europe. The specific aims of the PACE study are situated on two levels, that

(*continued*)

Box 1 (continued)
of the resident and that of care staff (i.e., nurses and care assistants). The study aim on the resident level is to examine the quality of dying as well as costs of end-of-life care in nursing homes. The study aim on the staff level is to examine palliative care knowledge and attitudes among care staff. The PACE study uses the term "nursing home" to refer to "collective institutional settings where care, on-site provision of personal assistance in daily living, and on-site or off-site provision of nursing and medical care, is provided for older people who live there, 24 h a day, 7 days a week, for an undefined period of time" (Van den Block et al. 2016).

In each country, a sample of nursing homes was drawn through proportionally stratified random sampling to obtain representative samples in terms of region within country, facility type, and bed capacity. Sampling was done based on national lists of nursing homes in all countries, except Italy, where no national lists exist and a previously created cluster of nursing homes with interest in research participation was used. The English research team additionally recruited through ENRICH, a network of nursing homes with interest in research participation, to improve the participation rate. The sampling frame consisted of all deaths of the previous 3 months among residents of the sampled nursing homes. Questionnaires were distributed to four different respondents linked to each death: (1) the nurse most involved in the care of the deceased resident or a care assistant in case a nurse could not be identified, (2) the nursing home administrator/manager/head nurse, (3) the resident's treating physician (GP or elderly care physician), and (4) a closely involved relative (family or friend). Questionnaires for care staff were distributed to all care staff on duty on the day the researchers visited the nursing home for data collection.

The resident-level questionnaires assessed residents' quality of dying, health-related quality of life of residents and relatives, quality and processes of palliative and end-of-life care (including psychosocial and spiritual care, advance care planning, medication use, life-prolonging treatments, treatments discontinued or not initiated, palliative sedation), and costs and resource use. The staff-level questionnaires assessed staff knowledge and attitudes regarding palliative care, self-efficacy in providing palliative care, interdisciplinary communication and ethics in the work environment, and communication with residents and family. The PACE study has provided evidence from six countries regarding the quality of dying and quality of end- of-life care of nursing home residents (Pivodic et al. 2018), as well as palliative care knowledge of nursing home care staff (Smets et al. 2018).

3 Death Certificate Data to Study Place of Death

Most countries worldwide register deaths in a systematic and standardized manner using death certificates that are handled by a government agency. These records primarily serve administrative purposes, but they are also being used in public health research. The analysis of information from death certificates is a classic method applied in epidemiology. All major descriptions and projections of mortality, including causes of death and life expectancy, such as those regularly published by the WHO, rely on death certificate data. Death certificates typically contain information on the deceased's identity; birth details; gender; date, cause, and location of death; date on which the death was registered; informant details; name of coroner (in case the death was referred to

one); details of the registrar handling the registration; and the date on which the death certificate was produced. These are limited data, but they are highly standardized across most countries worldwide which makes them particularly useful for cross-national comparisons.

The research potential of death certificates has also been recognized in palliative care (Cohen et al. 2007b). Death certificate data on place of death have become one of the most frequently used tools in public health research in palliative care (Pivodic et al. 2016c; Gao et al. 2013; Sleeman et al. 2014). Studies using place of death data have shown to be useful for identifying the care settings that have an important role in the delivery of end-of-life care in different countries (Cohen et al. 2007b). This has made them a cornerstone in the planning, implementation, and evaluation of policies aimed at enabling people to die in their place of choice. Data on where people die can also provide a scientific evidence base for the allocation of financial, material, and human resources for palliative care (Pivodic et al. 2016c).

The major advantage of death certificate data is that they allow phenomena to be studied in full populations (e.g., all deaths of one country during 1 year) rather than samples and thus do not carry the risk of sampling bias. This fact, together with the high level of standardization of death certificate data, facilitates cross-national comparisons of place of death (Pivodic et al. 2016c; Cohen et al. 2015). Several cross-national studies of the place of death have been conducted to date and revealed countries with higher or lower proportions of deaths in certain locations (Houttekier et al. 2010; Cohen et al. 2008; Pivodic et al. 2015; Cohen et al. 2015). Next to cross-national standardization, there is also standardization of place of death data over time *within* countries. This has made death certificates the tool of choice for monitoring trends over time in place of death in different populations (Sleeman et al. 2014; Houttekier et al. 2011; Gao et al. 2013). These analyses can be used, for instance, to study the potential impact of changes in healthcare policy (e.g., additional funding for home palliative care) or societal changes (e.g., decrease in availability of family care).

The unique identifiers on death certificates, which unambiguously link them to a particular individual, usually enable linkages across population-level databases administered by government agencies. This has been important for obtaining relevant predictor variables in analyses of place of death that are not recorded on death certificates, such as certain sociodemographic data, economic indicators, or regional indicators of healthcare resources (e.g., hospital bed capacity) (Pivodic et al. 2016c). In principle, there lies even greater potential in linking individual death certificate data to other population-level data, such as health claims data. These possibilities are discussed in the next section. A further advantage of death certificate data lies in the large sample size one can obtain with them. This provides sufficient statistical power for studying subpopulations (e.g., people who died from lung cancer, people living in regions with low socioeconomic indicators) and for conducting tests of association with a large number of independent variables (Cohen et al. 2007b).

Studies of place of death using death certificate data carry several challenges. Firstly, the primary use of these data is administration and not research. As a result, important information for research purposes (e.g., sociodemographic information, individual socioeconomic status rather than regional aggregates) is often not included in them. Death certificates do not contain some information that is important for predicting a person's place of death, such as information on the course of disease, treatments received toward the end of life, or the persons' preferred place of death (Cohen et al. 2007b). Although it is possible to study the place of death in a population that could potentially benefit from palliative care as judged by the cause of death (Pivodic et al. 2016c), we cannot know from death certificates whether palliative care was a realistic option for a specific individual. Secondly, despite the high level of cross-national standardization of death certificates, place of death is not uniformly coded across countries. Some countries register it only in a limited way, for instance, by distinguishing merely "home" versus "other" (Pivodic et al. 2016c). This calls for a more complete registration and better standardization of place of death

records across countries (Pivodic et al. 2013). Finally, studies using death certificates may be affected by issues of validity regarding the cause of death (Burger et al. 2012). This seems less of a problem when aggregated categories of causes of death are used (e.g., cancer versus non-cancer disease), but it appears particularly problematic when dementia is concerned. A study using linked administrative data showed that only around half of people who die with dementia have it listed as their cause of death on the death certificate (Perera et al. 2016). The likelihood of having dementia recorded was higher if the person died in a nursing home rather than at home. These findings should warn researchers to be cautious in their conclusions from studies that investigate associations between cause and place of death.

Box 2 describes the International Place of Death study as an example of a population-level investigation of place of death. This study has been conducted in multiple countries, allowing for cross-national comparisons, as well as multiple times within the same country (Belgium) with the aim to study trends in place of death.

Box 2 Example of a Study Using Death Certificate Data

International Place of Death (IPoD) study

The International Place of Death (IPoD) study investigated the place of death in the total population of deaths of 1 year in 14 countries worldwide (Cohen et al. 2007b). The study collected complete death certificate data in countries that are situated across different levels of palliative care integration into mainstream healthcare. Next to place of death, the death certificates provided limited clinical (i.e., cause of death) and sociodemographic data. In some countries, sociodemographic and environment-related variables are not recorded on death certificates and were obtained by linking death certificates with other databases (e.g., census data). Additionally, healthcare resource statistics per capita (e.g., number of hospital beds/1000 inhabitants) and data on the degree of urbanization were linked with the deceased's municipality/local authority of residence.

These data were used for large-scale studies of the place of death in different populations (e.g., people in potential need of palliative care (Pivodic et al. 2016c), people who died from cancer (Cohen et al. 2015)) as well as for trend analyses (Houttekier et al. 2011). Among other findings, these analyses revealed that people who die from cancer were more likely to die at home rather than in hospital in many countries, but not all. This led to the hypothesis that the relatively predictable course of disease of cancer might facilitate a home death only in those countries where cancer care is not centered in hospitals (Pivodic et al. 2016c). IPoD data also revealed important similarities across countries, such as the finding that people who died from hematological cancer were more likely to die in hospital than people who died from a solid tumor in 14 countries across four continents. This raises the possibility that there might be clinical characteristics that make a certain place of death more likely, independent from healthcare organization (Cohen et al. 2015).

4 Routinely Collected Population-Level Administrative Data

A growing body of public health research in palliative care makes use of routinely collected health data. These data are generated by and serve administrative and clinical processes, as opposed to data generated solely for research purposes, such as survey data. Routinely collected data in palliative care research include, for instance, death registry data; activity data from primary, secondary, and tertiary care settings; health claims data; and cancer registries (Davies et al. 2016; Maetens et al. 2016).

Routine health data can be collected at three different levels, and this has an influence on their possibilities for research use: (1) the personal level, which includes disaggregated information about individual people including clinical records of care received; (2) the service level, which includes summary information about a healthcare service, e.g., number of patients seen in a year; and (3) the area level, which includes summary information about an area, e.g., proportion of home deaths or number of hospitals (Davies et al. 2016). The second and third levels allow comparisons to be made between areas and services. The first level, the person level, contains the richest information about a patient's clinical and sociodemographic characteristics and treatments. It is this level on which the most meaningful data on quality of care can be collected. Hence this section focuses on the use of person-level routine data in palliative care research.

Earle and colleagues were among the first to explore the potential of using systems of routinely collected data in palliative care research, specifically to assess and implement quality indicators for end-of-life cancer care (Earle 2003). Since then, increasing digitalization has further facilitated the process of generating, storing, and exchanging large amounts of individual patient data that can be used for public health research in palliative care (Murdoch and Detsky 2013). Routinely collected health data are a source of comprehensive information concerning service and medication use and associated costs, as these are well-recorded for billing purposes in many countries (Maetens et al. 2016).

The use of routinely collected administrative data has several important advantages for public health research in palliative care. Just like death certificates, they are population-level data and hence not prone to sampling bias. They allow different subpopulations, including difficult-to-reach subgroups to be studied (Billings 2003). Individual person-level routine data can be aggregated on multiple levels (e.g., by diagnosis, treatment, service provider, geographical region), which gives them an important advantage over routinely collected data on the service level that do not offer the possibility to identify unique cases. Given that most administrative data are collected at regular intervals, they permit time trend analyses and longitudinal studies. Lastly, obtaining administrative data is relatively inexpensive compared to original large-scale data collection (Maetens et al. 2016).

Using routine administrative data in research also carries limitations (Maetens et al. 2016). Obtaining comprehensive routine data for research purposes often requires linking data from different sources. This process brings about potential challenges for researchers, including identifying relevant data, completeness of data, obtaining access to data from different organizations, technical difficulties when linking data, creating useful variables for research purposes, and maintaining strict ethics and privacy procedures (Davies et al. 2016; Maetens et al. 2016). Health services not covered by insurers are usually not included in these databases, and it may be region- and country-specific which services are and are not covered. This places additional demands on researchers to identify the regulations applicable to the region or country they intend to study. Furthermore, the use of certain services cannot be identified because there is no individual reimbursement per patient (e.g., mobile hospital palliative care teams in Belgium) or because reimbursements are not regulated or generalized (e.g., consultations of a psychologist in Belgium) (Maetens et al. 2016). An additional limitation is linked to the fact that administrative databases are not primarily research instruments. This means that they do not contain more in-depth data on quality of care (e.g., patient reported outcome measures), quality of dying, and details of the course of disease and symptoms experienced.

Box 3 describes a study that used linked administrative data to study palliative and end-of-life care in Belgium.

Box 3 Example of a Study Using Routinely Collected Administrative Data

Belgian study using linked data from eight administrative databases (Inter-Mutualistic Agency [IMA] study) (Maetens et al. 2016)

(*continued*)

Box 3 (continued)

The Inter-Mutualistic Agency (IMA) study was conducted in Belgium and linked eight administrative databases from three different administrators with the aim of studying the use, quality, and costs of end-of-life care on the population level and their association with various clinical, sociodemographic, socioeconomic, and environmental factors.

The data sources included:

1. Sociodemographic database of all individuals with health insurance (legally mandatory in Belgium)
2. Medical claims database containing health and medical care use characteristics of all reimbursed healthcare services of home, nursing home, and hospital care, except medication dispensed in public pharmacies
3. Pharmaceutical database containing medication supply characteristics of medications dispensed in public pharmacies
4. Belgian Cancer Registry database with diagnostic information on all new cases of cancer including type of cancer and date of diagnosis
5. Death certificate database containing causes of all reported deaths
6. Population registry database including household composition
7. Census database including housing characteristics and educational level
8. Fiscal database including net taxable income

The combination of these databases can provide information for the full population of deceased persons on formal healthcare use and related costs, medication prescription, causes of death, main diagnoses, and various sociodemographic and socioeconomic information. However, the data will likely be an underestimation of costs for end-of-life care given that services not covered by insurers are not included and neither are out-of-pocket costs.

A published research article describes the procedures for accessing and linking these databases, the information they contain, and which data handling procedures were necessary to prepare the data for analysis (Maetens et al. 2016). This can help researchers in navigating possibilities for using routine data in Belgium. It also provides a thorough description of the possibilities and limitations, as well as procedures and considerations to make, when using routinely collected administrative data for palliative care research internationally.

Research that has resulted from this method includes an investigation of resource use in the last 6 months of life of people who died with versus from Alzheimer's Disease (Faes et al. 2018), as well as a study of quality indicators for end-of-life care in the population who died from cancer (De Schreye et al. 2017).

5 Existing Epidemiological Monitoring Tools

A further research method derived from public health research to examine large population-based samples of people at the end of life includes the monitoring of care through epidemiological surveillance networks, such as sentinel networks of general practitioners (GPs) (Van den Block et al. 2013). Sentinel networks are networks of practices or community-based physicians who conduct epidemiological surveillance of one or more specific health problems on a regular basis (Fleming et al. 2003; Deckers and Schellavis 2004; Vega et al. 2006). The networks are typically set up and managed by national public health institutes to monitor various health problems such as the incidence of flu, diabetes, stroke, or suicide

(Fleming et al. 2003; Devroey et al. 2003; Lobet et al. 1987). In doing so, they monitor the health of the entire population in a country or wider region (Fleming et al. 2003; Deckers and Schellavis 2004). The general objectives of sentinel networks are (1) to evaluate public health problems and their importance within the general population; (2) to observe the change in certain health problems over time to evaluate, for instance, the impact of prevention campaigns; and (3) to study the management and follow-up of health problems in general practice (Van den Block et al. 2013).

Epidemiological surveillance through sentinel networks of GPs has a long tradition in scientific research. In countries in which close to everyone has a GP these networks capture representative samples of the population and thereby constitute a good research tool for studying population health (Van den Block et al. 2013). General practice is highly accessible in Europe; in the countries included in the Euro-Sentimelc study (see Box 4), almost all of the population have a GP whom they consult regularly (Schäfer et al. 2010; García-Armesto et al. 2010; Gerkens and Merkur 2010; Ferré et al. 2014). The yearly turnover of GPs in the sentinel networks is low which contributes to the scientific quality of the data collected. In contrast to death certificates and other routinely collected data, data generated by sentinel networks have primarily a research rather than an administrative purpose. This means that they are more comprehensive and include important sociodemographic and health- and healthcare-related information that is not captured in administrative databases and often not even in patients' medical files (e.g., whether GPs were aware of a patient's preferred place of death). Furthermore, researchers can rely on the routine quality assurance procedures employed by the public health institutes that manage the networks. This includes checks of data for inconsistencies and completeness, measures to reduce non-response, and instructions to physicians to use patient records and information coming from hospitals when registering information. Sentinel networks have regular and frequent registration intervals (e.g., weekly registration of deaths in the study described in Box 4), which makes recall bias less likely than in retrospective surveys with non-continuous registration where the interval between a person's death and data collection is typically longer (see Box 1).

Studies using sentinel networks of GPs also carry challenges. Obtaining in-depth data of care aspects is usually not possible as registration forms have to be kept short and simple so as not to overburden GPs. GPs are also asked to report on care that patients received outside of general practice (e.g., in hospital) of which they may not be fully informed. Hence there may be an underestimation of certain treatments provided or decisions taken by hospital physicians. It was also shown that GPs underreport deaths that occurred in hospital (Van den Block et al. 2013). Lastly, some countries' healthcare organization poses specific challenges to this research method. For instance, Belgium does not have patient lists per practice which means that the population denominator cannot be precisely defined. In the Netherlands, sentinel networks of GPs do not capture deaths in nursing homes as the treating physicians in these facilities are specialized nursing home physicians.

Box 4 describes one, and so far the only, study that used population-based data from sentinel networks of GPs to study end-of-life care.

Box 4 Example of a Population-Based Study Using an Existing Epidemiological Surveillance Network to Study Palliative Care

European Sentinel Network Monitoring End-of-Life Care (Euro-Sentimelc) study

The European Sentinel Network Monitoring End-of-Life Care (Euro-Sentimelc) study is a continuous cross-national mortality follow-back study with the aim to examine end-of-life care in the population of four European countries (Van den Block et al. 2013). It is called continuous because, unlike in the VOICES or ELD studies (Box 1), deaths were not identified at one point in time but continuously over a 3-year period. The sampling frame was individual

(*continued*)

Box 4 (continued)
adult deaths that were registered by general practitioners (GPs) belonging to sentinel networks of Belgium, the Netherlands, Italy, and two autonomous communities in Spain, i.e., the Valencian Community and Castile and Leon.

The GPs belonging to the sentinel networks completed a standardized registration form for every deceased patient of their practice and answered questions regarding several aspects of their end-of-life care. GPs registered deaths on a weekly basis to keep response bias at a minimum. The information collected by the registration forms is anonymous, and the topics surveyed include places of care and place of death, transitions between care settings, communication between physician and patient/family, advance care planning, palliative care provision, symptoms in the last week of life, and costs and burden of end-of-life care for patients and family carers. A particular characteristic of this study is that GPs were asked to indicate whether the death they were reporting on was "sudden and totally unexpected." The authors excluded sudden deaths from the analyses in order to focus on patients for whom care in the terminal phase of life, including palliative care, was a realistic option (Van den Block et al. 2013).

An analysis of deaths registered by the sentinel networks showed that they were representative for all deaths in the participating countries in terms of age, gender, and place of death (Van den Block et al. 2013). Deaths in nursing homes in the Netherlands were an important exception to this, as nursing home residents are treated by specialized elderly care physicians as opposed to GPs. Furthermore, GPs underreported a small number of sudden hospital deaths in all countries as well as non-sudden hospital deaths and deaths of people under 65 years in Belgium (Van den Block et al. 2013).

Box 4 (continued)
Over several years of data collection, the Euro-Sentimelc study (and its predecessor studies in Belgium and the Netherlands Meeussen et al. 2011) provided monitoring data on several aspects of end-of-life care in the last 3 months of life in four European countries.

These include, but are not limited to, transitions between care settings (Van den Block et al. 2007, 2015), hospital admissions at the end of life (Pivodic et al. 2016b), trends over time in specialist palliative care involvement in Belgium (Penders et al. 2018), preferred and actual place of death (Ko et al. 2013), and patient-GP communication about end-of-life topics (Evans et al. 2014).

6 Qualitative Methods in Public Health Research in Palliative Care

Public health research is dominated by quantitative research methods, and public health research in palliative care is no exception to this. As a result, there are many *descriptions* of end-of-life care processes and outcomes in populations but few studies that aim to provide *understanding* or *meaning* to these phenomena (Sallnow et al. 2016a). The spread of traditional, quantitative, methods in public health research across a growing number of health topics has led to calls for more reflection on the appropriateness of the questions asked in public health research, the ways in which they are addressed, and the conclusions drawn from research into health practice and policies (Faltermaier and Faltermaier 1997). Authors have argued that the complexity inherent to public health initiatives in palliative care is insufficiently captured by the dominant quantitative methods outlined in the previous sections (Sallnow et al. 2016a). They do not provide sufficient information to answer questions such as when and where people with a life-threatening

illness seek professional help, how they perceive and interpret their illness, how they view the care provided to them, their preferences for care, and how this is shaped by societal factors. Understanding these phenomena, all of which influence the circumstances in which people die, can aid in the development of appropriate and effective public health interventions. However, studying them places new demands on study designs.

Qualitative methods provide a possibility to study the complexity inherent to public health approaches in palliative care. Qualitative research has been particularly used and promoted within "new public health" approaches to palliative care (Sallnow et al. 2016b). It is seen as the method of choice for studying social, personal, and environmental resources for health, next to curative and restorative approaches that have guided "classic" conceptions of public health. According to this view, qualitative methods are essential for research that represents patients not as mere objects of compliance to expert-based interventions but as active and conscious individuals capable of making informed decisions, seeking professional help only under certain circumstances, with special needs and expectations (Faltermaier and Faltermaier 1997). Box 5 presents two studies as examples of the research questions asked, methods applied, and insights gained from qualitative approaches to public health research in palliative care.

Box 5 Examples of Qualitative Public Health Research in Palliative Care

The impact of a community volunteer program in Uganda

This study explored the impact of a Community Volunteer Program (CVP) run by Hospice Africa Uganda that provides practical, emotional, physical, and spiritual support to people with cancer and HIV/AIDS in their own home (Jack et al. 2011). It engages members from the local community (i.e., community volunteers) to augment the work of a local hospice team by identifying patients, who often live in rural communities and who would normally not be seen by the hospice team, or even know of it. Community volunteers are acting as a link between patients in the community and healthcare professionals. The research was conducted with a sample of key stakeholders involved with the service, i.e., 21 patients (who had been attended by the CVP team for at least 3 months), 11 hospice clinical staff, and 32 community volunteer workers (CVWs). Data from patients and CVWs was collected through group interviews using a semi-structured schedule. Hospice clinical staff participated either in focus groups or individual semi-structured interviews. Data collection focused on the participants' experience of the CVW program. Data were analyzed using thematic analysis. The authors found that the CVP was having a positive impact on patients and families by being a "bridge" to the hospice and enabling palliative care to reach out into the rural community. Identified challenges included distances that volunteers are required to travel on poor transport (bicycles in bad condition) and expected reductions in funding.

Usefulness of digital stories as research method for palliative care in Māori communities

Digital stories are short first-person videos comprised of images, video clips, voice-overs, text, and music that tell a story of great significance to the creator. They have been described as a useful emergent method for public health research and specifically community-based participatory research (Williams et al. 2017). This study explored how this method might be applied in palliative care and specifically for studying Māori(Indigenous people of New Zealand) experiences of caring for their older relatives at the end of life. This method is based on the position that

(*continued*)

Box 5 (continued)
community-centered palliative care approaches call for community-centered research methods, especially ones that can be adapted to the particularities of a certain locality. Previous research using digital storytelling (DST) with indigenous communities suggested that it might fulfill the imperative for culturally appropriate methods.

This study adopted an exploratory qualitative research design using a constructivist conceptual framework. Constructivism acknowledges the presence of multiple realities; the understanding of phenomena is derived through participants' subjective views that have been shaped by social interaction with others and from their own personal histories (Williams et al. 2017). The research approach involved making Māori concerns and priorities the focal point of the research, which was centered within Māori culture and practice. Participants, who had to be involved in the care of an older relative, were recruited through snowball sampling based on a group of Māori who had participated in previous research. The digital stories were created in a workshop facilitated by the researchers. Additionally, participants were asked to complete an anonymous, written questionnaire consisting of open-ended questions on their views of the workshop and digital story. Thematic analysis was used to analyze the questionnaires.

The authors identified several facilitating factors for this method as well as hindering factors with regard to recruitment, use of technology, and integration of the pōwhiri process (Māori formal welcome of visitors) into the research. Overall, they concluded that DST is a useful method to study Māori end-of-life caregiving. Differences between cultures among countries worldwide mean that people face different palliative and end-of-life care scenarios. This diversity necessitates a diversity in research methods to better understand ways in which care can be most effectively delivered in different communities. DST may be a useful method for studying palliative care in a participatory research environment built on community involvement and specifically with indigenous groups.

7 Conclusion

Public health research is an essential element of palliative care research. It allows us to study circumstances of dying, patients' and families' needs, and the provision and quality of care toward the end of life, including palliative care, in populations. This chapter provides an illustrative overview of quantitative and qualitative methods that have been used in public health research in palliative care. All methods described here, both quantitative and qualitative, are well-established in public health research. This chapter explains how they can be applied in the specific field of palliative care and which knowledge can be gained through them. We distinguished several quantitative approaches according to their sampling frame, the data source and the primary purpose of the data (administrative versus research), and types of respondents (in the case of surveys). Next to the dominant quantitative methods, this chapter also pays attention to qualitative public health research methods, which are increasingly being employed, particularly in the context of community-centered approaches to dying and palliative care. This chapter aimed to highlight their importance and the potential they offer for a better understanding of public health phenomena in palliative care that are insufficiently or not at all captured by quantitative data.

Next to showing the possibilities that public health research offers to palliative care, this chapter also makes apparent that no single method can answer all relevant questions. In this regard, public health research is no different from other domains, including clinical research. Recognizing

this, this chapter describes the advantages and limitations of each method presented and gives examples of research questions they are particularly suited to address.

We acknowledge that our illustrative overview of research methods and studies likely overlooks several other public health research designs that have led to important insights in palliative care. Likewise, there are many examples of studies using the methods we presented that we did not mention. However, we do hope that the examples presented in this chapter convey to interested readers the diversity and possibilities of public health research in palliative care, help them identify similar studies in the literature, appraise their possibilities and limitations, and guide future research endeavors.

Ultimately, we argue that the best possible view on and understanding of the circumstances of dying and provision of palliative care in populations can be achieved only by applying a diversity of public health research methods, each of which is suited to answer specific sets of questions.

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Development and Evaluation of Complex Interventions in Palliative Care

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Nilay Hepgul, Wei Gao, Matthew Maddocks, and Irene J. Higginson

Contents

Abstract

Evaluations of complex interventions are of utmost importance to identify and deliver clinically and cost-effective palliative and end-of-life care for future populations. They are however challenging and resource intensive. The Medical Research Council (MRC) framework together with the Methods Of Researching End of Life Care (MORECare) collaboration provides clear standards on best research practice in evaluating services and treatments. These guidelines emphasize the need to consider implementation at all phases of evaluation, rather than only at the end. Furthermore, they highlight the need for flexible and pragmatic approaches to develop, examine, and evaluate complex interventions in palliative and end-of-life care. In this chapter we outline what a complex intervention is, discuss the challenges of developing and evaluating complex interventions in palliative and end-of-life care, and provide examples of complex interventions which have reached the evaluation phase.

1 Introduction

Conducting research in palliative and end-of-life care can be demanding, especially when evaluating the effectiveness of complex palliative care interventions. There are multiple challenges associated with involving people with advanced illness in research, for example, people have

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_108

progressive and unpredictable illness trajectories, and high attrition from studies is common (Lorenz et al. 2008). The "gold standard" randomized controlled trial (RCT) is particularly challenging to conduct, as it demands a position of equipoise and a readiness to allocate to trial arms, by chance, people living with troublesome symptoms and a high level of need. A flexible and pragmatic approach is therefore needed to identify, examine, and evaluate palliative care interventions.

In 2000, the Medical Research Council (MRC) published its landmark framework for developing and evaluating complex interventions (Craig et al. 2008; Medical Research Council 2000). This provided an internationally agreed definition of what is meant by a "complex" intervention and a robust framework for the design of evaluative trials in this area. Complex interventions in health care were said to comprise a number of separate elements that seem essential to the proper functioning of the intervention, although the "active ingredient(s)" of the intervention are difficult to specify (Medical Research Council 2000). In their guidance the MRC advocates for the use of distinct iterative phases of intervention development, feasibility/piloting, evaluation, and implementation. Subsequent to this, the MRC jointly with the UK National Institute for Health Research (NIHR) established the Methods Of Researching End of Life Care (MORECare) collaboration. The aim was to identify, appraise, and synthesize best practice methods for research evaluating palliative and end-of-life care. In particular, it focused on the evaluation of complex interventions around service delivery and reconfiguration. In this chapter we outline what a complex intervention is, discuss the challenges of developing and evaluating complex interventions in palliative and end-of-life care, and provide examples of complex interventions which have reached the evaluation phase.

2 What Is a Complex Intervention?

There are several definitions of complex interventions. Most highlight the presence of multiple, interacting components and emphasize variability in the content, context, and mode of delivery, as well as the unpredictability of the overall effect (Lewin et al. 2017; Petticrew 2011; Wells et al. 2012). According to the MRC definition, a complex intervention (e.g., treatment, service) is one with several interacting components which may act both independently and interdependently. The components usually include behaviors, parameters of behaviors (e.g., frequency, timing), and methods of organizing and delivering those behaviors (e.g., type(s) of practitioner, setting, and location) (Medical Research Council 2000). As such, it can be difficult to know which are the "active ingredients." Complex interventions may be delivered at the individual, organizational, or population level and be targeted toward patients either directly or indirectly via health professionals and/or health systems. Taking these defining attributes into account, palliative and end-of-life services are clearly complex interventions, which comprise multiple interacting components and dimensions (Campbell et al. 2007).

Box 1 What Makes an Intervention Complex?

- The number of and interactions between components within the experimental and control interventions.
- Number and difficulty of behaviors required by those delivering or receiving the intervention.
- Number of groups or organizational levels targeted by the intervention.
- Number and variability of outcomes.
- Degree of flexibility or tailoring of the intervention.

Taken from Craig et al. (2008)

3 Evaluation

There is a growing interest in understanding the effectiveness of complex interventions in order to accurately describe and replicate them. Evaluation

of a complex intervention is key to help identify and examine the "active ingredients" and how they tend toward an effect. Through this understanding, it becomes possible to know how an intervention can be transferred to other contexts, how generalizable an intervention might be, and how it can be most effectively implemented in clinical practice. A challenging aspect of evaluating a complex intervention is defining the intervention itself, to standardize its content and delivery by determining the critical components of the intervention and how they relate to and impact on each other (Medical Research Council 2000). Evaluations of complex interventions can be problematic simply because the researchers have not fully defined and developed the intervention prior to undertaking a trial. Added to this, the evaluation of palliative and end-of-life care interventions can be particularly difficult due to patients having complex and often multiple needs (physical, psychological, social, and spiritual) making standardization of the intervention more difficult. There are also often many people involved, not just patients but their families and those who support and care for them. Finally, there are issues around recruitment and retention of patients into studies and defining and measuring outcomes on a background of rapidly changing clinical situations and limited survival times.

4 MRC Framework/Guidance

In 2000 the MRC presented a stepwise approach to the evaluation of complex interventions. These steps can be compared with the sequential phases of drug development from the initial preclinical experiments through to post-marketing surveillance studies (Campbell et al. 2000). The sequential framework is useful as it sets out the objectives to be met at each stage prior to moving forward. However, it fits more readily with typical routes for drug development, and therefore for complex interventions, not all stages will be relevant for all research questions. Nonetheless, as a definitive effectiveness trial can be highly costly, it is important to systematically develop, test, and refine an intervention and the research methods before one takes place. The guidance was intended to help researchers choose and implement rigorous methods to develop and evaluate complex interventions, leading to theory-driven interventions with well-understood components.

Preclinical or theoretical phase – The first step is to establish the theoretical basis and identify evidence that suggests the intervention might lead to the expected effect. Reviewing the theoretical basis for an intervention may lead to changes in the hypothesis and improved specification of potentially active ingredients (Campbell et al. 2000). Some interventions may already be widely practiced or have evidence from previous studies from different contexts, and therefore a theoretical phase may not be essential. Consulting available evidence may help to eliminate implausible interventions or highlight any facilitating factors or barriers in developing a specific intervention.

Phase I or modelling – This phase involves identifying the components of the intervention as well as their underlying mechanisms and interrelationships. Paper modelling (diagrams or flowcharts) or simulations may be used. It is essential to clarify important components in order to devise clear and reasoned protocols for subsequent trial design. This phase may also involve qualitative testing, for example, through focus groups, preliminary surveys, case studies, or small observational studies. Qualitative testing during this early phase can also be helpful to understand how the intervention might work and to identify potential barriers to it being delivered.

Phase II or exploratory trial – In this phase, all the evidence gathered so far is put to the test to develop the optimal intervention and trial design. This can involve testing the feasibility of delivering the intervention as well as its acceptability to patients and providers. It may be appropriate to experiment with the intervention by adjusting different components to see what effect each change has on the intervention as a whole and to understand which variations seem to be the most appropriate for a full-scale effectiveness trial. Evidence can be obtained to support the theoretically expected treatment effect and to identify an appropriate control group, outcome measures, and recruitment estimates for a main trial.

Phase III or main trial – The central step in the evaluation of a complex intervention is the main randomized controlled trial. This requires addressing the issues usually posed by RCTs such as adequate sample size, eligibility criteria, adequate randomization and blinding (where feasible), appropriate outcome measures, and informed consent of participants. Complex interventions can pose challenges in these areas. Individual randomization may not always be feasible, for example, if the intervention requires training and upskilling staff who will interact with all trial participants. Allocation concealment or blinding is often not possible given that treatments involve face-to-face contact.

Phase IV or long-term implementation – The purpose of the final phase is to examine the implementation of the intervention into practice and establish the long-term, real-life clinical effectiveness. This can help inform about the stability of the intervention, the broader applicability, and the safety profile, including adverse effects that might not become apparent until large groups of people experience the intervention.

In 2008, the MRC framework was updated to provide a more cyclical model that placed greater emphasis on early phase piloting and evaluation work and recognized that complex interventions work best when tailored to local contexts rather than being completely standardized (Fig. 1) (Craig et al. 2008). The framework superseded the 2000 guidance, and this updated version presented a more iterative process of development, feasibility/piloting, evaluation, and implementation. As an example, the theoretical basis and components of an intervention may be reexamined following the results of an exploratory trial. The 2008 guidance has a broader scope than the 2000 version, covering observational and experimental methods as well as implementation of interventions (Anderson 2008).

Development – Before any substantial evaluation occurs, the intervention must be developed to the point where it can reasonably be expected to lead to an effect (Craig et al. 2008). This requires the identification of an evidence base, which may be achieved through a systematic review of the existing literature. Based on the available evidence, a theory or model of how the proposed intervention is going to work can be developed. Often it can be useful to draw on disciplines outside of palliative care and end-of-life care and even beyond health sciences.

Feasibility/piloting – Piloting is crucial to assess and test intervention procedures and their acceptability. An important step is to estimate likely recruitment and retention rates in order to inform sample size calculations (that take attrition into account) and avoid smaller than expected effect sizes (Eldridge et al. 2004). Similarly, missing data is to be expected; therefore piloting can help determine the expected level of missing data in advance. Pilot studies do not need to be a scale model of the planned evaluation but function to

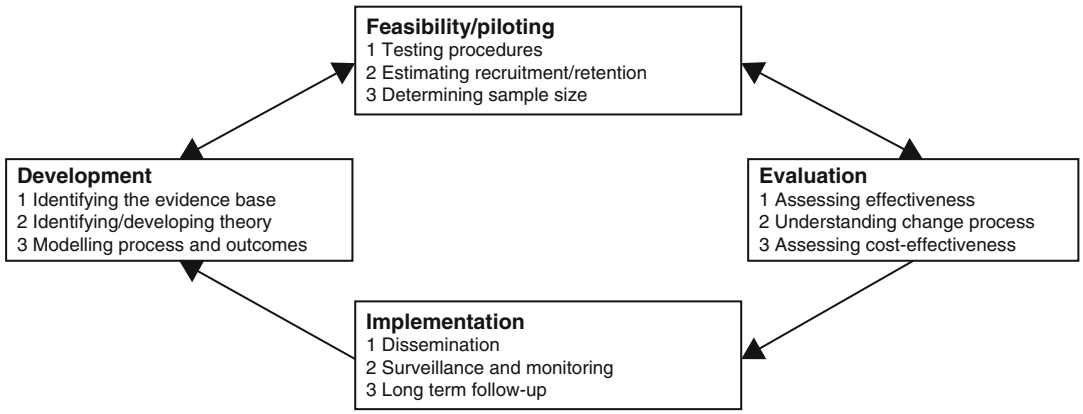

Fig. 1 Key elements of the development and evaluation process. (Taken from Craig et al. 2008)

examine the key uncertainties that have been identified during the development (Craig et al. 2008).

Evaluation – The choice of study design and how the intervention will be evaluated need careful consideration. Randomization should always be considered where possible in order to avoid selection bias. It is critical to think about the outcome measures, most importantly the primary outcome but then also secondary outcomes. The chosen timing of data collection is also important, and long-term follow-up may be required to establish whether any immediate effects of an intervention persist. Understanding the processes involved in the implementation and delivery of an intervention can provide valuable insights into why an intervention works or fails and how it can be optimized in clinical practice. An embedded process evaluation can be helpful to assess implementation fidelity and understand the contextual factors associated with variations in outcomes (Oakley et al. 2006).

Implementation – Reports of evaluations should include detailed description of the intervention to enable replication, evidence synthesis, and wider implementation (Craig et al. 2008). It is critical to utilize the findings from an evaluation of a complex intervention either for clinical practice or to inform policy.

5 MORECare

A major barrier to progress the science of palliative and end-of-life care is the lack of high-quality research (Higginson 2004). While the number of clinical trials in palliative and end-of-life care is on the increase (Tieman et al. 2008), questions remain about the quality of research being undertaken, particularly with regard to rigorous designs. Reviews have concluded that palliative care studies are largely descriptive, with wide variations in sample size, demographic and clinical aspects, and a lack of recognized standardized measures (Aoun and Nekolaichuk 2014; Bakitas et al. 2006; Hui et al. 2011). A recent review of evidence-based practice in palliative care highlights common problems including underpowered studies, recruitment difficulties and high attrition, inadequate follow-up periods, difficulty defining outcomes, and performance bias (Visser et al. 2015). In response to this need, the UK Medical Research Council (MRC) and National Institute for Health Research (NIHR) established the Methods Of Researching End of Life Care (MORECare) collaboration. The aim of the collaboration was to identify, appraise, and synthesize "best practice" methods for research evaluating palliative and end-of-life care. In particular, it focused on complex service delivery reconfiguration interventions (Higginson et al. 2013).

Building on the MRC guidance, MORECare involved systematic literature reviews, transparent expert consultations (involving consensus methods of nominal group and online voting), and stakeholder workshops to identify challenges and best practice in palliative and end-of-life research (Higginson et al. 2013). The transparent expert consultations identified three shortcomings for the MRC guidance:

- Moving from feasibility and piloting to implementation without robust evaluation;
- Failing to develop the feasibility of the evaluation methods alongside the feasibility of the intervention;
- Lack of a theoretical framework underpinning interventions.

There is a need to build simultaneously the intervention and research methods and consider implementation at all phases of evaluation rather than only at the end (Higginson et al. 2013). The findings were synthesized to develop a guidance statement (the MORECare statement) on the best methods to research end-of-life care. The statement provides a first step in setting common, much-needed standards for evaluative research in palliative and end-of-life care. It is designed to be used alongside existing reporting statements, e.g., CONSORT and STROBE. The MORECare statement is relevant to all research stakeholders, researchers, funders, ethical committees, and editors, and presents 36 best practice solutions to improve study quality and set the standard for future research. In addition it

includes 13 recommendations to improve the national/international environment for complex intervention research in palliative and end-of-life care (Higginson et al. 2013). The recommendations focus in particular on five key areas of uncertainty, as identified by the literature reviews, of: ethics (Gysels et al. 2013); outcome measurement (Evans et al. 2013a); statistics (managing missing data and attrition) (Preston et al. 2013); mixed methods research (Farquhar et al. 2013); and health economics (Preston et al. 2012). We discuss ethics, outcome measurement, and statistics in more detail below.

Participation and Ethics – Whether patients who are at the end of their lives should be invited to participate in research has been debated (Casarett and Karlawish 2000; Gysels et al. 2012, 2013). It can be difficult to obtain informed consent in circumstances where time is restricted, and patients may have fluctuating/declining mental capacity (Vig et al. 2010). In such situations the likely influence of family members on research participation must be considered, and their concerns must be addressed. These ethical issues must be taken into account when designing and evaluating complex interventions in palliative and end-of-life care. The MORECare transparent expert consultation reasoned that it can be unethical to assume that patients should not be offered research opportunities purely because they have advanced disease (Higginson et al. 2013). In fact there is evidence suggesting patients and families are willing to engage in research near the end of life and find it a positive, rewarding experience (Gysels et al. 2012). Steps should be taken during the study design stage to ensure studies are flexible and researchers are equipped with methods that can enable patients and carers to participate (Gysels et al. 2012).

Box 2 MORECare Considerations for Participation and Ethics

- Work within legal frameworks on mental capacity and consent to ensure that those who may benefit from interventions are offered the opportunity to participate.
- Collaborate with patients and caregivers in the design of the study, vocabulary used in explaining the study, consent procedures, and any ethical aspects.
- Attend the ethics committee meeting with a caregiver or patient to help the committee better understand the patient perspective.
- Ensure proportionality in patient and caregiver information sheets, appropriate to the study design and level of risk, as excessive information in itself can be tiring/distressing for very ill individuals.
- Adjust eligibility criteria to recruit those patients who may benefit most from the intervention, ensuring equipoise.

Taken from Higginson et al. (2013)

Outcome measurement – Outcomes in palliative and end-of-life care can be equally as complex as interventions. There is a need to capture change in needs across a variety of functional domains (physical, emotional, social, and spiritual) at a time when participants may be deteriorating rapidly or approaching death. In both research and clinical practice, multiple measures exist including many which have often not been validated in palliative care populations (Harding et al. 2011). The use of outcome measures which have not been developed or validated in palliative care populations, compromises the evaluation of intervention/service effectiveness (Harding et al. 2010; Tang and McCorkle 2002; Zimmermann et al. 2008). The nature of palliative and end-of-life care requires outcome measures with properties that accommodate multiple domains of care, change over time and increasing levels of debility, the use of proxies, and the timing to detect change (Evans et al. 2013a). The MORECare transparent expert consultation identified three main areas which are of critical importance for the evaluation of palliative care interventions: priority measurement properties, incorporating proxy data, and identifying time points. These aspects each

require careful consideration during the development and feasibility/piloting phases.

Box 3 MORECare Considerations for Outcome Measures

- Choose outcome measures which:
  - Have established validity and reliability in the relevant population;
  - Are responsive to change over time;
  - Capture clinically important data;
  - Are easy to administer and interpret;
  - Are applicable across care settings (e.g., patients' home, hospital, hospice);
  - Are able to be integrated into clinical care;
  - Minimize problems of response shift.
- Consider including patients' experience of care.
- Select time points of outcome measurement to balance the value of early recording, to reduce attrition, but to allow enough time for the intervention to have had an effect.
- Consider the potential effect of response shift (that is, a change in a person's internal conceptualization of the aspects measured). Questionnaires that include anchor points or descriptions of each response category may be less problematic.

Taken from Higginson et al. (2013)

Missing data – Attrition and missing data are inevitable in palliative and end-of-life care research. A recent systematic review of missing data in published RCTs of palliative care interventions found 23% of data was missing for the primary endpoint of included studies (Hussain et al. 2016). This level of missing data can make statistical analysis problematic, especially when evaluating complex interventions as it results in the loss of statistical power and the introduction of bias. When designing studies in palliative and end-of-life care, it is recommended that high rates of attrition should not be seen as indicative of poor design (Preston et al. 2013). The causes of "missingness" should be clearly recorded, and an analysis plan should consider how to account for missing data and attrition based on cause. In keeping with the considerations for the choice of outcome measurement, data from proxies may be used to account for missing data as appropriate. The feasibility/piloting phase can provide valuable estimates of attrition which may occur in a full-scale evaluation, and these should be used to test and model the impact of different forms of imputation.

Box 4 MORECare Considerations for Missing Data and Attrition

- Estimate in advance levels of, and reasons for, attrition and missing data, integrating these into sample size estimates and planned collection of data from proxies.
- Monitor and report all levels of, and reasons for, attrition and other missing data.
- Assume missing quantitative data not to be at random unless proven otherwise.
- Test results from different methods of imputation – noting that "using only complete cases" is a form of imputation.
- Use the MORECare classifications of attrition: attrition due to death (ADD), attrition due to illness (ADI), and attrition at random (AaR).
- Consider reasons for missing data which are not due to attrition, and consider these in the analysis and the potential imputations.

Taken from Higginson et al. (2013)

6 Real Case Examples

The examples below demonstrate the successful use of an iterative and phased approach to developing complex interventions in palliative care. The knowledge in each stage of development

helps build and improve the design, execution, and generalizability of these large-scale effectiveness trials.

The OPTCARE Neuro Trial – This is a multicenter, mixed methods Phase III trial investigating the clinical and cost-effectiveness of short-term integrated palliative care (SIPC) for patients with long-term neurological conditions. The SIPC being trialed is a complex intervention in that it:

- Contains several components (assessment, symptom management, future care planning, follow-up visits);
- Aims to change behaviors by those staff delivering the intervention, those providing usual care to this patient group, and some changes on the part of patients and families;
- Targets patients, families, and staff in primary, hospital, and voluntary care, thus including different groups and organizational levels;
- Has several complex outcomes, including change in symptom management and hospital admissions;
- Is tailored to individual patient need and circumstances by those delivering the SIPC;
- Operates in a context where there may be some variability between patient groups and settings in the usual care provided to patients with long-term neurological conditions.

The SIPC was developed following the MRC guidance and modelled on previous work. This included a literature review (Gruenewald et al. 2004) and qualitative studies (Edmonds et al. 2007a, b) to determine need and to develop the theoretical underpinning of the intervention, appraisal of trial methods (Higginson et al. 2006a, b), service modelling, and a successful phase II trial randomizing 52 patients (Edmonds et al. 2010; Higginson et al. 2008, 2009). The main trial will randomize 356 patients with a range of long-term neurological conditions, a sample size which accounts for 20% attrition in keeping with recent evidence and the MORECare considerations.

Following MORECare recommendations, the trial has involved a patient and public involvement group at all stages with a particular emphasis on the vocabulary used in explaining and promoting the trial. In the early stages of the trial, further development work included a mapping exercise (van Vliet et al. 2016) and an online survey of professionals (Hepgul et al. 2017) in order to explore the current levels of integrated working between palliative care and neurology services. The complexity of delivering and evaluating a palliative care intervention requires the accumulation of knowledge from multiple sources and will depend on interprofessional behaviors (Craig et al. 2008; Evans et al. 2013b). Furthermore, the effects of an intervention may be dependent on the existing clinical context and provider factors (Lewin et al. 2017). It is therefore valuable to explore clinicians' views and opinions when implementing and evaluating emerging services and informing future requirements. The recruitment of participants into the trial as well as the delivery of the intervention has relied heavily on "buy-in" from clinicians, and so this early work exploring their views has contributed greatly to building good working relationships. As this is a multicenter trial, a key aspect of evaluating the intervention will be implementation fidelity. The SIPC requires individualized care and may become ineffective if any of its vital interacting components are left out. Therefore, understanding how to maintain and improve implementation fidelity in palliative care is especially important in order to avoid errors of poor implementation of complex interventions (Ang et al. 2017).

The Breathlessness Intervention Service (BIS) – This program of work aimed to establish the effectiveness and cost-effectiveness of a Breathlessness Intervention Service (BIS) as compared to standard care, for patients with advanced cancer or non-cancer conditions. The program followed the MRC framework for the development and evaluation of complex interventions. The preclinical phase included a literature review followed by a qualitative study which explored the experience of breathlessness for patients and carers living with cancer or COPD. This provided the evidence around the need for the intervention, its role, and the way it should work, for example, it should be community based and address carer, as well as patient need (Booth et al. 2003). This was

followed by a Phase I qualitative evaluation of the first model of the BIS (Booth et al. 2006), the results of which led directly to the refinement of the complex intervention to be tested in a Phase II exploratory trial (Farquhar et al. 2009, 2010). In addition, the Phase I data informed the choice of primary outcome for the Phase II RCT: patient distress due to breathlessness.

The Phase II used a mixed methodology which integrated qualitative interviews with quantitative outcome measures for patients and carers as well as qualitative interviews with referrers to, and providers of, the intervention. The development and evaluations of complex interventions in palliative care benefit from the application of mixed methodology as this can provide evidence from a variety of sources, enabling better understanding of how an intervention does or does not work and inform the design of subsequent studies (Farquhar et al. 2011). Indeed, this mixed methods approach allowed for further refinement of the BIS, for example, it provided evidence that the length of intervention should be reduced – an important finding for a palliative care intervention. The BIS subsequently underwent a Phase III RCT with two sub-protocols: one for advanced cancer and one for advanced nonmalignant disease (due to differing service models) (Farquhar et al. 2014, 2016).

7 Conclusion and Summary

Developing and evaluating complex interventions in palliative and end-of-life care involves overcoming many challenges. The complexity involved requires the accumulation of knowledge to fully understand the processes and mechanisms of palliative care interventions. Evaluations provide important information irrespective of trial outcome. If a trial is negative, it can be unclear if that was due to the intervention being truly ineffective or whether the intervention was poorly applied or used in an inappropriate context. If a trial demonstrates a positive effect, it can be hard to judge how the results of the trial might be applied to a different context if the active ingredients and mechanisms are not well understood (Campbell et al. 2007). The use of an iterative and phased approach where knowledge can build should improve the design, execution, and generalizability of large-scale effectiveness trials. Mixed methods can be employed at all phases of development and evaluation. The MORECare statement sets clear standards on best research practice in evaluating services and treatments in palliative and end-of-life care. It emphasizes the need for considerations about implementation to be integrated into all phases of evaluation rather than only at the end. This approach ensures that when the intervention is ready to be implemented more widely, it is feasible, and the context and processes of implementation are understood, planned for, and resourced (Higginson et al. 2013).

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Mixed Method Research in Palliative Care

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Catherine Walshe

Contents

Abstract

This chapter focuses on the use of mixed methods research designs in palliative care. Mixing methods is increasing in popularity as a research approach, but study quality can be poor. This chapter highlights key issues and resources for those interested in mixed methods research, to encourage researchers to focus on important principles and debates to inform study planning. First, the defining features of mixed methods research are explored and definitions presented. Second, the paradigm challenges of mixed methods research are discussed, with a focus on current epistemological thinking in the area. Third, the issues of design are presented. This includes consideration of the purpose of mixed methods studies, a continuum of study characteristics, and a typology of core mixed methods designs. Approaches to mixing data are given particular consideration. Barriers to high-quality mixed methods studies are presented and recommendations on mixed methods research in palliative care discussed. Throughout, contemporary examples from palliative care mixed methods research are used to illustrate key points.

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_109

1 Introduction

Humans, it is argued, are intuitively mixed methods researchers. When we make decisions in our day-to-day lives, we frequently draw from a range of data sources. For example, when making a decision on which household appliance to purchase, we may turn to quantitative data such as energy efficiency ratings, price, or customer review ratings. We are also likely to be influenced by qualitative data such as feedback from friends and colleagues about their experiences and decisions. Our final choice will probably involve weighing up these different strands of information. Mixed methods research can tap into that instinctive approach to understanding the world around us and is gaining popularity with funders and researchers, although it still represents less than 3% of published health services research (O'Cathain et al. 2007; Coyle et al. 2016; Wisdom et al. 2012). Mixed methods research is, essentially, shorthand for research that uses qualitative and quantitative research approaches within a single project, where there are likely a combination of methods and where the data are mutually illuminating, and inferences are drawn using both (or multiple) approaches (Bryman 2012; Tashakkori and Cresswell 2007). This integration is frequently seen as vital, as without it the contribution to knowledge is the same as that from a qualitative and quantitative study undertaken independently, rather than the whole being the sum of the parts (O'Cathain et al. 2010).

The focus of this chapter is to explore the issues associated with mixed methods research, highlight important debates, present essential information, and illustrate with examples from palliative care research. The focus is on why, when, and how mixed methods research can be appropriately used in palliative care, to facilitate apt research choices and enable high-quality, impactful work. While much of the focus of this chapter is on research involving empirical data collection, mixed method systematically constructed research reviews are also possible, and similar considerations apply (Pearson et al. 2015; Sandelowski et al. 2012).

2 Defining Mixed Methods Research

Mixed methods research is often characterized as a "third" methodological movement or paradigm, following the examinations and developments of quantitative and qualitative research (Tashakkori and Teddlie 2010; Johnson and Onwuegbuzie 2004). There is clear evidence of an evolving trajectory of thinking about what mixed methods research is and how it is characterized. The focus of definitions has shifted and developed from those focusing on methods to methodology, philosophy, purpose, and characteristics (Creswell and Plano Clark 2018). An analysis of 19 definitions of mixed methods research identified a number of important themes within existing definitions, which are explored in Box 1 (Johnson et al. 2007).

Box 1 Analysis of Definitions of Mixed Methods Research

What is mixed: Qualitative and quantitative research but may also include within paradigm mixing (e.g., two forms of qualitative research).

The mixing stage: May occur at data collection, analysis, or throughout the research phases. Some considerations that there are perspectives on the same research question.

Breadth: Definitions can encapsulate mixing of data, mixing at all stages, and mixing of worldviews and paradigms.

Why mixing occurs: Definitions include a number of purposes for mixing including breadth, corroboration, understanding, validation, and social justice.

Orientation: Some definitions are "bottom-up," where the research question drives the approach, others are "top-down" where the philosophy or paradigm of the researcher drives the approach.

Johnson et al. (2007, pp. 118–123)

Johnson et al. (2007) conclude by offering a general definition:

> Mixed methods research is the type of research in which a researcher or team of researchers combines elements of qualitative and quantitative research approaches (e.g., use of qualitative and quantitative viewpoints, data collection, analysis, inference techniques) for the broad purposes of breadth and depth of understanding and corroboration.
>
> This definition refers to mixed methods research as a type of research:
>
> A mixed methods study would involve mixing within a single study; a mixed method program would involve mixing within a program of research and the mixing might occur across a closely related set of studies. (Johnson et al. 2007, p. 123)

What this definition does not address, however, is an understanding of the social world, and worldview, of the researcher nor an acknowledgment of the importance of paradigmatic, epistemological, or ontological issues in this field. These issues are explored in the writings of Jennifer Greene (2006, 2007, 2008). She argues that a methodology for social inquiry engages four domains of issues and assumptions: philosophical assumptions and stances, inquiry logics, guidelines for practice, and sociopolitical commitments in science (Greene 2006). These issues are debated later in this chapter, but the argument that mixed methods offer different ways of framing an understanding of the world is important to acknowledge in definitions. Mixed methods research draws on the strengths and perspectives of different methods, recognizing the existence and importance of the physical, natural world as well as the importance of reality and influence of human experience (Johnson and Onwuegbuzie 2004).

Creswell and Plano Clark (2018) and Creswell et al. (2011) offer a number of evolving definitions which incorporate these core characteristics, including a highly cited definition provided as part of commissioned guidance for the National Institutes of Health and which is used in this chapter:

Mixed methods research will be defined as a research approach or methodology:

> focusing on research questions that call for real-life contextual understandings, multi-level perspectives, and cultural influences; employing rigorous quantitative research assessing magnitude and frequency of constructs and rigorous qualitative research exploring the meaning and understanding of constructs; utilizing multiple methods (e.g., intervention trials and in-depth interviews); intentionally integrating or combining these methods to draw on the strengths of each; and framing the investigation within philosophical and theoretical positions. Creswell et al. (2011 p. 4)

3 Foundations of Mixed Methods Research: History and Philosophy

A good overview of the evolution of mixed methods is provided by Creswell and Plano Clark (2018), who identify five overlapping stages. They characterize these stages as formative (arguing for the use of mixed methods), the paradigm debate (discussing stances, reconciliation), procedural development (rationales, design, typologies), expansion (positioning as a distinctive approach), and reflection and refinement (mapping onto frameworks, critique, presenting new paradigms). Despite these stages, the existence of mixed methods studies is not new but has not always been explicitly labelled as such (Pelto 2015). Suffice to say here that palliative care researchers interested in adopting mixed methods may wish to consider these developments, so that their work is grounded in contemporary understandings of mixed methods approaches. As with most areas of health service research, there has been an expansion in the use of mixed methods approaches in palliative care, but not necessarily with an explicit description of how developments in the ways that mixed methods are conceptualized have informed designs (Farquhar et al. 2011a). A more important focus for this chapter is the exploration of philosophical and theoretical debates in mixed methods research and a consideration of how this can and should shape palliative care research in the field.

A framework for how to consider different domains of thinking associated with issues of ontology, epistemology, methodology, design, and purpose is offered by Jennifer Greene (2008) and outlined in Table 1, together with key questions for consideration.

Table 1 A framework for social science methodology

Domain	Descriptor	Issues for mixed methods research
Philosophical assumptions and stances	Philosophical and theoretical stance. Anchored in philosophy of science and includes assumptions about *ontology* (nature of social world) and *epistemology* (social knowledge)	Is it possible to hold competing or contrasting assumptions?
		What influences the decisions made by researchers in the field?
		Is mixed methods an alternative paradigm itself?
Inquiry logics	Justificatory logic. The *methodology* considerations, such as purpose, question, and design which are internally congruent and coherent	How best can methods follow purpose and question?
		How can research designs be developed and better focus on integration?
		How do we judge the quality of mixed methods research?
Guidelines for practice	Practical advice. The "*how to*" of research, with guidance on specifics such as sampling, data collection, etc.	How best to mix different approaches?
		How to choose best methods in an inquiry context?
Sociopolitical commitments	Location of the design in society The *interests* and *purpose* of the research in *context*	Is mixed methods a distinctive methodology?

Derived from Greene (2008)

The arguments against mixed methods research primarily fall into the epistemological domain. Some consider that because qualitative and quantitative research are believed to be separate paradigms, encapsulating different ways that the world can be understood and interpreted, it is not possible, or desirable, to mix them (Bryman 2012). While there are technical arguments associated with this debate, with discussions of the practical aspects of data collection and analysis, understanding arguments associated with a paradigmatic debate is an important conceptual first step for a researcher. A number of different positions have been articulated (Greene 2008; Creswell et al. 2011):

PURIST STANCE: The assumptions of qualitative and quantitative research are incompatible, and so it is not possible to combine them in research. The paradigms are coherent wholes that must be respected (Lincoln and Guba 1985; Sale et al. 2002).

COMPLEMENTARY STRENGTHS STANCE: Rather than seen as incompatible, paradigms have valuable differences that should be maintained. Methods are kept separate from one another, but within a single study (Brewer and Hunter 1989; Morse 2003).

DIALECTIC STANCE: Paradigmatic assumptions are different and valuable, but the paradigms are historical and social constructions and are not immune to change. Engagement can bring new, transformative, insight, but must be made explicit (Greene 2007, 1997; Maxwell and Loomis 2003; Greene and Hall 2010). *Dialectical pluralism suggests that different world views should be carefully considered, stakeholder values should guide projects, and collaborations conducted with attention to fairness, justice and equality* (Burke Johnson and Stefurak 2013; Stefurak et al. 2015).

*ALTERNATIVE PARADIGM: Emergent paradigms (*e.g. *pragmatism, realism, transformative) actively promote mixing of methods* (Johnson and Onwuegbuzie 2004). *This thinking has been expanded to a consideration of a 'best' worldview for mixed methods* (Creswell and Plano Clark 2018). *Some authors privilege pragmatism as an approach that prioritises the question over the paradigm, focusing on 'what works', and recommend abandoning*

a dichotomy between approaches (Morgan 2007; Florczak 2014). *Others suggest transformative paradigms* (Mertens 2003)*, or critical realism* (Maxwell and Mittapalli 2010) *as perspectives which support aspects of combining qualitative and quantitative approaches.*

A-PARADIGMATIC STANCE: Assumptions of paradigms are logically independent, and hence can be mixed. Priority given to demands of the research problem (Patton 2002). *Worldviews may relate to different designs, related to different project phases, but need to be explicit* (Creswell and Plano Clark 2018). *These views may be tied to a common perspective from the community of scholars relevant to the research, who form a shared identity, with common problems* (Morgan 2007; Denscombe 2008).

SUBSTANTIVE THEORY STANCE: Paradigmatic assumptions embedded with or intertwined with substantive theories relevant to conduct of study. They enable thinking, but do not guide practice.

Contemporary thinking on mixed methods tends toward adopting dialectic, pragmatic, realistic, or transformative approaches. Examples of mixed methods studies guided by the realist, pragmatic, and transformative perspectives are summarized in Tables 2, 3, and 4.

4 Mixed Method Research Designs

Mixed methods study designs should take account of standard considerations when planning any robust research study, and each study is likely to have unique features. However, there are concepts that are particular to, or emphasized within, mixed methods research studies that require attention. First, the purpose of the mixed methods study needs to be considered. Second, operationalising a continuum of study characteristics. Third, selecting a core design from a typology of studies. These are now considered in turn.

4.1 Purpose of Mixed Methods Research

Five primary purposes of mixed methods research have been determined, based on a conceptual framework developed from theoretical literature and refined through the analysis of 57 empirical mixed method evaluations:

Table 2 Example palliative care study using a REALIST perspective

Question/aim	To find if how and under what circumstances palliative care registrations are made for patients with nonmalignant diseases in primary care
Design	GP practice data were analyzed statistically, and qualitative data was collected from healthcare professionals and members of relevant organizations
Perspective	Realism
Findings	The Integrated Care Pathway began to enable the reduction of inequalities in care by identifying, registering, and managing an increasing number of palliative patients with nonmalignant diseases. Consensual and inclusive definitions of palliative care were developed in order to legitimize the registration of such patients
Contribution of mixed methods	Mixed methods uncovered not only whether palliative care registrations are increasing but also for whom, by what means, and in which circumstances
Key references	Dalkin SM, Jones D, Lhussier M, et al. Understanding integrated care pathways in palliative care using realist evaluation: a mixed methods study protocol BMJ Open 2012;2:e001533. https://doi.org/10.1136/bmjopen-2012-001533
	Dalkin SM, Lhussier M, Philipson P. et al. Reducing inequalities in care for patients with non-malignant diseases: Insights from a realist evaluation of an integrated palliative care pathway. Palliat Med 2016;30(7):690–697
	(Dalkin et al. 2012, 2016)

Table 3 Example palliative care study using a PRAGMATIC perspective

Question/aim	To examine the use of specialist palliative care in relation to age, after controlling for need
Design	Mixed methods: focused ethnography of specialist palliative care services, systematic literature review, cross-sectional survey
Perspective	Pragmatic philosophy, drawing upon a health capability account of equitable healthcare
Findings	The findings suggest equitable use of specialist palliative care. However, a comprehensive account of equity must consider both use and quality of care. There were some suggestions that, within a resource-limited context, the quality of care may vary
Contribution of mixed methods	Mixed methods enabled broader research questions and deeper inferences. Ideas about need were interwoven with need measurement. Pragmatic grounding enabled use of best-fit methods to answer questions
Key references	Burt JA. Equity, need and access in health care: a mixed methods investigation of specialist palliative care use in relation to age. Doctoral thesis, UCL (University College London). 2010 http://discovery.ucl.ac.uk/19633/1/19633.pdf [accessed 12.10. 17]
	Burt JA, Plant H, Omar R, Raine R. Equity of use of specialist palliative care by age: cross-sectional study of lung cancer patients. Palliat Med. 2010; 24(6):641–50 https://doi.org/10.1177/0269216310364199
	Burt J, Raine R. The effect of age on referral to and use of specialist palliative care services in adult cancer patients: a systematic review, Age Ageing. 2006; 35(5):469–76, https://doi.org/10.1093/ageing/afl001
	(Burt 2010; Burt et al. 2010; Burt and Raine 2006)

Table 4 Example palliative care study using a TRANSFORMATIVE perspective

Question/aim	To report the meta-synthesis of a research project investigating delirium epidemiology, systems of care, and nursing practice in palliative care units
Design	A two-phase sequential transformative mixed methods design with knowledge translation as the theoretical framework. The project answered five different research questions about delirium epidemiology, systems of care, and nursing practice in palliative care units. Data integration and meta-synthesis occurred at project conclusion
Perspective	Transformative
Findings	There was a moderate to high rate of delirium occurrence in palliative care unit populations; and palliative care nurses had unmet delirium knowledge needs and worked within systems and team processes that were inadequate for delirium recognition and assessment. The meta-inference of the DePAC project was that a widely held but paradoxical view that palliative care and dying patients are different from the wider hospital population has separated them from the overall generation of delirium evidence and contributed to the extent of practice deficiencies in palliative care units
Contribution of mixed methods	The meta-inference was that a widely held but paradoxical view that palliative care and dying patients are different from the wider hospital population has separated them from the overall generation of delirium evidence and contributed to the extent of practice deficiencies in palliative care units
Key references	Hosie A, Agar M, Lobb E, Davidson PM, Phillips J. Online First. Improving delirium recognition and assessment for people receiving inpatient palliative care: a mixed methods meta-synthesis. Int J Nurs Stud. https://doi.org/10.1016/j.ijnurstu.2017.07.007
	Hosie et al. (2017) https://www.journalofnursingstudies.com/article/S0020-7489(17)30157-8/fulltext

triangulation, complementarity, development, initiation, and expansion (Greene et al. 1989).

1. ***Triangulation:*** *This implies convergence, corroboration, correspondence of results from different methods. The emphasis can be on seeking corroboration between qualitative and quantitative data.*
2. ***Complementarity:*** *This implies elaboration, enhancement, illustration or clarification of*

Table 5 Example palliative care study for a DEVELOPMENT purpose

Question/aim	To refine and evaluate a practical, clinical tool (SPICT) to help multidisciplinary teams in the UK and internationally, to identify patients at risk of deteriorating and dying in all care settings
Design	Participatory research with ongoing peer review process via an open-access web page, followed by prospective case-finding study in an acute hospital
Perspective	Instrument development
Findings	The SPICT was refined and updated to consist of readily identifiable, general indicators relevant to patients with any advanced illness and disease-specific indicators for common advanced conditions
Contribution of mixed methods	Enabled second phase of case finding to be informed by international development work
Key references	Highet G, Crawford D, Murray SA et al. Development and evaluation of the supportive and Palliative Care Indicators Tool (SPICT): a mixed-methods study BMJ Support Palliat Care 2014;4:285–290. (Highet et al. 2014)

findings from one method with the results from another. Methods can be used to explore different aspects of phenomena to yield an elaborated understanding or explanation. This may include off-setting weaknesses of some approaches (Bryman 2006). *Complementarity differs from triangulation, as convergence requires that methods assess the same phenomenon.*

3. ***Development:*** *This implies sequential use of results from one method to help develop or inform the other method. This may include instrument development, or development of sampling approaches* (Bryman 2006).
4. ***Initiation:*** *This implies discovery of paradox and contradiction, such that results from one method can inform changes in the other. These may emerge rather than be a planned intent, or be intentionally analysed for fresh insights.*
5. ***Expansion:*** *This seeks to extend breadth and range by using different methods for different or multiple components. For example, qualitative methods can be used to assess processes and quantitative methods to assess outcomes, or qualitative data to generate hypotheses, and quantitative data to test them* (Greene et al. 1989).

When this categorization was used to explore health services research, the main purposes were complementarity, expansion, and development (O'Cathain et al. 2007), while triangulation and expansion were common in social sciences (Bryman 2006). Inherent in this categorization of purpose is that some imply fixed designs, planned in advance, and others a more flexible or emergent approach where the use of mixed methods develops or commences during the research (Creswell and Plano Clark 2018). Researchers should be clear and explicit about the purpose of their study and why a mixed methods design is appropriate to meet this purpose. A critique of this categorization is that it focuses too much on analysis (Collins et al. 2006). Example palliative care studies, categorized by the purpose of the study, are summarized in Tables 5 and 6.

4.2 The Characteristics of Mixed Methods Research

Once the overarching purpose of the research is determined, attention can be paid to specific design characteristics of the study. These are often typified on a sliding scale, continuum, or dichotomy depending on the specific characteristic and the choices available within that characteristic. Greene et al. (1989) identified seven characteristics in their study: methods, phenomena, paradigms, status, independence, timing, and study. These are displayed in Table 7, interspersed with three exemplars from palliative care research. These are a study of a breathlessness intervention (Farquhar et al. 2009, 2011b, 2014, 2016), a study of spiritual well-being (Selman et al. 2013),

Table 6 Example palliative care study for a CONVERGENT, TRIANGULATION purpose

Question/aim	To investigate the interactions between organization and culture as conditions for integrated palliative care in hospital and to suggest workable solutions for the provision of generalist palliative care
Design	A convergent parallel mixed methods design. Two independent studies: a quantitative study, in which three independent datasets were triangulated to study the organization and evaluation of generalist palliative care, and a qualitative, ethnographic study exploring the culture of generalist palliative nursing care in medical department
Perspective	Theories of integrated care, convergent design
Findings	Two overall themes emerged: (1) "generalist palliative care as a priority at the hospital," suggesting contrasting issues regarding prioritization of palliative care at different organizational levels, and (2) "knowledge and use of generalist palliative care clinical guideline," suggesting that the guideline had not reached all levels of the organization
Contribution of mixed methods	Valuable in addressing the complexity of palliative care provision in hospital culture and organization
Key references	Bergenholtz H, Jarlbaek L, Hølge-Hazelton B. Generalist palliative care in hospital – Cultural and organisational interactions. Results of a mixed-methods study. Palliat Med. 2016;30(6):558–66 (Bergenholtz et al. 2016)

Table 7 The characteristics of mixed methods research

SIMILAR	***Methods***	DIFFERENT
	Degree to which methods selected are similar to or different from each other in form, assumptions, strengths, or limitations (Greene et al. 1989). Most health service studies prioritized quantitative methods or gave equal weighting to methods. Rare that qualitative methods given priority (O'Cathain et al. 2007)	
DIFFERENT: Farquhar et al., used a wait-list randomized controlled trial and qualitative interviews		
SIMILAR: Selman et al. used cognitive interviews and outcome scales		
DIFFERENT: Morita et al. used a pre-post survey study and qualitative interviews and focus groups		
SAME	***Phenomena***	DIFFERENT
	Degree of intention to assess different, similar, or the same phenomena. This can be caused by a response to different research questions. Mixed methods tend to be used with broad and complex questions, with multiple facets (Tariq and Woodman 2013)	
SIMILAR: Farquhar et al. investigated the phenomena of both response to treatment (same) and the experience of treatment (different)		
SIMILAR: Selman et al. investigate constructs of peace and well-being through two different means		
DIFFERENT: Morita et al. examine a complex range of outcome and process phenomena		
SAME	***Paradigms***	DIFFERENT
	Degree to which different method types implemented within same or different paradigms. This is a dichotomous choice	
DIFFERENT: Farquhar et al. used a trial and qualitative interviews from different paradigms		
SIMILAR: Selman et al.'s cognitive interviewing and outcomes both examined different aspects of validity		
DIFFERENT: Morita et al. used a pre-post survey and qualitative data collection from different paradigms		
EQUAL	***Status***	UNEQUAL
	Degree to which methods have equally important or central roles to meet the study objectives	
UNEQUAL: Farquhar et al. give prominence to trial results in reporting		
EQUAL: Selman et al. give equal weight to both methods in reporting		
UNEQUAL: Morita et al. give prominence to survey data in reporting		

(*continued*)

Table 7 (continued)

INTERACTIVE	***Independence***	INDEPENDENT
	Continuum of how qualitative and quantitative methods are conceptualized, designed, and implemented interactively or independently	
INTERACTIVE: Farquhar et al. appear to have designed and implemented the methods interactively		
INTERACTIVE: Selman et al. appear to have designed and implemented the methods interactively		
INDEPENDENT: Morita et al. appear to have conducted the methods in independent phases		
SEQUENTIAL	***Timing***	SIMULTANEOUS
	Methods typically implemented concurrently or sequentially but can be interspersed. Decisions important on sequencing and timing (Morgan 1998)	
SIMULTANEOUS: Farquhar et al. conduct data collection using multiple methods simultaneously		
SIMULTANEOUS: Selman et al. conduct data collection using multiple methods simultaneously		
SEQUENTIAL: Morita et al. conduct data collection sequentially, but with qualitative and quantitative methods interspersed		
MULTIPLE	***Study***	ONE
	Categorical choice between one or multiple studies. Typically one study	
ONE STUDY: Farquhar et al.'s study is a single study		
ONE STUDY: Selman et al.'s study is a single study		
SINGLE STUDY: Morita et al.'s study appears to be a single study, although the protocol recognizes design changes over time		

Greene et al. (1989), Farquhar et al. (2009, 2011, 2014, 2016), Selman et al. (2013), Morita et al. (2012, 2013), and Morgan (1998)

and the study of a program of interventions on palliative care for people with cancer (Morita et al. 2012, 2013).

4.3 Typology of Mixed Methods Research

Many authors have created typologies of mixed methods designs, including those who have changed and refined their typology over time (Creswell and Plano Clark 2018). Creswell and Plano Clark (2018) tabulate 15 typologies, and their own four iterations, refined over time. Their current typology has three core designs: explanatory sequential, exploratory sequential, and convergent designs. These are summarized in Table 8. They consider these parsimonious and practical, positing that one or more of these three core designs are at the heart of a mixed methods study. The labels reflect the *primary intent* of the researcher for using and integrating data – intent being the outcome that the researcher hopes to attain by mixing data. Intent is implied with the first label (e.g., explanatory, exploratory, and convergent). The sequencing of data is reflected in the second label (e.g., sequential). They consider that these changes shift the conceptualization from timing and sequence to purpose and intent (Creswell and Plano Clark 2018).

A review of mixed methods studies in healthcare published between 1999 and 2009 identified 168 papers, primarily from the USA, the UK, and Canada, categorized using an earlier typology of Creswell and Plano Clark (Östlund et al. 2011). Most common ($n = 98$) were approaches using parallel analysis, but with little articulation of purpose, method status, or expected outcomes. Other studies used sequential approaches ($n = 46$) both explanatory and exploratory, but concurrent approaches were rarer. Their critique of the papers highlights the lack of explicit theoretical assumptions and poor clarity on whether the conclusions primarily stemmed from qualitative or quantitative findings (Östlund et al. 2011).

The use of each of these core designs is now discussed with a worked example in palliative care.

4.3.1 Convergent Design

This design is illustrated with a study developing and evaluating the Dignity Talk framework for

Table 8 Outline of three core mixed methods research designs

Design	Features
Convergent design (previously called concurrent or parallel design)	To bring together results of quantitative and qualitative data analysis. Comparison may bring more complete understanding, validate one set of findings with another, etc.
	Example: conducting survey and focus group on same topic with similar group(s) of people. Separately analyzed, but datasets compared to see similarity and difference
	Also called simultaneous triangulation, parallel study, convergence model, concurrent triangulation
Explanatory sequential design (or explanatory design)	Occurs in two distinctive interactive phases. Starts with collection and analysis of quantitative data, followed by collection and analysis of qualitative data to explain or expand on first phase results
	Example: collect survey data on one topic, but find surprising association in data. Conduct focus group targeted at those who experience particular phenomenon to attempt to explain unexpected result
	Also called sequential model, sequential triangulation, qualitative follow-up, iteration design
Exploratory sequential design (or exploratory design)	Occurs in two phases but begins with and typically prioritizes the qualitative data in first phase. Quantitative feature is built on the exploratory results from the qualitative phase and typically incorporates a development phase (e.g., instrument development) followed by quantitative testing
	Example: collects interview data about a phenomenon, used to create a survey instrument, which is used to assess prevalence of activities
	Also called instrument development design

Extracted from Creswell and Plano Clark (2018)

people receiving palliative care (Guo et al. 2018) (Table 9).

4.3.2 Explanatory Sequential Design

This design is illustrated with a study designed to provide insight into what nurses know, do, and need to provide support to anxious patients in hospice care (Zweers et al. 2017) (Table 10).

4.3.3 Exploratory Sequential Design

This design is illustrated with a study to examine the effect of using the interRAI PC on the quality of palliative care in nursing homes (De Almeida Mello et al. 2015; Hermans et al. 2014, 2016, 2018) (Table 11).

4.4 Approaches to Mixing Data

The mixing of data is considered to be the most conceptually challenging and practically difficult areas of mixed methods research (Collins and O'Cathain 2009). The approach taken has to be grounded in the purpose and design of the research and occurs at different times, depending in this, as can be seen from the earlier discussions of core designs. With this in mind however, it is worth examining mixing and integrating data in more depth. Typical approaches include merging data, connecting data, building data, and embedding data (Creswell et al. 2011; Fetters et al. 2013).

Merging data is commonly used in convergent designs and implies combining both qualitative data (e.g., text) and quantitative data (e.g., numeric information). Some of the exemplar studies presented in this chapter achieve this through reporting quantitative results, followed by qualitative data that explore, support, or expand upon the quantitative data. Diagrams are also possible, for example, (Selman et al. 2013) display merged data figuratively. Different forms of data matrices or displays can also be used (Miles and Huberman 1984). Merging may also be possible through

Table 9 Palliative care example of a convergent mixed methods design

Feature	Discussion	Example
Guo Q, Chochinov HM, McClement S, Thompson G, Hack T. et al. Development and evaluation of the dignity talk question framework for palliative patients and their families: a mixed-methods study. Palliative Med. 2018 (First published 13 Nov 2017. https://doi.org/10.1177/026921631773469)		
Intent	To obtain different but complementary data on the same topic, bringing together strengths and weaknesses of quantitative and qualitative methods (Patton 2002). Also corroboration, validation	To develop a novel means of facilitating meaningful conversations for palliative patients and family members, coined Dignity Talk, explore anticipated benefits and challenges of using Dignity Talk, and solicit suggestions for protocol improvement
Reasons for choice	Facilitates collection of both data types at once, when both sorts of data needed from participants, researchers, or team have both sorts of skills	Not explicitly stated
Assumptions	Pragmatic paradigm can be appropriate, as this worldview holds with merging qualitative and quantitative data	No paradigm explicitly stated
	If multiple philosophical frameworks, should be reported	
Procedures	(a) Collect both qualitative and quantitative data on the topic. Usually concurrent but separate, often equally important	Described as a convergent parallel mixed methods design
	(b) Separate and independent data analysis	The Dignity Talk guidelines and questions were evaluated using both quantitative and qualitative data. Data were collected simultaneously and priority was given to both forms of data
	(c) Merging results through comparison or transformation, e.g., joint data display table, graphical display, transforming qualitative data into counts	Descriptive statistics were used to describe demographic data. Feedback obtained from patients and family members regarding clarity, sensitivity, relevance, and importance of Dignity Talk questions was analyzed quantitatively (endorsement rate). Chi-square analysis was employed to compare the overall endorsement rate by patients and family members. Qualitative data were analyzed line by line using the constant comparative techniques to identify recurrent themes by the first two authors. Quantitative and qualitative results were finally merged and interpreted, based on which the Dignity Talk question framework was revised
	(d) Interpretation of convergence or divergence, relationships	
Advantages and disadvantages	Efficient, can be conducted by a team, gives a voice to participants	The research team included members from psychiatry, psychology, and nursing, as well as research personnel
	Consequences of different sample sizes and merging datasets of different sizes, how to explain divergence	Strengths of the study include Dignity Talk being developed and modified based on both qualitative and quantitative data. It is one of very few psychosocial interventions targeting patient/family dyads and is meant to be self-administered by patients and families. Limitations include a relatively small sample size, although rich qualitative data were collected

Creswell and Plano Clark (2018) and Guo et al. (2018)

transforming data to the same form, mostly commonly through counting within qualitative data (Sandelowski et al. 2009). Matrices can facilitate focusing attention on cases rather than variables or themes and allow patterns to be sought (O'Cathain et al. 2010).

Table 10 Palliative care example of an explanatory sequential mixed methods design

Feature	Discussion	Example
Zweers D, de Graaf E, Teunissen S. Suitable support for anxious hospice patients: what do nurses 'know', 'do' and 'need'? An explanatory mixed method study. BMJ Supportive & Palliative Care. 2017. (Published Online First: 30 June 2017. https://doi.org/10.1136/bmjspcare-2016-001187)		
Intent	To use a qualitative strand to explain initial quantitative results, to form groups based on quantitative results, sampling	The primary aim of this mixed methods study was to gain insight into what nurses know, do, and need to support patients in hospice care suffering from anxiety. The secondary aim was to explore which additional factors influence knowledge about anxiety, performed interventions, and the needs of hospice care nurses
Reasons for choice	Teams are more quantitatively oriented, important variables are known, ability to return to participants, time for two phases, only resource to collect one type of data at a time	Not explicitly stated
Assumptions	Often greater focus on quantitative aspects, leading to positivist assumptions, but which can shift to constructivism, be dialectic	No paradigm explicitly stated
Procedures	(a) Design and implement qualitative strand, analyze	A prospective explanatory and triangulated component design was conducted using quantitative and qualitative methods
	(b) Use quantitative results to determine which results will be explained, refine qualitative questions, sampling, etc.	
	(c) Design and implement qualitative strand, analyze	An online survey was conducted to establish a broad understanding of the current practice regarding anxiety management. Data were analyzed with descriptive and inferential statistics
	(d) Interpret connected results	
		The focus groups (FGs) provided a deeper and multifaceted insight with a subset of nurses who had completed the survey. Data were analyzed using thematic analysis
		Results presented in a connected manner.
Advantages and disadvantages	Appeals to quantitative researchers, straightforward and manageable design, and reporting requirements, second phase can be emergent	The combined quantitative and qualitative approach allowed the researchers to acquire an in-depth insight into the current practices of anxiety management
	Can take time for two phases, second phase not known in advance	They report nonrandom non-response to the online survey, with a risk of socially desirable answers. However the focus groups mitigated this risk as clear from the exchange of experiences that is perceived as safe environment to share practice

Creswell and Plano Clark (2018) and Zweers et al. (2017)

Building and connecting data share some characteristics and are more common in sequential designs. Connecting involves data links through the sampling frame and building through informing data collection approaches (Fetters et al. 2013). Two techniques which may be helpful both in connecting data and merging data are the use of a triangulation protocol and following a thread (O'Cathain et al. 2010). Triangulation protocols in mixed methods research usually take place at the interpretation stages of studies, examining data for convergence, complementarity, or contradiction. Again coding matrices are recommended to display data to consider where there is agreement, partial agreement, silence, or disagreement (O'Cathain et al. 2010). Following a thread means taking a question or theme from

Table 11 Palliative care example of an exploratory sequential mixed methods design

Feature	Discussion	Example
Hermans K, Spruytte N, Cohen J, Van Audenhove C, Declercq A. Informed palliative care in nursing homes through the interRAI Palliative Care instrument: a study protocol based on the Medical Research Council framework. BMC Geriatr. 2014; 14, 132		
Hermans K, Spruytte N, Cohen J, Van Audenhove C, Declercq A. Usefulness, feasibility and face validity of the interRAI Palliative Care instrument according to care professionals in nursing homes: A qualitative study. Int J Nurs Stud. 2016; 62, 90–99		
Hermans K, De Almeida Mello J, Spruytte N, Cohen J, Van Audenhove C, Declercq A. Does using the interRAI Palliative Care instrument reduce the needs and symptoms of nursing home residents receiving palliative care? Palliat Support Care. 2018; 1–9		
Intent	Results of first, qualitative method can help develop the quantitative method that follows, e.g., to develop a new tool or intervention based on experience/culture, etc.	Main research aims:
		(a) To evaluate the effect of the interRAI PC on the quality of palliative care in nursing homes
		(b) To evaluate the feasibility of using the interRAI PC in nursing homes
		(c) To evaluate the face validity of the instrument
Reasons for choice	Used when instruments not available, variables not known, no guiding framework, need for cultural adaption of measure/tool	Not explicitly stated
	Teams are qualitatively oriented, time is available for phased study, interested in transferability of new measure/tool/intervention	
Assumptions	Can start from constructivist stance and move to post-positivist stance	No paradigm explicitly stated, but individual papers reported in a way congruent with paradigms of individual phases
Procedures	(a) Collect and analyze qualitative data to explore phenomenon	The study has a longitudinal, quasi-experimental pretest-posttest design
	(b) Identify results on which quantitative feature will be built	Care professionals evaluated the needs and preferences of all nursing home residents receiving palliative care by means of the interRAI Palliative Care instrument. Data on the usefulness, feasibility, and face validity of the interRAI Palliative Care instrument were derived from notes, semi-structured interviews, and focus groups with participating care professionals and were thematically analyzed and synthesized
	(c) Development phase (instrument, measure, intervention)	
	(d) Implement quantitative strand to examine salient variables/test with new set of participants	
		Care professionals made a series of recommendations in order to optimize the usefulness of the instrument
		A quasi-experimental pretest-posttest study was conducted to compare the needs and symptoms of residents nearing the end of their lives. Care professionals at the intervention nursing homes filled out the interRAI PC over the course of a year for all residents aged 65 years and older who were nearing the end of their lives
Advantages and disadvantages	Sequential nature straightforward, qualitative aspect acceptable to some audiences as associated with quantitative component, clear product from research	Part of a large, funded, long-term study which facilitated the use of different study phases. This also means the study is reported across different papers, which makes the mixed-method element challenging to report comprehensively
	Time-consuming, can be difficult to specify in advance, may require multiple samples, need to determine which qualitative results to use, requires skilled team	

Creswell and Plano Clark (2018) and Hermans et al. (2014, 2016, 2018)

one component and following it through across methods, and potentially phases, of a study.

A particular form of integration is seen when one of the datasets has lesser priority and is embedded within a larger design. The classic example of this is an embedded qualitative process evaluation within a trial or other evaluation designs (Grant et al. 2013; Linnan and Steckler 2002; Oakley et al. 2006). Qualitative data collection embedded within a trial is increasingly common, although still only seen in a minority of published studies, especially in palliative care, and not always well conducted or described (Lewin et al. 2009; Flemming et al. 2008). Such embedded work can occur before the trial (e.g., to generate hypotheses, refine the intervention, or develop outcome measures), during the trial (e.g., to assess fidelity, change processes, or responses to the intervention), or after a trial (e.g., to explore reasons for the findings, generate further hypotheses) (Lewin et al. 2009).

5 Barriers to High-Quality Mixed Methods

Both Bryman (2007) and O'Cathain et al. (2009) studied barriers to mixed methods and the integration of data within studies. They identify eight issues:

***Audience**: Mixed methods research is frequently written for publication as separate studies, with different parts of the research written for different audiences. An example is the research examining palliative care in nursing homes used as an exemplar earlier, reported across separate, multiple, publications* (Hermans et al. 2014, 2016, 2018). *Priority can be given to the reporting of quantitative data, particularly those from randomised controlled trials that are considered a 'gold standard' in health services research. An example here is some of my own research which mixed both randomised controlled trial and qualitative case study data, but where the trial report contained no qualitative data, as requested by reviewers* (Dodd et al. 2018; Walshe et al. 2016a, b, c).

***Methodological preferences:** Researchers can report having particular skills in, predilection towards or a greater faith in a particular approach as a component of a mixed method study.*

***Research structure:** Sometimes insufficient planning or conceptualisation of design mitigates against good data integration. Time issues in planning and conducting research can exacerbate these issues, as can funding which can limit the length of studies.*

***Timelines:** A barrier can be that results from different parts of a study are available at different times, and sometimes to different parts of the research team(s).*

***Research skills and specialisms:** Apposite skills need to be present within an individual or team. An issue to note is that the skill mix within a team may impede integration by compartmentalising roles, or privileging a particular form of data. There remain few opportunities to train in mixed methods research, and examples in the literature are scant due to the publication issues alluded to already.*

***Nature of the data:** One set of data may be more intrinsically interesting or novel.*

***Ontological divides:** Most mixed methods researchers are pragmatists, but the divide can lead to issues within teams and more widely*

***Publication issues:** The requirements of journals, funders or institutions can shape the conduct of studies, with perceived preference assumed to be quantitative studies. Guidelines to publishing mixed methods studies exist, and should be consulted* (Leech et al. 2011). *However there are few examples of mixed methods research to draw from as exemplars as less than 3% of studies in health services research are mixed methods studies* (Wisdom et al. 2012).

The challenge of reporting mixed methods research and demonstrating that it has been

conducted appropriately and rigorously is important and worth separate consideration. Methodological reviews point to deficiencies of reporting of mixed methods research, especially with regard to issues associated with rigor (Brown et al. 2015). Readers are pointed toward two resources: first the Good Reporting of a Mixed Methods Study (GRAMMS) reporting guidelines which should be used when reporting mixed methods studies (O'Cathain et al. 2008) and, second, a scoring system for mixed studies' reviews (Pluye et al. 2009).

Perhaps more complex are the debates surrounding how to ensure high quality in and subsequently judge mixed methods research. Disputes and inconsistencies are evident in understanding whether the qualitative and quantitative components of a study should be assessed separately and how to assess the "mixing" of methods and its appropriateness (Tashakkori and Teddlie 2010). One approach to rigor is legitimation, a term proposed to avoid the connotations associated with terms more usually used with purely qualitative or quantitative designs (Onwuegbuzie and Johnson 2006; Onwuegbuzie and Leech 2007). Legitimation in mixed research, rather than being viewed as a procedure that occurs at a specific step of the mixed research process, is better conceptualized as a continuous iterative, interactive, and dynamic process (Onwuegbuzie et al. 2011; Collins et al. 2012). In addition to the quality criteria inherent in GRAMMS (O'Cathain et al. 2008), quality criteria based on literature review and meta-summary are also proposed by (Fàbregues and Molina-Azorín 2017). Readers are encouraged to consider the recommendations of these writers and also directed to the textbook of Creswell and Plano Clark (2018).

5.1 Recommendations on Mixed Methods Research in Palliative Care

The MORECare study into methodological issues in palliative care research examined the use of mixed methods in this field using a transparent expert consultation design (Farquhar et al. 2013). They made nine recommendations, which they categorized as fully endorsed, partially endorsed, or refined draft recommendations (Table 12).

While the authors recognize that many of these recommendations are also apt to research outside palliative care, they also argue that mixed methods research may address some of the key challenges of palliative care research. In particular they highlight that mixed methods research approaches may mitigate some of the known issues of recruitment, attrition, respondent burden, and outcome measurement known to affect palliative care research (Higginson et al. 2014; Preston et al. 2013). They argue that this is because mixed methods could provide valuable data that could inform recruitment and sample-retention strategies, address issues of gatekeeping, and ensure that outcome measures are fit for purpose (Preston et al. 2016; White and Hardy 2008; Bausewein et al. 2016). Palliative care research often explores issues which are complex and context dependent, where interventions are complex, and with challenging ethical issues. Such complexity is likely to require research designs that are themselves more complex and mixed methods designs part of that picture.

6 Conclusions

Mixed methods research designs have much to offer the field of palliative care. Research in palliative care brings particular challenges, and the use of mixed methods can assist in ameliorating some of these. Caution must be exercised, as mixing methods requires particular considerations associated with understanding of paradigm and attention to design choices and the order and function of data collection and analysis. Hopefully there are pointers to these considerations in this chapter which will facilitate researchers in accessing resources to guide excellent mixed methods design choices. This should further the field of palliative care research and hopefully enhance the quality of palliative care in the future.

Table 12 The MORECare recommendations on mixed methods research in palliative care

Endorsement	Recommendation
Fully endorsed	Mixed methods (integrating quantitative and qualitative methods) research is a particularly useful approach for palliative and end-of-life care research: the exact choice of method will depend on the research question, and each method needs to be justified
	The degree of respondent burden needs careful consideration in palliative and end-of-life care research, and researchers should consider prioritization of key outcome measures and qualitative questions, whether splitting data collection sessions may be necessary, and the place and mode of data collection. Piloting and user involvement inform respondent burden concerns, but decisions about respondent burden should be taken with participants and not for them
Partially endorsed	Where justified, qualitative exploration of experiences of participation in randomized controlled trials and other "well-designed studies" should be carried out and should include all participant groups, e.g., patients, carers, and clinicians; this is in addition to qualitative exploration of experiences of the intervention
	Trial registers need to include fields for registration of qualitative components of the study or parallel qualitative studies, and similar non-trial registers should be established
	Depending on the research question, palliative and end-of-life care research may benefit from a multidisciplinary team-working approach; thus in most cases, teams will need to consist of requisite disciplines (clinical and academic) to answer the research question proposed
	Greater emphasis is required on implementation studies in palliative and end-of-life care research than is presently the case: this may develop naturally as the specialty establishes, but researchers should be encouraged to move from phase III RCTs to phase IV implementation studies and consider the contribution a mixed methods approach could make to them
	Researchers working on mixed methods studies need both quantitative and qualitative skills (and training) that should come from separate relevant professionals at the design stage and potentially also at the data collection stage, but given the sensitivity of research in palliative and end-of-life care, researchers conducting interviews need additional empathy and communication skills. Researchers from differing paradigms need an openness to, and understanding of, other paradigms within the team. Support and debriefing of all team members is important
Refined draft recommendations	Given the current state of (under-)development of palliative and end-of-life care research, the explicit use of theoretical perspective is encouraged from the outset, and investigators should be open to developing new theoretical frameworks for the field
	Given the nature of the sensitivities involved in palliative and end-of-life care research, there are potentially particular problems of therapeutic effects of research interviews that can be confounding: this should be considered when designing studies and interpreting findings. The lack of evidence of the nature and duration of therapeutic effects requires further research

Farquhar et al. (2013, pp. 1157–1158)

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Ethics in Palliative Care Research

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Kasper Raus and Sigrid Sterckx

Contents

Abstract

Today, there is near universal consensus on evidence-based medicine (EBM) as the preferred approach to medical practice. In palliative care, however, a strong evidence base is lacking in many respects, which could result in less than optimal care being provided to patients. Establishing a solid evidence base requires much research to be conducted in palliative care. Such research in palliative care faces both empirical and ethical challenges. In this chapter, we focus on several ethical issues and challenges that are relevant to palliative care research. Many legal and ethical

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_110

frameworks exist for dealing with research on ethical issues, but this chapter examines how these general frameworks apply more specifically to the domain of palliative care research. We will discuss the key issue of vulnerability in palliative care research. Other issues that will be touched upon are: (1) respect for research participants; (2) the need for independent review; (3) the requirement of social and/or scientific value; (4) issues related to informed consent; (5) challenges regarding scientific validity; (6) favorable risk-benefit ratio; and (7) fair participant selection. In touching upon these issues, most ethical challenges for palliative care research are examined. The chapter aims to show that although many ethical challenges may exist when conducting palliative care research, these challenges should in no way be deemed insurmountable. Research in palliative care is both needed and possible, provided sufficient attention is given to possible ethical sensibilities.

1 Introduction

Within medicine, there has been a clear paradigm shift toward the use of empirical evidence in both clinical practice and policy making. Today, there is near universal consensus on evidence-based medicine (EBM) as the preferred approach to medical practice (Sackett 1997). However, in this respect, palliative care has been argued to lag behind. The evidence base supporting palliative care is there, but is not as good as it could be (Higginson 1999). Other research suggests that there is an increasing amount of research in palliative care and that the level of evidence is rising (Tieman et al. 2008).

There are many reasons for this gap in research and evidence base. Part of it concerns the funding of palliative care research (Higginson 2016), but other factors include the challenges to conducting palliative care research that is both maximally scientifically valid and ethically justified. In this chapter, we will deal with the second of those challenges, namely, the research ethics challenges that arise when conducting palliative care research.

The need for palliative care research hardly requires justification. It is clear that more evidence is needed, as only good and solid evidence provides the best guarantee for good and ethical practices. An example is the well-known Liverpool Care Pathway for the Dying Patient which was developed in the UK as a care pathway to explore and implement good end of life care for all patients. It was widely used but sparked considerable controversy because it was seen by many as a mere tick box exercise. In 2013 an independent review found that there was no evidence on the potentially adverse events of the LCP and that "[n]o research has yet produced evidence by robustly comparing these pathways with other forms of care" (Neuberger et al. 2013). Subsequently, it was recommended that the LCP should be phased out and abandoned. This case provides a striking example of how the lack of research and evidence in palliative care might potentially lead to improper care being provided. This is but one example of the fact that there are strong ethical reasons, in addition to scientific ones, for conducting research in palliative care and thereby improving the evidence base.

Nevertheless, although necessary, palliative care research is also particularly challenging from an ethical perspective. In this chapter, we will look at some of the ethical issues that are particular to research in palliative care. Two remarks are in order. First, this chapter does not pretend to provide an exhaustive overview of all research ethics issues. Our goal is to discuss some of the most pertinent issues with regard to palliative care research. Second, this chapter does not pretend to address any of the issues at length. Each of the issues discussed in this chapter is themselves subject to considerable debate. We examine each issue in some detail and provide essential literature references for those interested in more in-depth discussions of that particular issue.

For sake of clarity, in the next two sections, we explain the focus of this chapter and the ethical framework that is used. Subsequently, we will discuss the key issue of vulnerability in palliative care research. Other issues that will be commented upon are (1) respect for research participants, (2) the need for independent review, (3)

the requirement of social and/or scientific value, (4) issues related to informed consent, (5) challenges regarding scientific validity, (6) favorable risk-benefit ratio, and (7) fair participant selection.

2 The Focus of This Chapter

To avoid conceptual confusion, we believe it is important to be clear that we will focus on palliative care research, a category which should be distinguished from other types of research that will not be our focus.

Palliative care research ought to be distinguished from the more broad category of research involving terminally ill or dying patients. Although there may be significant overlap (since much of palliative care research involves terminally ill or dying patients), distinguishing them is essential. First, not all research involving terminally ill or dying patients constitutes palliative care research. For example, terminally ill or dying patients might be enrolled in clinical trials to test potential new *curative* drugs. No doubt the involvement of terminally ill or dying patients in such research raises specific and highly relevant ethical issues, yet these are not the focus of this chapter.

Second, not all palliative care research involves terminally ill or dying patients. Research can take many forms (survey, interview, focus group, clinical trial, etc.) and involve many different types of participants (nurses, relatives, caregivers, physicians). With regard to the ethical evaluation, this diversity in research types and research populations is particularly relevant. Although roughly the same ethical principles apply to all types of research, in the application of these principles, the research type and participant population recruited play an important role. For example, the ethical requirement for a favorable risk-benefit ratio applies to all research, but interventional research with terminally ill or dying patients evidently involves a different risk-benefit calculation compared to epidemiological research involving palliative care physicians. Nevertheless, both will be considered to be examples of palliative care research. Whenever relevant, we will explicitly distinguish between research types and participant population throughout the chapter.

In short, what characterizes palliative care research is not the population of participants it involves. Rather, palliative care research, as we use the concept, should be seen as *research of any type, regardless of participant population, that is intended to further the evidence or knowledge base of palliative care.*

3 Ethical Frameworks

When considering the ethical aspects of research ethics, a wide variety of possible ethical framework exists. There is currently no framework that enjoys universal consensus, although there is considerable overlap and near universal consensus on several items.

A first important source for clinical research ethics can be found in various authoritative international guidelines. An argument could be made that serious thinking about research ethics started only after WWII (Rothman 1987) and in the wake of particular scandals (e.g., the WWII research atrocities and the Tuskegee syphilis research scandal). Following these revelations, several international guidelines were drafted. Well known are the Nuremberg Code, the Declaration of Helsinki, and the CIOMS guidelines. Although not legally binding, many of these guidelines form the basis for national legislation in various countries.

However, these guidelines do not always provide definite answers to research ethical dilemmas in palliative care research. First, considerable differences exist between these guidelines. A recent study by Bernabe and colleagues, looking at the well-known international guidelines, found that:

> There is no consensus on the majority of the imperatives and that in only 8.2 % of the imperatives were [sic] there at least moderate consensus (i.e., consensus of at least 3 of the 5 ethics guidelines). (Bernabe et al. 2016: 1)

Second, these guidelines have a wide scope and thus rarely specifically address issues that are directly relevant to palliative care research. Therefore, merely consulting internationally

recognized guidelines will not suffice to find definite research ethical recommendations for palliative care research.

Another often cited and highly influential framework is that of Emanuel and colleagues (Emanuel et al. 2000). This is an attempt to construct a coherent ethical framework based on the international guidelines cited above. More specifically, the framework consists of seven key ethical requirements that should all be met in order for any clinical research to be considered ethical. Ethical clinical research must (1) be valuable (enhance health or knowledge), (2) be scientifically valid, (3) select participants fairly, (4) have a favorable risk-benefit ratio, (5) be subject to independent ethical review, (6) have informed consent from participants, and (7) show respect for enrolled participants.

Although many other frameworks might be possible, for the present chapter we will make use of this framework. We believe the seven requirements provide a good overview of the key ethical issues in clinical research. As our chapter is focused on palliative care research, we will examine how these requirements relate to palliative care research.

4 Vulnerability of Terminally Ill Patients

Before dealing with the seven ethical requirements, we first want to highlight one of the most common concepts in research ethics: "vulnerability" (for a recent and extensive exploration of the concept, see Bracken-Roche et al. 2017). Some groups or individuals are considered to be vulnerable, meaning they are at increased likelihood of being harmed or wronged (The difference between harming and wronging is the topic of considerable debate. In general harming seems to involve some form of damaging (e.g., physical or psychological harm). Wronging is a more broad concept that refers to acts that are contrary to moral principles such as fairness, justice, and beneficence or acts which involve unjustified breaches of moral rights (e.g., the right not to be harmed or the right to privacy). Understood in this way, wronging does not necessarily coincide with harming. Although it is possible to wrong someone through the infliction of unjustifiable harm, one can also wrong someone without harming them (e.g., breaching someone's privacy without them ever knowing) or harm someone without wronging them (e.g., harm inflicted in a medically and ethically justified amputation).) *in research contexts*. All guidelines acknowledge the issue of vulnerability and maintain that when vulnerable individuals are recruited for health-related research, additional or special protective measures should be taken or considered. Classic examples are pregnant women, prisoners, and children.

It is important to emphasize two particular points. First, there are many different kinds of vulnerability, and the concept of vulnerability discussed here relates to the research context. The *Oxford English Dictionary*, for example, defines "vulnerable" as "susceptible of receiving wounds or physical injury" (*Oxford English Dictionary*). In this sense every human being is vulnerable by virtue of being human, but this broad interpretation of vulnerability is not helpful when considering protection for particular groups or individuals participating in palliative care research. Therefore, labelling potential research participants as either vulnerable or not vulnerable implies nothing with regard to these participants' vulnerability in other contexts. Second, it should be stressed that vulnerability is best interpreted as a comparative concept (Wendler 2017). When a particular group or individual is labelled as vulnerable, this should be taken to mean that this group or individual is *more likely* to be harmed or wronged in research and that therefore *additional* protective measures are in order. Considering a particular group or individual to be non-vulnerable hence does not necessarily mean that they cannot be harmed or wronged through their participation in research. Adequate protective measures should be taken for *all* research participants, but *additional* measures should be considered for vulnerable participants.

Vulnerability is an established concept in research ethics, but the relevant question for this chapter is whether participants in palliative care research should be considered vulnerable

and, thus, be awarded additional or special protection. As argued above, palliative care research can include a variety of different participants (e.g., terminally ill patients, relatives, nurses, physicians, etc.). Within that group of possible research participants, the most likely candidates to be labelled as vulnerable are terminally or seriously ill patients. These potential participants have indeed been argued to be vulnerable. The influential CIOMS guideline argues that the category of potentially vulnerable participants includes "people with incurable or stigmatized conditions or diseases" (CIOMS 2016: 58). This position has also been taken in academic literature (Nickel 2006).

However, the usefulness of vulnerability as a concept has also been questioned to some degree (e.g., Levine et al. 2004). There seem to be several arguments against using vulnerability as a broad label, especially for terminally ill patients.

First, applying the concept in a way that automatically covers entire groups or populations might incorrectly consider these groups as more homogeneous than they really are. Those with terminal or serious illnesses form a highly heterogeneous group that cuts across age, gender, socioeconomic background, etc. Again, this is not to say that particular patients with serious terminal illnesses might not be considered vulnerable but rather that there seems to be no reason to *automatically* consider them to be vulnerable. Indeed, vulnerability could be argued to be a context-dependent rather than a category-wide concept. For example, a socioeconomically disadvantaged patient might be vulnerable to coercive financial offers to participate, but need not be vulnerable with regard to other ethically relevant risks. Many guidelines, for example, the CIOMS guideline, explicitly address this issue and seek "to avoid considering members of entire classes of individuals as vulnerable" (CIOMS 2016: 57).

Second, and related, there are no agreed upon criteria to determine vulnerability. The Declaration of Helsinki, for example, argues that some groups or individuals are potentially vulnerable, but provides no examples or criteria to help determine what constitutes such vulnerability. The CIOMS guideline and the WHO, on the other hand, use a very broad concept that may cover or include a large majority of patients, including seriously ill ones. However, if the concept of vulnerability is used in such a way that it covers nearly all potential research subjects, its usefulness in practice is limited (Levine et al. 2004).

Third, vulnerability as a broad concept has led to problematic practices. Many of the populations that have been labelled vulnerable have, as a result, been systematically excluded from research as this was sometimes seen as the only way to guarantee protection for vulnerable patients. However, this could lead to injustice and an unfair participant selection (for instance, if they are automatically withheld the benefits from participating in research). This could, paradoxically, actually lead to increased vulnerability for these patients. This might be relevant to the context of palliative care since, as mentioned earlier, palliative care lags behind in its evidence base. As we will explain below, there may be a significant extent of so-called gatekeeping in palliative care research whereby institutions, researchers, families, or health-care providers prevent access to research recruitment (see Sect. 10).

This has led to calls for a pragmatic conception of vulnerability. The question then is not so much "is this patient vulnerable or part of a vulnerable population" but rather "which steps should be taken to maximally protect the participants recruited within a particular study" (Wendler 2017). It would seem to be a fundamental ethical requirement that every participant in a research study should be granted the best possible protection, regardless of whether they should be deemed vulnerable or non-vulnerable. Therefore, in the remainder of this chapter, we will not focus on the question as to whether participants in palliative care research should be labelled vulnerable, but rather on particular potential ethical risks within palliative care research and ways of handling those risks.

As mentioned above, we will be using the well-known framework developed by Emanuel and colleagues which focuses on seven ethical requirements. Some of these requirements are

more relevant than others in the context of palliative care research, but in the interest of completeness, we will discuss all of them.

5 Independent Review

There is widespread consensus that, for any study involving human participants to be ethical, a research protocol has to be in place which needs to be independently reviewed. Many jurisdictions around the world legally require ethics committees or Institutional Review Boards (IRBs) to be established. The drafting of a protocol is required to guarantee valid informed consent (see Sect. 7), since without it patients cannot know what they are consenting to, making their consent invalid. Such a protocol is also essential for guaranteeing scientific validity (see Sect. 8) since ad hoc changes to the research while underway are unlikely to positively benefit the ethical nature and scientific validity of the research.

It has been suggested that getting approval from an ethics committee or IRB may be particularly challenging for palliative care research involving terminally ill patients or their loved ones (Casarett and Karlawish 2000; Lee and Kristjanson 2003). Abernethy et al. (2014) suggest that many ethics committees or IRBs may not be familiar with the particularities of palliative care research or may be hesitant to approve research that involves terminally ill patients or their loved ones. In turn, this may shun researchers away from palliative care research which is seen as overly ethically contentious and not likely to obtain approval from an IRB.

There is no reason to assume, however, that palliative care research involving terminally ill patients or relatives cannot be done in an ethical manner. A strategy for getting approval that has repeatedly shown to be effective, is early communication with the ethics committee or IRB (e.g., Hickman et al. 2012; Abernethy et al. 2014). This allows researchers to more quickly respond to possible concerns from the ethical committee and to collaboratively create a palliative care research protocol that is scientifically valid and ethically justified.

6 Social or Scientific Value

Another general ethical requirement for research involving human participants is that the research that is being considered is expected to have social or scientific value. This is crucial since research puts patients at risk (however slight), and this should only be considered when social value can reasonably be expected. Additionally, social or scientific value is essential from the perspective of making responsible use of finite funds for research. It is therefore highly recommended for researchers to reflect in advance on the potential beneficial contributions of their research to science or society. Within the research community, there is a growing emphasis on translational research which focuses on translating research findings into everyday practice in order to improve health care for patients (Westfall et al. 2007; Woolf 2008).

When applied to palliative care research, this ethical requirement clearly strengthens the case for conducting palliative care research. In view of the gap in evidence base and the existing reservations toward palliative care, there is a huge potential for societal and/or scientific value of research in this area.

7 Informed Consent

Informed consent is the best known and often seen as the main requirement for research involving human participants. Hence we will devote a bit more attention to this requirement. Many of the well-known research scandals, such as the Nazi experiments or the Tuskegee study, raised (among other things) significant concern due to the lack of informed consent or even the lack of *any* consent whatsoever (Vollman and Winau 1996). Today, there is near universal consensus that informed consent is a conditio sine qua non for ethical research. Of course, ethical issues pertaining to research should not be limited to issues of consent. As famously argued by Emmanuel and colleagues, research can be unethical even when there is informed consent (Emanuel et al. 2000). As such, consent is a

necessary condition, but it should not be considered a sufficient one.

Generally, a person is deemed to be able to provide informed consent if (1) she has the cognitive capacities to understand information about the study and the effects of participation and (2) she is not subject to coercion, manipulation, or undue influence. Those who cannot meet these conditions are deemed unable to provide consent.

Note that for this chapter we will use the formulation "unable to provide informed consent" rather than "incompetent," which has sometimes been used in the past. Competence is clearly task-specific, and labelling patients as incompetent might create the wrong impression that they have lost all capacity to consent. Persons unable to provide informed consent in a research context might still be able to provide informed consent in a variety of other contexts.

In palliative care research, the issue of informed consent is clearly pertinent, particularly with research involving dying patients or their relatives. We will deal with each of these two categories in turn.

7.1 Dying Patients

Dying patients may face an increased risk of failing to meet the two essential conditions of informed consent: the cognitive capacity to understand information and the absence of undue influence.

7.1.1 Reduced Cognitive Capacity

With regard to the capacity to understand information, dying patients may face an increased risk of having a reduced capacity to understand and assess information due to their life-threatening illness or general physical condition. This is the case for patients who suffer from conditions such as dementia or brain tumors, but also for imminently dying patients whose consciousness is frequently reduced. Hence, three possible scenarios might unfold. Terminally ill patients might be incapable of providing informed consent if they are not conscious, if they have reduced cognitive capacities that give reason to question their ability to provide informed consent, or if they lose their ability to provide consent while participating in the research study. We will briefly discuss each of these situations.

Scenario 1: Terminally Ill Patients Who Clearly Lack the Ability to Provide Consent

The Nuremberg Code drafted in response to the WWII atrocities includes the requirement that research may only be conducted following "the voluntary, well-informed, understanding consent of the human subject in a full legal capacity" (paragraph 1) (The full text of the Nuremberg Code can be found online at https://archive.hhs.gov/ohrp/references/nurcode.htm.). This clearly makes it impossible to conduct research with, for example, children and persons who are unable to consent. Since then the realization has grown that, if particular conditions are met, research involving persons who lack the ability to consent can be ethical. In fact the CIOMS guidelines provide that including patients who are unable to consent should be the default and that it is their exclusion which must be justified.

> Adults who are not capable of giving informed consent must be included in health-related research unless a good scientific reason justifies their exclusion. (CIOMS 2016, guideline 16)

Of course, all clinical research ethics guidelines agree that when research is done involving persons who are unable to provide informed consent, particular conditions must be met. **First** of all, research involving persons unable to consent should only be considered if the research cannot be conducted with patients able to provide consent. **Second**, even though patients may be unable to provide informed consent, they should always be informed and *refusal* to participate should always be respected. **Third**, informed consent has to be obtained from a legally recognized representative of the patients. **Fourth**, according to the Declaration of Helsinki, persons unable to provide consent should not be included in research that is unlikely to benefit them, unless "it is intended to promote the health of the group represented by the potential subject" (World Medical Association 2013, section 28). **Fifth**, research

involving participants unable to provide informed consent must present no more than minimal risk.

For palliative care research, the fourth condition seems to be particularly relevant. It has been observed that one of the challenges of palliative care research with terminally ill patients is that it is less likely to be directly beneficial to these patients. However, according to the Declaration of Helsinki, this does not automatically invalidate the study but requires the study to be intended to promote the health of palliative care patients. It is clear that in this respect "health" should be interpreted broadly, as in the well-known WHO definition which states that health is: "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (WHO).

Scenario 2: Terminally Ill Patients Who Have Reduced Cognitive Capacities

Although sensitive, this scenario does not seem to pose an insurmountable ethical challenge. Patients are normally believed to be able to provide consent unless there is reason to believe otherwise, and capacity assessment tools exist to determine the presence or absence of capacity (Karlawish 2008). Dying patients should thus be assessed for this purpose. In cases where these patients are found to lack the ability to provide informed consent, scenario 2 effectively collapses into scenario 1 in which case special provisions apply.

Scenario 3: The Situation Changes While the Study Is Ongoing

A less often discussed scenario concerning palliative care research with dying patients is the scenario where a patient has given informed consent beforehand, but *becomes* unable to provide informed consent during the study period. This raises problems because the requirement of informed consent should be seen as more than merely required before the study is initiated. It revolves around respect for the patient as a person and also covers the patient's right to withdraw consent (and thus participation) at any given time. If participants become unable to provide informed consent during the study, they might thereby lose the ability to protect their own interests. How should such participants be protected? Note that for research protocols that require participants' full cognitive capacities throughout the study, this is less of an issue. Participants who are likely to become unable to provide informed consent will then fail to meet the inclusion criteria and hence will be excluded. However, studies that do not require participants' full cognitive capacities throughout the study are faced with an ethical challenge.

A far-reaching protective measure would be to automatically exclude from *any* study patients who are likely less able or unable to provide informed consent during the study. The effect of such an automatic exclusion, however, would be that those in physically poor condition (and therefore more likely to become less able to provide consent) would be systematically excluded from research. This could result in an evidence gap for those patients, which in turn might lead to a higher likelihood of improper palliative or end of life care. Less far-reaching protective measures therefore seem to be preferable.

As mentioned earlier, all international guidelines allow health research to be conducted on participants incapable of providing informed consent, provided that various additional conditions are met. It would thus seem obvious that when participants *become* unable to provide informed consent during the study, the same additional conditions apply. For example, there is widespread agreement that research on participants incapable of consenting can only take place either if an advance directive for participation is available or if the participant's legal representative approves. For participants who *become* incapable of providing consent, continued participation in the study must, in our view, also be justified by an advance directive and/or a proxy consent. For studies including participants who are likely to become less able or unable to provide consent, this scenario needs to be addressed beforehand.

Another crucial requirement for research involving participants unable to provide informed consent is that the research can reasonably be expected to benefit the participant directly or to serve the health needs of the group of which the

participant is a member. As argued above, a significant need exists for valuable research on end of life care, and the concept of health is a broad concept, so this condition can arguably be met by palliative care research. However, this should never automatically be assumed.

In short, we would argue that even when participants becoming unable to provide informed consent have provided informed consent beforehand, this does not automatically justify their continued participation in the study. Continued participation must be justified by an advance directive or a proxy consent, and in this context the abovementioned additional ethical requirements apply. For studies involving terminally ill patients who are more likely to become less able or unable to provide informed consent, these situations should be addressed beforehand.

7.1.2 Undue Influence

Another particular concern that is relevant to dying patients is the risk that the presence of a terminal illness might unduly influence them in their decision to participate in palliative care research (Agrawal et al. 2006).

In this regard, we should first and foremost mention the risk of therapeutic misconception (Appelbaum and Roth 1982) which has become a standard concept in research ethics. Therapeutic misconception has been defined in many different ways (Henderson et al. 2007). It can be argued to occur when participants in a study:

> Do not understand that the defining purpose of clinical research is to produce generalizable knowledge, regardless of whether the subjects enrolled in the trial may potentially benefit from the intervention under study or from other aspects of the clinical trial. (Henderson et al. 2007: 1736)

Some studies indicate that dying patients might be willing to undergo significant risks in the expectation of a mere glimmer of therapeutic hope (e.g., Agrawal et al. 2006). In doing so, they might overestimate the benefits of participating in a particular research. If they are willing to try anything, dying patients might find it impossible to refuse an offer to participate in a study. This would invalidate their informed consent.

Although the issue of therapeutic misconception is most pertinent in research pertaining to therapeutic interventions, it is also a source of concern in palliative care research. For informed consent to be valid, it is essential that potential participants have a realistic understanding of the risks and benefits of participation. Therefore, when a study includes dying patients, who are well known for being at risk of therapeutic misconception, particular attention should be paid to this issue. This is true even for palliative care research where no possibility of therapeutic effect is present.

Another matter of concern is the relationship between the dying patients and their treating physician. There is no doubt that terminally ill or dying patients may depend to a considerable extent on their treating physician or health-care institution. If the physician then asks for their participation in a research study, they may well feel unable to refuse. This may be due to gratitude or alternatively to a fear that refusal will negatively affect their relationship with their physician or even the quality of their care. As regards the fear that refusal will adversely affect care, it is an established ethical principle that refusal to participate in a study or a decision to withdraw from a study should never adversely affect the patient-physician relationship. However, this in no way excludes the possibility that dying patients may perceive this to be the case and, as a result, *experience* an inability to refuse, however unfounded this may be. Particular care must therefore be taken in such cases to avoid this perception.

In general, there seems to be a potential risk when dying patients are asked to participate in a research study by the health-care professional responsible for their care. The Helsinki Declaration specifically discusses this issue and recommends the following:

> When seeking informed consent for participation in a research study the physician must be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent must be sought by an appropriately qualified individual who is completely independent of this relationship. (WMA 2013, paragraph 27)

The CIOMS guideline provides a similar recommendation in the case of a dependent relationship. We would argue that, in cases of palliative or terminally ill patients, there is definitely a relationship of strong dependency. Due to their physical condition the patients may not be easily transferable, and due to their limited life expectancy, there may be no opportunity to establish a relationship with a new physician.

7.2 Relatives or Loved Ones

It is important not to limit issues regarding informed consent in palliative care research to research involving dying patients. Indeed, relatives or loved ones might also be involved in palliative care research, either directly as research participants or as proxy for involvement of a participant who is unable to provide consent.

As with dying patients, relatives or loved ones may be influenced by considerations of gratitude toward physicians involved in treating their relative or loved one. Moreover, the risk of therapeutic misconception may also exist for relatives or loved ones who operate as a proxy for a participant unable to provide consent. They are expected to protect the interests of their relative or loved one, and they are only fully able to do so when they have an adequate and correct understanding of the risks and benefits.

8 Scientific Rigor or Validity

Any research study must be as scientifically rigorous as possible. As was made clear by Emmanuel and colleagues in their classic ethical framework for clinical research, scientific validity is a key ethical requirement. Having patients participate in a study that is not conducted in a way that it can reasonably be expected to generate valid results is simply unethical as it amounts to (potentially) harming patients for no reason.

For palliative care research this might result in somewhat of a catch-22. The "gold standard" of clinical research is still the randomized controlled trial (RCT). However, in some palliative care research, for example, studies involving terminally ill patients, randomization might be particularly challenging (Grande and Todd 2000) or even ethically unjustified (de Raeve 1994). Hence research would only be ethical when maximally scientifically rigorous, but cannot be made maximally scientifically rigorous due to other ethical considerations. By way of example, let us consider the question of whether continuous deep sedation at the end of life (often referred to as palliative sedation) shortens life. The scientifically most valid way of testing this assumption is by performing an RCT with dying patients, half of whom would receive continuous deep sedation and half of whom would not. Obviously this would not be possible for ethical reasons (Beller et al. 2015). The question of whether continuous deep sedation shortens life therefore remains a topic of considerable debate (Sterckx et al. 2013).

Unsurprisingly, in view of the above, research indicates that RCTs are rare in palliative care research and often methodologically flawed. Rinck and colleagues have conducted a systematic review of all RCTs investigating the effectiveness of palliative care services (Rink et al. 1997). They examined 11 trials and found that all had methodological shortcomings. A more recent study from 2008, reviewing 25 Cochrane systematic reviews, found that RCTs in palliative care remain small scale and methodologically problematic (Wee et al. 2008). This conclusion was reaffirmed in a 2017 systematic review (Bouça-Machado et al. 2017). In a framework that judges the gold standard of evidence to be evidence gathered through RCTs, palliative care may be at an inherent disadvantage. This might in turn affect the ethical acceptability of palliative care research.

As a proposed way out of this, catch-22 calls have been made to rethink the framework of evidence for palliative care research (Aoun and Kristjanson 2005) and to move away from RCTs as the only "gold standard." Many commentators indeed emphasize the need to further the evidence base of palliative care using other research methodologies than RCTs, for example, qualitative research, mixed method methodologies, etc. (e.g., Aoun and Nekolaichuk 2014; Visser et al.

2015). Such a shift does not necessarily imply a loss of scientific validity, since, as argued in a highly influential article on trial design, large-scale observational trials can be scientifically equivalent to RCTs (Concato et al. 2000). Numerous other commentators likewise challenge the RCT as being the one and only gold standard (e.g., Grossman and Mackenzie 2005; Bothwell et al. 2016). Of course, RCTs are not necessarily impossible in palliative care research and are often used to good effect. However, if an RCT can only be performed in an ethical way with far-reaching concessions on scientific validity, different research designs need to be considered.

We would submit that it is possible for researchers in palliative care research to fulfill their ethical obligation or scientific validity even where RCTs are not possible. In fact, there is reason to believe that finding valid alternatives for RCTs in palliative care may in some case actually be the ethically correct way of moving forward. Researchers in palliative care research thus have a continuous ethical obligation to critically select the research methodology that best meets both ethical and scientific requirements.

9 Favorable Risk-Benefit Ratio

Another fundamental ethical requirement on which near universal consensus exists is that every study should have a favorable risk-benefit ratio. This is notoriously difficult since, as emphasized in international guidelines and in the academic literature, there is no clear mathematical formula for determining risks and benefits or for determining what constitutes an acceptable or favorable ratio.

In order to determine risk, researchers need to consider (1) the magnitude of possible physical, psychological, social, or other harms and (2) the likelihood of that harm occurring. A low likelihood of substantial harm can in this way be compared to a high risk of minor harm. For palliative care research, especially research involving seriously or terminally ill patients, careful harm assessment needs to be undertaken in advance. What represents minor harm for a healthy participant might be a more substantial harm for a vulnerable patient. Interviews or surveys, for example, might take a limited amount of time, but for patients with a terminal illness, this may represent a serious investment of time they would rather spend otherwise. For relatives, on the other hand, there exists the risk that they become distressed.

As regards the benefits, there are two kinds of benefits to consider. First, the direct benefits for the research participants, and, second, there are potential benefits for the group of which the research participant is a member. Both kinds of benefits can be considered in a risk-benefit analysis. As regards palliative care research with terminally ill patients, it has been suggested that there is little chance of real benefit for the participants themselves as they have a limited life expectancy (De Raeve 1994). Nevertheless, this has been argued to potentially underestimate the variety of potential benefits. A systematic review of research into the attitudes of terminally ill patients and their relatives toward participation in palliative care research suggests that these groups are often interested in participation in research and may even experience some form of benefit (White and Hardy 2010). Participation in palliative care research has, for example, been found to provide some palliative and/or dying patients with an increased sense of meaning because of the opportunity "to give something back." According to other studies, participation in palliative care research "assisted [palliative care patients] in coping in their situation and reduced their feelings of isolation" (White and Hardy 2010).

Finally, there must be an acceptable or favorable balance between the risks and the benefits of a study. What counts as acceptable or favorable is a matter of debate, but seems to depend on two things. First, and most obviously, a risk-benefit ratio is acceptable or favorable when the risks are offset by the study's benefits. The higher the risk (more likely or more substantial harm), the higher the potential benefits should be in order for the study to be justified.

A related and equally important condition is not only that the risks and benefits should weigh up but also that they should be divided fairly. If a

particular group bears all the risks while another group enjoys the potential benefits, this is arguably unfair and even exploitative (for a good and extensive overview of exploitation in clinical research, see Wertheimer 2008). It is thus not sufficient for researchers in palliative care to list the potential risks and benefits; they should also reflect on the allocation of those risks.

10 Fair Participant Selection and Gatekeeping

A final important requirement for a research study to be ethical is that participants be selected fairly. This involves the formulation of clear and justified inclusion and exclusion criteria. The inclusion of a certain participant population must not be based on mere convenience, but must be both ethically and scientifically justified. Care must also be taken that no individuals or groups are unjustifiably excluded from research.

For palliative care research, a particular challenge arises concerning fair participant selection. A well-known issue in research is gatekeeping, which has been defined as "the ad hoc denial of access to individual patients or systematic denial for particular groups of patients for reasons outside the framework of the trial eligibility criteria" (Sharkey et al. 2010: 363). Such gatekeeping has repeatedly been reported in palliative care research contexts (Hudson et al. 2005; Kars et al. 2016). The reasons for gatekeeping are often paternalistic concerns for the well-being of the research participant (White et al. 2008). Although no doubt often well-intended, the result of such gatekeeping is that recruitment in palliative care research becomes ad hoc and dependent on the willingness of physicians to recruit patients or relatives. This might not only threaten the scientific validity of a study; it might also be ethically unfair if potential participants are not even given the opportunity to consider participation in a research study. It has been reported that for palliative care trials a high percentage of patients are willing to participate (Ling et al. 2000), strengthening the argument that paternalistic gatekeeping might be unjustified.

Therefore, care must be taken to minimize gatekeeping. Strategies that have been suggested include anticipating possible misconceptions, continuously checking the inclusion for potential biases, and involving clinicians. Of course, there may still be ethical grounds for excluding particular vulnerable individuals, but that exclusion should be based on clear and study-wide criteria rather than on ad hoc grounds for exclusion.

11 Respect for Potential and Enrolled Subjects

Although respect for enrolled subjects is no doubt essential, it might be somewhat unclear how this requirement should be translated into the practice of doing research. What does it mean to show respect for potential and enrolled subjects?

In philosophy, perhaps one of the most famous elaborations of the concept of respect for persons is that of Immanuel Kant (2012 (1785)). The precise interpretation of Kant's idea of "respect" is a matter of extensive philosophical debate. However, key to the Kantian interpretation is that persons, by virtue of being rational human beings, should never be treated solely as a means, but always also as an end in themselves. One fails to respect human beings when one treats them as mere passive instruments, means, or objects in the achievement of a certain goal, however good that goal might be. This is particularly relevant for a research context, since in research involving human participants, human beings *are* used as a means to gather data and/or generate knowledge.

However, although human beings are used as a means in this context, investigators can still make sure they are shown respect and are not *solely* or *merely* used as a means. For example, when persons freely and autonomously consent to participation, they can be said to subscribe to the goal of the research study, thereby making it their own. In this scenario the participant is not a passive object, but an active participant. In essence, the principle of respect revolves around the researchers' attitudes and the acknowledgment that every single participant in a research study is a human being with dignity, dreams, desires, beliefs, and interests

that need to be protected. As the Declaration of Helsinki states:

> While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects. (WMA 2013)

Fulfilling the requirements of clinical research is in the *interest of the participants* and should not be seen as a mere safety measure for the (legal) protection of researchers.

Although the requirement of respect for research participants is not limited to palliative care research, it is too important to leave out. When applied to palliative care research, it requires researchers to be aware of and concerned for the situations that are specific to the participants in their study. In research including terminally ill patients and/or their loved ones, care must be taken to always take a respectful attitude toward these participants and to do this *throughout* the entire research study. The requirement to show respect does not stop when, for example, the informed consent form is signed nor when the active involvement of the participant is finished. Data gathered from patients should equally be treated with sufficient respect when stored, analyzed, and put into publishable form. Participants have a continued interest in what happens to their data, and this interest may even continue to apply when they pass away (a situation that is more likely to occur in palliative care research involving seriously ill patients). No matter how scientifically relevant or valuable one might deem the research to be, the dignity, integrity, and general interests of participants should always come first.

12 Concluding Remarks

In this chapter we have sought to provide an overview of some of the relevant ethical issues pertaining to palliative care research. In general it is hard to make broad and general statements on this topic, for palliative care research can involve a great variety of research methodologies and a wide diversity of participant populations.

What is clear, however, is that palliative care research can be ethically justified, and we arguably even have a moral obligation to engage and invest in palliative care research in order to create a much more solid evidence base. It is also clear that particular ethical requirements give rise to particular challenges in the field of palliative care research. For example, for research involving terminally ill patients, scientific validity and informed consent may be particularly problematic. However, none of these challenges are impossible to overcome.

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Evidence-Based Practice in Palliative Care

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Contents

Abstract

Many of the chapters in this Textbook provide state of the art, that is, evidence-based recommendations for the practice of palliative care and palliative medicine. This chapter on "Evidence-based practice in palliative care" will focus on the principles, advantages, and limitations of evidence-based medicine (EBM) and evidence-based practice (EBP) in general and specifically within the field of palliative care. We will discuss the concepts of EBM/EBP from a historical perspective, their role within the field of palliative care, the way EBM/EBP is practiced by a clinician in a stepwise approach, and critically reflect on how these concepts have developed over the past decade. The development of EBM/EPB has had an enormous impact on the way medicine is practiced today. It should not however be considered cookbook medicine. Its future lies

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_111

in generating useable evidence that can be combined with context, professional expertise, and patient preferences to provide optimal treatment and care to individual patients.

1 What Is Evidence-Based Medicine (EBM) and Evidence-Based Practice (EBP)?

For over a century (between the eighteenth and nineteenth century), physicians have debated the role of statistics, mathematics, and probabilistic knowledge in the practice of medicine, particularly in Europe and the USA. Only by the start of the twentieth century, medicine had moved from the empirical observation of cases to the scientific application of basic sciences to determine best therapies or diagnoses (Mayer 2010). After 1950, the randomized clinical trial became the standard for excellent research, following the work of British men such as Sir Ronald Fisher, Austin Bradford Hill, and particularly Archie Cochrane. The latter was the first to publish a quality-rated systematic review of the literature on a particular topic in medicine (Mayer 2010). This was the beginning of a true paradigm shift in thinking and reasoning in medicine. The Cochrane Collaboration Network, founded in 1993, grew out of this work.

In 1996, Sackett published his ground-breaking publication in the *British Medical Journal*, defining **evidence-based medicine (EBM)** as "the conscientious, explicit, and judicious use of the best evidence in making decisions about the care of individual patients" (Sackett et al. 1996). More simply stated, EBM concerned the application of the best possible evidence from medical literature to the individual patient's problem, resulting in the best possible care for each patient (Mayer 2010). The movement of EBM that grew out of this work has led to a profound innovation in medical teaching and medical research. It resulted in the development of professional guidelines and standards of care to support professionals in making decisions in individual patient care (Dutch Council for Public Health and Society 2017).

Evidence-based practice (EPB) – sometimes referred to as evidence-based clinical practice (EBCP) – is a term that was introduced later. While both terms EPB and EBM considerably overlap, the term "EBP" is considered "broader" than EBM, and it implies the use of evidence-based knowledge by multiple professional disciplines in health care. Historically, EBM primarily involved physicians and concentrated on the treatment aspect of medicine. EBP is considered to be more multidisciplinary, targeting nurses, clinicians, nurse practitioners, physical and occupational therapists, hospital administrations, etc. (Adriaenssens et al. 2018). For reasons of readability and because of the broader concept of EBP, we will use this term throughout the chapter.

Initially, EBP focused primarily on the use of evidence in clinical decision-making, while at the same time de-emphasizing other important determinants of clinical decisions such as the individual clinical experiences. In later definitions, it was emphasized more that research evidence alone is not sufficient to guide clinical decisions. Clinicians should apply their expertise to assess the patient's problem and incorporate the evidence together with patient preferences and values. Evidence-based decision-making was then defined as the integration of best research evidence with clinical expertise and patient values. This model is depicted in Fig. 1.

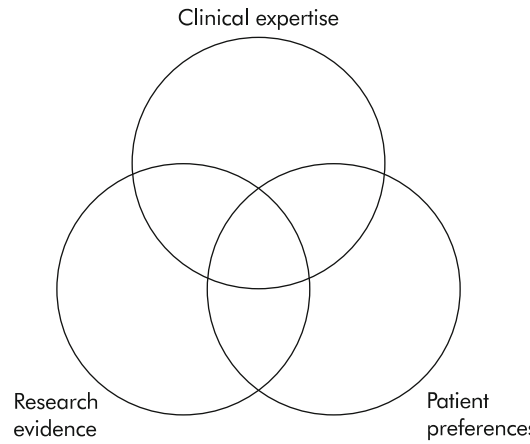

Fig. 1 Early model of the key elements for evidence-based clinical decisions. (Reproduced from Haynes et al. 2002, with permission from BMJ Publishing Group Ltd)

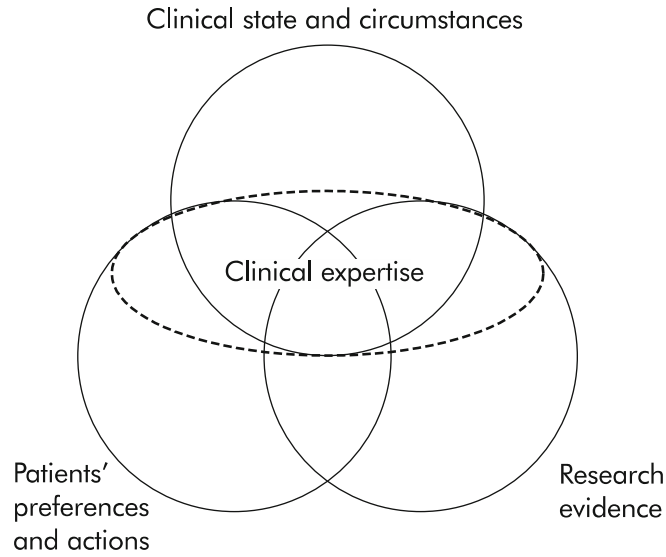

Fig. 2 An updated model for evidence-based clinical decisions. (Reproduced from Haynes et al. 2002, with permission from BMJ Publishing Group Ltd)

In a more advanced and recent model, as shown in Fig. 2, **evidence-based health care combines the best available evidence, clinical situation of the patient, patient preferences and actions, all bound together by clinical experience** (Mayer 2010; Adriaenssens et al. 2018; Haynes et al. 2002). At the top of Fig. 2 are the patient's clinical state, the clinical setting, and clinical circumstances she/he is in, which are dominant factors in clinical decisions. Regarding preferences, patients might have varying views on treatment options (or they might have no clear preference) depending on several factors such as previous experiences, personal values or traits, or the values of their families. Such preferences should be explored and taken into account. In particular for end-of-life and palliative care, with its important focus on patient values and preferences in decision-making, this component in the updated EPB model is highly relevant. The factor "patient actions" was mainly added due to the inconsistencies that might occur between patient preferences or physician's advice and actual patient behavior, for example, patients who prefer to stop smoking but still smoke. A third obvious factor is the research evidence available, which includes all sorts of observational and interventional studies in basic and applied health research. However, a lot of research evidence will not easily or automatically apply to the individual patient at hand. Hence, personalizing the evidence to fit a patient's specific circumstances is a key part of evidence-based decision-making. Finally, the role of clinical expertise is very central and important in evidence-based decision-making. This includes the general basic skills of clinical practice as well as the experience of the individual practitioner. It is the clinical expertise that integrates and balances the other elements in the model and often involves sorting through trade-offs (Haynes et al. 2002).

The EBP community has grown rapidly over the past 20 years to become an "energetic intellectual community committed to making clinical practice more scientific and empirically grounded and thereby achieving safer, more consistent, and more cost-effective care" (cited from Pope 2003; in Greenhalgh et al. 2014). The EBP community has achieved to set up the Cochrane Collaboration to summarize evidence from clinical trials; it has set methodological and publication standards for research, built national and international infrastructures for developing and updating clinical practice guidelines, and developed resources and courses for teaching critical appraisal and building the knowledge base for implementation and knowledge translation (Greenhalgh et al. 2014). Regarding the latter, a whole body of literature has developed regarding EBP development, dissemination, and implementation. It addresses the importance of three distinct stages as part of the

evidence-based process: knowledge creation and distillation; diffusion and dissemination; and adoption, implementation, and institutionalization (Nieva et al. 2005; Adriaenssens et al. 2018). Additionally, EPB has also gained a lot of attention within health-care policy work. EBP can provide important means to improve efficacy, efficiency, and quality of care, and sometimes it might help in keeping health-care expenses under control (Adriaenssens et al. 2018). Developing methods to produce evidence-based policies in health care has become an important research field of its own.

Although these developments are highly relevant in the field of EBP, this chapter will focus mainly on the viewpoint of the individual clinician and how he/she uses EBP in real practice. We will first highlight the need for more evidence in palliative care and on how EBP can/should be practiced or what skills are needed by clinicians to perform EBP adequately. Because the model of EPB outlined here is not without critics, we will also discuss these further on in the chapter.

2 Evidence-Based Practice in Palliative Care: The Need for High-Quality Evidence

EBP has grown rapidly over the past 20 years across the field of medicine and has resulted in much improvement in clinical practice for patients. Every year, an enormous amount of trials and reviews are produced in the medical research community (Visser et al. 2015). It has been argued that palliative care has been lagging behind compared to other medical disciplines and that the evidence-base is still too limited in terms of high-quality trials to ensure high-quality practice (Aoun and Nekolaichuk 2014; Higginson et al. 2013; Dy et al. 2012).

The number of researchers in the field of palliative care has grown substantially over the past decades. Multiple disciplines – medicine, public health, social health, sociology, psychology, anthropology, etc. – are studying this highly complex and multidisciplinary field using different methodological approaches. The number of clinical trials in palliative care has also grown accordingly. For example, a 2017 Cochrane review on the effects of early palliative care in cancer patients summarized the work of 7 published trials, but also reported 20 additional trials that are currently ongoing (Haun et al. 2017). A systematic review of published clinical trials assessing therapeutic interventions in palliative care (up to 2015) retrieved 107 trials in Medline (Bauça-Machado et al. 2017).

However, a number of reviews (Bauça-Machado et al. 2017; Dy et al. 2012; Hui et al. 2012; Kaasa and Radbruch 2008; Visser et al. 2015, Wee et al. 2008b) evaluating the strength of the evidence in palliative care have highlighted some important problems with current evidence:

- RCTs are proportionately limited in number, for example, while the proportion of original studies have increased between 2004 and 2009, the proportion of interventions studies remained stable over time (Hui et al. 2012).
- Many clinical trials are methodologically flawed. Existing study designs show important quality deficiencies including poor recruitment, high attrition, small sample sizes leading to a lack of study power, and lack of thoroughly executed pilot studies to carefully select outcome measures or understand possible biases or confounders, the absence of an explicit defined primary outcome, etc. (Aoun and Nekolaichuk 2014; Dy et al. 2012; Luckett et al. 2014; Smith et al. 2014).
- Even trials that are judged to be of high quality are often underpowered (Wee et al. 2008b).
- The overall quality of the reporting of key trial methodology is too poor (e.g., lack of reporting of random sequence generation, allocation concealment, blinding (Bauça-Machado et al. 2017, Hui et al. 2012)).
- Due to a lack of well-designed and well-executed studies, reviews "fail to provide good evidence to guide clinical practice because the primary studies are few in number, small, clinically heterogeneous, and of poor quality and validity" (cited from Wee et al. 2008b).

Hence, effectiveness research in palliative care has been described as lacking the quality to contribute to evidence-based medicine or to inform practice and policy-making well enough. This

lack of high-quality research and evidence is considered to be a major barrier to improving quality of care provided in the final phases of life (Higginson et al. 2013).

Recently, important work was done to improve the design and conduct of intervention research in palliative care, which resulted in the MORECare statements for palliative care research (Higginson et al. 2013). It starts from the idea that all palliative care interventions are inherently complex interventions. The development and evaluation of such interventions can follow the UK Medical Research Council's guidance on developing and evaluating complex interventions, but because of the complexities and specificities in palliative and end of life care research, the MORECare work leads researchers through all phases of intervention development and provides advises on how to optimize research methods. In this Textbook, a whole chapter ("Development and Evaluation of Complex Interventions in Palliative Care") is devoted to this important work and the reader is referred to that chapter for further information.

With these efforts, researchers in palliative care have attempted to increase the quality of their research with the aim of providing better evidence to improve EBP decision-making. Nevertheless, a number of authors have also argued that some of the fundamental assumptions underlying EBP are incompatible with palliative care, and the methodologies used in randomized controlled trials are often not feasible in the palliative care context. A review outlining the challenges of conducting high-quality research in palliative care and the limitations attached to the traditional EBP approach in the field of palliative care was published in 2015 by Visser et al. We will address these criticisms more in detail at the end of this chapter, after describing in detail how EBP should be practiced.

3 How to Practice Evidence-Based Practice: A Stepwise Approach

Three skills are identified as important for practitioners practicing evidence-based medicine: (1) information mastery, (2) critical appraisal, and (3) knowledge translation (Mayer 2010). These skills are used throughout the different steps involved in the process of EBP. While different authors have identified slightly different versions of this stepwise approach, they all involve the same processes. From a learner's perspective, it would be best to start learning EBP by learning and practicing the different steps, taking a specific patient scenario as a starting point. For details, we refer the reader to other Textbooks on EBM and EBP, of which there have been written many, for many different disciplines and professions. Here, we will summarize the different steps involved in the complete process of EBP.

3.1 Step 1: From Clinical Problem to Clinical Question

A first step is the translation of a clinical problem of a patient to an adequately formulated clinical question. Clinical questions are usually formulated in the form of a PICO, that is, what is the problem of the patient (P), what is the intervention of interest (I), what is the control-intervention (C) that is used for comparison, and what is the outcome of interest (O)? This is a very important step since the answer to your clinical question will co-determine how you deal with the patient's problem.

In Table 1, a PICO is defined using an example. The clinical question could be for example: "Is medically assisted hydration more effective than no medically assisted hydration for maintaining quality of life in a patient who is considered in the last days of life and unable to maintain sufficient oral fluid intake?" In some cases, time is also added to PICO. This relates to the period over which the intervention is studied (i.e., whether the study was carried out for a sufficient amount of time).

3.2 Step 2: Searching for Evidence

There is an enormous amount of literature to be found in medicine. There are several types of research studies (e.g., case-control, cross-sectional, cohort, randomized controlled trials), many different peer-reviewed and non-peer-

Table 1 PICO is used to identify the clinical question (Mayer 2010)

Structure of the clinical question (PICO)	Explanation	Example from palliative care
The Patient	Population group to which your patient belongs	Adults who are considered to be in the last days of life and are unable to maintain sufficient oral fluid intake
The Intervention	The therapy, etiology, or diagnostic test you are interested in applying to your patient	Effect of medically assisted hydration
The Comparison	A comparison group (that is commonly encountered in clinical practice) to against which the intervention is measured	Compared to no medically assisted hydration
The Outcome of interest	The endpoint of interest to you or your patient. The most important outcomes are those that matter to the patient, often death, disability or full recovery	Quality of life

reviewed journals, focused on specific disciplines or a more general medicine audience. In step 2, the clinician needs to have good searching skills and use medical informatics, to search the literature for those studies that are most likely to give the best evidence to answer the identified question. This requires that one develops an effective, hence systematic search strategy for a clinical question. To ensure that all relevant information can be retrieved when searching the literature, it will be important to access several databases. One of the most widely known database is Medline. Medline was developed by the National Library of Medicine at the National Institutes of Health in the USA, and it is the world's largest general biomedical database. In psychological science, other databases are more relevant such as PsycINFO, or in the field of nursing and allied health studies, CINAHL. It is beyond the scope of this chapter to provide the reader with a full overview of databases available or specific instructions on how search strategies can be made in the different databases.

In this chapter, we will focus on the different sources available to clinicians when seeking the answer to a clinical question for a particular patient. When a clinician is looking for an answer to his question at the point of care, when the patient is "in his office," she/he will not perform comprehensive Medline searches, but instead will look for pre-appraised sources and high-quality meta-analyses such as those published by the Cochrane Collaboration, or search for clinical guidelines or decision supports available on the topic.

3.2.1 Knowledge Acquisition Pyramid

To help clinicians search for evidence among the large amount of publications and tools available to them, the Haynes **knowledge acquisition pyramid** (Haynes 2006, in Mayer 2010) was developed, sometimes also referred to as the "**waterfall or cascade" approach.** Following this approach would mean that clinicians should search the literature in a number of consecutive steps, as shown in Fig. 3.

Clinicians start by looking at the highest level of systems, standards, and guidelines to help with decision-making. Computerized decision support systems are newly developing approaches to providing clinicians with online support at the point of care via linking with patient file data. The IT system links directly to high-quality information needed "on the spot." There are a few of these systems being developed to support the implementation of guidelines; some are local or national linked to specific institutions (further details are provided later in this chapter). Second, clinicians should search for summaries and synopses which provide critical overviews of reviews and studies. These can be evidence-based textbooks or critical overviews of reviews and studies such as *BMJ* best practice or ACP Journal Club

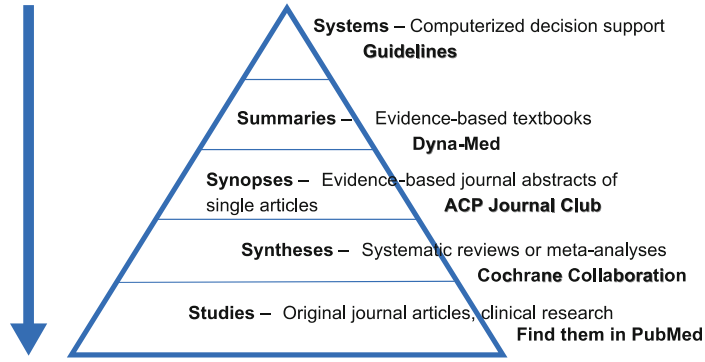

Fig. 3 The knowledge acquisition pyramid of Haynes. (Reproduced from Mayer 2010, by permission of Oxford University Press)

(these sources can also have different names in different countries). A third source of evidence concerns the systematic reviews and meta-analyses of which Cochrane reviews is one of the most important. Lastly, when all other sources do not provide clinical guidance, clinicians are bound to evaluate primary sources of evidence and look for original studies in different databases such as Medline or Cinahl.

Clinicians go "down the pyramid" and stop when they have (or estimate that they have) sufficient high-quality information to answer their clinical question. For all these steps, it will be crucial to also understand the quality of the evidence or the strength of recommendations that are made by these different sources. Hence, step 3 of EBP is a crucial element of decision-making.

3.3 Step 3: Critical Appraisal of Available Evidence

Once the evidence has been found, a third step in EBP is to perform a critical appraisal of the evidence found. When appraising individual studies, clinicians should search in this step for sources of bias within those studies. More specifically, they should systematically evaluate whether a study addresses a clearly focused question, whether valid methods were used to address that question, and whether the valid results of the study are important. When appraising clinical practice guidelines or other aggregate sources of evidence, they should evaluate the development process of these sources, and several important tools have been developed to help clinicians in this task. This section addresses the most important elements to consider when appraising the available evidence for the different types of sources identified in the knowledge acquisition pyramid, starting with individual studies up to guidelines and decision-support systems.

3.3.1 The Appraisal Pyramid: From Animal Research to Meta-analyses

Clinicians usually are taught to appraise literature following an **appraisal pyramid**. Such pyramids exist in multiple formats with slightly different terminologies used. Important is the distinction between literature that is already critically and systematically appraised by others and individual studies of various designs. An example of such a pyramid can be found in Fig. 4. The higher on the appraisal pyramid, the easier the source is to use, and the least amount of critical appraisal is needed by the user, of course considering the quality of the methods used in the different studies or analyses.

In recent literature, there have been some alternative proposals for this evidence pyramid. Murrad et al. (2016) have proposed to chop off the meta-analyses and systematic reviews from the pyramid top. Instead, reviews should be a lens through which evidence is viewed and applied. Also, in their new pyramid, the lines separating the study designs have become wavy instead of fixed, referring to the fact that studies might differ substantially in the quality with which they are performed. The wave going up and down reflects the GRADE approach of rating up and down based on the various domains of the

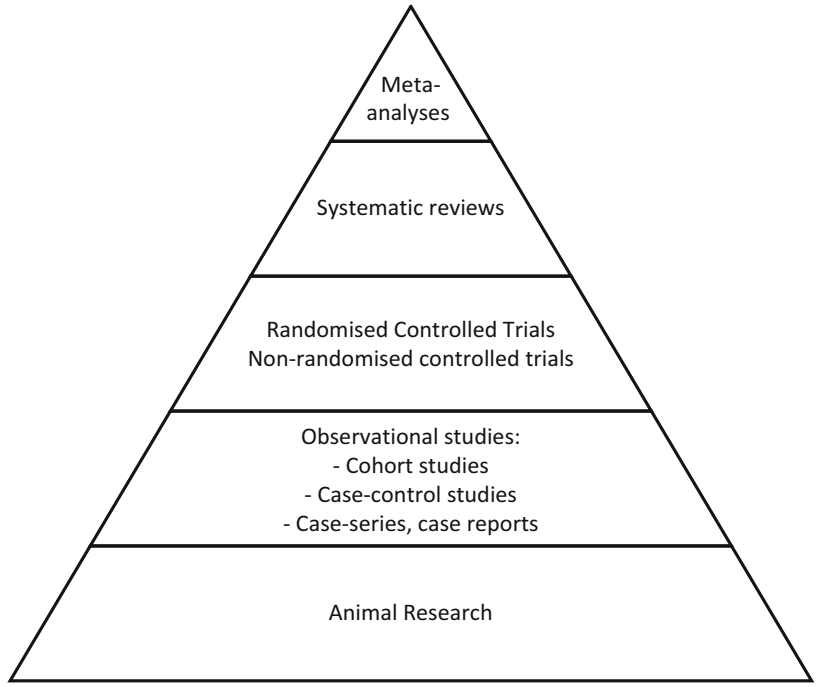

Fig. 4 The pyramid of appraisal of the literature (Mayer 2010)

quality of evidence (see further). The quality of studies, and not only the study design, determines how high or low they should be rated. For example, even though RCTs are considered high on the pyramid, there are also several biases that might lead an RCT to have a lower quality of evidence, and this should be taken into account by clinicians when evaluating the literature (Murrad et al. 2016).

In the following section of this chapter, we have highlighted what is most important for clinicians when appraising the literature and information available to them. First, meta-analyses and reviews are discussed. Secondly, the most important issues related to individual studies (RCT and other) are addressed. Finally, the strengths and weaknesses of summaries and guidelines available to clinicians are described.

3.3.2 Meta-analyses and Systematic Reviews

Meta-analyses or systematic reviews are techniques that aim to provide a comprehensive and objective analysis of all clinical studies on a specific topic. In many cases, statistical techniques are applied to quantify the combined effect of selected studies (Mayer 2010). (An important organization occupied with producing meta-analyses on a variety of topics in health care is the Cochrane Collaboration http://www.cochrane.org/). Cochrane is an international nonprofit organization that aims to "gather and summarize the best evidence from research to help you make informed choices about treatment." It is a global independent network of researchers, professionals, patients, carers, and people interested in health. Worldwide, there are more than 37,000 Cochrane contributors from 130 countries. It is organized via different Cochrane groups such as review groups, thematic networks, groups concerned with methodology of systematic reviews, and regional centers (with a regional focus for Cochrane activities within a defined geographical or linguistic area).

The Cochrane Library (http://www.cochranelibrary.com/) is a collection of databases that contain different types of high-quality, independent evidence:

– Cochrane database of systematic reviews (CDSR): preparing peer-reviewed systematic reviews following the *Cochrane Handbook*

for Systematic Reviews of Interventions and the *Cochrane Handbook for Diagnostic Test Accuracy Reviews* (Higgins and Green 2011)
- The Cochrane Central Register of Controlled Trials (CENTRAL), a highly concentrated source of reports (usually the abstract with bibliographical details) of randomized and quasi-randomized controlled trials
- Cochrane Clinical Answers (CCA) providing a digestible clinically focused entry point to rigorous research from Cochrane Systematic Reviews, aiming to inform point-of-care decision-making

In the field of palliative care, the work of the PaPaS Cochrane Pain, Palliative Care and Supportive Care Collaborative Review Group is an important resource (http://papas.cochrane.org/). PaPaS is based in Oxford, UK, founded in 1998, and funded by the National Institute of Health Research (NIHR) as part of the Research and Development program. They are one of the Cochrane review groups that specialize in different areas of health based in different countries around the world. Their scope is defined as studies of interventions for:

- Acute pain arising accidentally or through deliberate injury
- Chronic pain (lasting 3 months or longer)
- Headache and migraine
- Palliative care for those with life-limiting disease or illness
- Supportive care of patients and significant others living with serious illness, defined as "the multi-disciplinary holistic care of patients with malignant and non-malignant chronic diseases and serious illness, and those that matter to them, to ensure the best possible quality of life. It extends as a right and necessity for all patients, is available throughout the course of the condition, concurrent to condition management and is given equal priority alongside diagnosis and treatment. It should be individualised, taking into account the patient's past life experiences, their current situation and personal goals" (Cramp and Bennett 2012).

Cochrane reviews are performed following a very strict methodology described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins and Green 2011). While Cochrane Reviews are considered of very high quality, not all systematic reviews follow the methodologies used by Cochrane. The quality of reviews might vary considerably; hence, it is important for clinicians to critically appraise them. To help with this process, checklists have been developed to assess the methodological quality of systematic reviews. Next to Cochrane (Higgins and Green 2011), there are several organizations who have produced such checklists among others the AMSTAR checklist (Shea et al. 2017), the CASP Systematic review checklist developed by the Critical Appraisal Skills Programme (https://casp-uk.net/), the Centre for Evidence-Based Medicine in Oxford (UK) (https://www.cebm.net/2014/06/critical-appraisal/), the Joanna Briggs Institute (http://joannabriggs.org/research/critical-appraisal-tools.html), and the toolkits provided by BMJ Best Practice, to name a few. Finally, important aspects for a clinician to take into account when appraising a review are the seven domains identified by Shea et al. (2017) that can critically affect the validity of a review and its conclusions: (1) Is the protocol registered before commencement of the review? (2) Is the literature search performed adequately? (3) Is the exclusion of individual studies justified well? (4) Does the review include an evaluation of risk of bias from individual studies; (5) Are the meta-analytical methods appropriate? (6) Is the risk of bias when interpreting the results of the review considered? and (7) Is there an assessment of presence and likely impact of publication bias?

3.3.3 Critical Appraisal of Individual Studies

While the evidence pyramid in Fig. 4 provides guidance on which study design is considered of better quality, it will also be important to evaluate the quality of the methods used for each of these studies. To determine the validity of individual study results, it will be important to understand the characteristics, strengths, and weaknesses of different study designs used in science and the

different sources of bias of each design. There are several manuals available describing validated checklists for critical appraisal of different types of study designs. Several organizations or centers specializing in EBP have critical appraisal checklists available online such as the Critical Appraisal Skills Programme (https://casp-uk.net/), the Centre for Evidence-Based Medicine in Oxford (UK) (https://www.cebm.net/2014/06/critical-appraisal/), the Joanna Briggs Institute (http://joannabriggs.org/research/critical-appraisal-tools.html), and the toolkits provided by BMJ Best Practice. Because the methodological assessment of the study design of reviews and individual studies is key in determining the validity of the results and conclusion drawn, clinicians in most countries have extensive courses on research methods, designs, statistics, and critical appraisal of them.

Since one of the most important skills when appraising the evidence is understanding and recognizing different sources of bias, we will elaborate on this issue here. In Table 2, different sources of bias that can occur in clinical studies are summarized (Mayer 2010). As defined by the Cochrane Collaboration, bias is a systematic error or deviation from the truth, in results or in inferences (Higgins and Green 2011). Bias can lead to over- as well as underestimation of an intervention effect. Some biases are small, but others might be substantial and limit the validity of the results found in a study. Cochrane has produced a Risk of Bias Tool to be used by authors performing systematic reviews. It explains the most important sources of bias in clinical trials. Clinicians should be aware of these types or sources of bias when critically appraising the literature.

The most likely limitations that have been identified in randomized controlled trials that result in biased results (Schünemann et al. 2013) are the following:

- Lack of allocation concealment
- Lack of blinding

Table 2 An overview of different sources of bias in clinical studies (Mayer 2010; The Cochrane Risk of Bias Tool in Higgins and Green (2011))

Sources of bias	When does this occur?
Selection or sampling bias	When patients are selected in a manner that will systematically influence the outcome of the study, for example, inadequate randomization or inadequate concealment of allocation
Referral bias	When patients are selected after being referred for a specific type of care. This is a special form of selection bias that particularly limits the external validity thus generalizability of the study
Performance bias	When participants and personnel are not blinded hence are knowledgably of the allocated interventions during the study
Detection bias	When patients are preferentially included if they have been exposed to a particular risk factor. This is also a form of selection bias where exposure causes a sign or symptom that precipitates a search for the disease and then is blamed for causing the disease
Attrition bias	Patient attrition occurs when patients drop out of a study or are lost to follow-up, leading to a loss of valuable information. Patients who drop out may do so because a treatment or placebo is ineffective or there are too many unwanted side effects
Recall bias	Occurs most often in a retrospective study, either a case control or nonconcurrent cohort study. When asked about certain exposures, subjects with the outcome in the study are more likely than controls to recall the factors to which they were exposed
Reporting bias	When there is selective outcome reporting
Observer bias	When there is conscious or unconscious distorting in perception of reporting the measurement by an observer
Nonrespondent bias	Is a bias in the results of a study because of patients who do not respond to a survey or who drop out of a study; it occurs because those people who do not respond to a survey may be different in some fundamental way from those who do respond
Confounding	The presence of several variables that can explain the apparent connection between the cause and effect, for example, when there is no adequate statistical adjustment for possible confounders
Contamination	When the control group receives the same therapy as the experimental group

- Incomplete accounting of patients and outcome events
- Selective outcome reporting
- And other such as stopping a trial early for benefit, use of unvalidated outcome measures, carry-over effects in crossover trials, and recruitment bias in cluster RCTs

Key study limitations identified in observational studies that can introduce bias are (Schünemann et al. 2013):

- Failure to develop and apply appropriate eligibility criteria (inclusion of control population)
- Flawed measurement of both exposure and outcome
- Failure to adequately control confounding
- Incomplete or inadequately short follow-up, especially within prospective cohort studies

These sources of bias are determining factors to what is called "**internal validity**" of a study. Internal validity exists when precision and accuracy are not distorted by bias in the study. A study that is judged to be internally valid, measures precisely and accurately what is intended. Another important type of validity to consider, in particular for clinical studies and trials, is "**external validity**." External validity means that the results of the study can be generalized or extrapolated beyond the study population to other clinical situation or populations. When a population of a study is too narrow or the actual intervention delivered cannot be implemented in real practice, external validity is threatened (Mayer 2010).

Finally, an important network involved with improving quality in health research is the **EQUATOR network**. The EQUATOR network "Enhancing the QUAlity and Transparency Of health Research" is an international initiative that seeks to improve the reliability and value of published health research literature by promoting transparent and accurate **reporting** and wider use of robust **reporting guidelines**. The EQUATOR website (http://www.equator-network.org/) provides an overview of all types of reporting guidelines available for different study design:

- CONSORT for RCTs (with several extensions for cluster trials, pilot trials, etc.) and SPIRIT for trial protocols
- STROBE for observational studies
- PRISMA for systematic reviews
- SRQR and COREQ for qualitative research
- AGREE for clinical practice guidelines
- SQUIRE for quality improvement studies
- CARE for case reports
- STARD and TRIPOD for diagnostic and prognostic studies
- CHEERS for economic evaluations

We refer the reader to http://www.equator-network.org/ for up-to-date information on all reporting guidelines for main study types and their recent extensions. The reporting guidelines are intended for authors and researchers to help them in adequately reporting as well as designing their studies. They can also be an important tool to teach clinicians to evaluate and appraise the quality of studies performed within the broad domain of health care.

3.3.4 Synopses and Summaries

Summaries and synopses aim to provide critical overviews of reviews and studies to be available and usable by clinicians at the point-of care. These can be evidence-based textbooks or critical overviews of reviews and studies. They aim to provide high-quality, frequently updated, and easily digestible evidence-based recommendations for clinical practice, in particular those that are available online. Examples are UpToDate, DynaMed, and BMJ Best Practice. They are usually logically grouped around common medical scenarios and translated into alternative options related to diagnosis, treatment, and management (Banzi et al. 2010, 2011). They are also advocated and advertised as products with regular updating systems.

It is however very important to consider that recent analyses have criticized these textbooks and point-of-care summaries. The authors (Banzi et al. 2010; Jeffery et al. 2012; Kwag et al. 2016) compared different sources and showed that they include evidence relevant to practice at different speeds, that the proportion of topics with

potentially outdated treatment recommendations varies substantially and that topic coverage varies substantially. Generally, a high proportion of the 200 common topics had potentially out-of-date conclusions, missing information from one or more recently published studies (Banzi et al. 2010; Jeffery et al. 2012; Kwag et al. 2016). Jeffery et al. (2012) concluded that "although there is variation in the rate at which the leading textbooks are updated, all of them can benefit from more frequent processing of high quality, clinically relevant, recently published studies."

3.3.5 Clinical Practice Guidelines and Decision Support Systems

Systematic reviews of the effects of certain health-care interventions are essential to perform; however, they often do not provide sufficient information for making well-informed decisions. Clinical guidelines are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances (Legido-Quigley et al. 2013). Clinicians should be aware that not all clinical practice guidelines available to clinicians are evidence-based. Quite a few guidelines, also in palliative care, are based on expert opinions and lack the necessary studies to substantiate the guidance provided. Some guidelines also combine statements that are evidence-based with consensus-based statements when there is no evidence concerning one of the clinical questions. It will be important for readers to consider how statements are developed and preferably guidelines make this explicit (e.g., via the GRADE approach).

Regarding palliative care guidelines, several institutions and organizations exist that produce guidelines for palliative or end-of-life care. While some organizations (e.g., NICE, ESMO) produce palliative care guidelines next to a wide range of other health-care topics, there are also several national palliative care organizations who have specific units working to develop guidelines for palliative care, and there are international organizations developing international guidelines, including the European Association of Palliative Care.

High-quality guidelines should be based on high-quality evidence or in the absence of such evidence, on high-quality consensus procedures. Preferably of course, high-quality evidence is available to guide decision-making. The AGREE criteria to evaluate guidelines can help professionals to evaluate the development process of a guidelines. The AGREE working group has developed six domains for the evaluation of the quality of the process of making a practice guideline: scope/purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence. However, these criteria only indirectly assess quality of the content of the guideline by focusing on the way it was developed. To evaluate the extent to which a recommendation is based on evidence (and the level of that evidence), GRADE quality assessment criteria have been developed.

GRADE Approach

The **GRADE (Grading of recommendations assessment, development, and evaluation)** working group was founded in 2000. Because guidelines varied in how they rated the quality of evidence and how they graded the strength of recommendations, this group of researchers developed a new approach to grading quality (or certainty) of evidence and strength of recommendations, which is now considered the standard in guideline development internationally. A systematic and explicit grading approach can help prevent errors, facilitate critical appraisal, and help to improve communication of the information.

Table 3 displays an overview of the GRADE approach to quality of the evidence. Although quality of evidence is a continuum, four grades are distinguished and specific instructions for guidelines panels and authors of systematic reviews are described in detail in the Grade Handbook as it was updated in 2013 (Schünemann et al. 2013). We refer the reader to the http://www.gradeworkinggroup.org/ for up-to-date information on the grading approach.

In the GRADE approach, the quality of evidence is determined by several factors. The rating begins with the study design (trials or observational studies) and then addresses several factors that can reduce the quality of evidence and factors that can increase the quality rating. These are

Table 3 Quality of evidence grades. (Reproduced from Schünemann et al. 2013, with permission from the editors)

Grade	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Table 4 Factors determining the quality of evidence in the GRADE approach. (Reproduced from Schünemann et al. 2013, with permission from the editors)

Factors than can reduce the quality of the evidence	Consequence for the evidence level assigned
Limitations in study design or execution (risk of bias)	Decrease 1 or 2 levels
Inconsistency of results	Decrease 1 or 2 levels
Indirectness of evidence	Decrease 1 or 2 levels
Imprecision	Decrease 1 or 2 levels
Publication bias	Decrease 1 or 2 levels
Factors than can increase the quality of the evidence	Consequence for the evidence level assigned
Large magnitude of effect	Increase 1 or 2 levels
All plausible confounding would reduce the demonstrated effect or increase the effect if no effect was observed	Increase 1 level
Dose-response gradient	Increase 1 level

summarized in Table 4. The GRADE Handbook explains all these elements in further detail (Schünemann et al. 2013).

GRADE also makes explicit how to go from evidence to recommendation. The strength of a recommendation reflects the extent to which a guideline panel is confident that desirable effects of an intervention outweigh undesirable effects or vice versa, across a range of patients for whom the recommendation is intended (Schünemann et al. 2013). A strong recommendation signifies that the guideline panel judges the desirable effects of an intervention outweigh its undesirable effects (strong recommendation for an intervention) or that the undesirable effects of an intervention outweigh its desirable effects (strong recommendation against an intervention).

GRADE has also identified implications for different users of guidelines (i.e., patients, clinicians, as well as policy makers) of strong and weak recommendations, to aid with the interpretation. These are shown in Table 5.

Finally, GRADE has suggested how quality of evidence and strength of recommendations should be visually or symbolically represented. Table 6 summarizes the different symbols and letters that are used in guidelines to summarize these evaluations.

Implementation of Guidelines and Clinical Decision Support Systems

It has become clear over the past decades that guidelines do not implement themselves. While there has been a lot of literature related to the development and identification of evidence-based practices and programs, it has become clear that the mere existence of this knowledge does not change practice (Eyssen and Sikken 2018). Real impact in practice can only be achieved if effective intervention practices are combined with effective implementation practices. Consequently, several models have been developed to explain and visualize the implementation process of EBP (Nilsen 2015; Benahmed et al. 2017), such as the PARiHS framework (Kitson et al. 2008), the "research-to-practice-pipeline" model (Glasziou and Haynes 2005), and the GUIDE-M model (Brouwers et al. 2014). It is beyond the scope of this chapter to describe these models in detail. A meta-analysis of Fretheim et al. (2015) concluded that strategies that will increase adherence to clinical practice guidelines with moderate certainty include: clinical decision-support systems (including reminders), educational outreach visits (including practice facilitation), audit and feedback, local opinion leaders, tailored interventions, and educational meetings. In particular the clinical decision-support systems (CDS), also called computerized decision support systems, are important EPB initiatives currently under development.

Table 5 Implications of strong and weak recommendations for different users of guidelines. (Reproduced from Schünemann et al. 2013, with permission from the editors)

	Strong recommendation	Weak recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not	The majority of individuals in this situation would want the suggested course of action, but many would not
For clinicians	Most individuals should receive the recommended course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences	Recognize that different choices will be appropriate for different patients and that you must help each patient arrive at a management decision consistent with her or his values and preferences. Decision aids may well be useful helping individuals making decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working toward a decision
For policy makers	The recommendation can be adapted as policy in most situations including for the use as performance indicators	Policy making will require substantial debates and involvement of many stakeholders. Policies are also more likely to vary between regions. Performance indicators would have to focus on the fact that adequate deliberation about the management options has taken place

Table 6 Suggested GRADE representations of quality of evidence and strength of recommendations. (Reproduced from Schünemann et al. 2013, with permission from the editors)

Quality of evidence	Symbol	Letter (varies)
High	⊕⊕⊕⊕	A
Moderate	⊕⊕⊕◯	B
Low	⊕⊕◯◯	C
Very low	⊕◯◯◯	D
Strength of recommendation	**Symbol**	**Letter (varies)**
Strong for an intervention	↑↑	1
Weak for an intervention	↑?	2
Weak against an intervention	↓?	2
Strong against an intervention	↓↓	1

CDS is a technology that provides patient-specific medical knowledge at the point of need, that is, during medical or other consultations, via linking with patient file data. An EU-funded project GUIDES (Guideline Implementation with Decision Support) aims to develop a checklist and tools to improve the use of CDS. Organizations such as Duodecim Medical Publications have, for example, developed EBMeDS (Evidence-Based Medicine electronic Decision Support), a platform-independent service which can be integrated into electronic health records containing structured patient data. The EBMeDS system brings evidence into practice by means of context-sensitive guidance at the point of care. It receives structured patient data from electronic health records (EHRs) and returns reminders, therapeutic suggestions, and diagnosis-specific links to guidelines. Such systems will become an important tool for clinicians in the future to help at the point of care.

3.4 Step 4: Apply Evidence to the Individual Patient

In the application of evidence, step 3 is of course crucial. The quality of the studies found and/or the strength of recommendations in guidelines should be carefully considered. However, a number of other factors are crucial for translating this evidence to the individual patient at hand. The last EBP step is the process of knowledge transition (Haynes 2010) and concerns the application or interpretation of the evidence found in clinical studies to an individual or specific patient. Instead of generalizing evidence, EBP focuses on individualizing evidence to a specific problem or patient. This process is often the most difficult for a clinician.

A first important element to consider is the **clinical significance or importance** of a result of a study. Often in research, odds ratios and relative risks are reported to describe whether an intervention works compared to a control group. They are limited in providing information about how well the intervention works, that is, the size of the effect. Effect size reporting is one method of estimating the amount of benefit. A useful help in interpreting effect sizes is offered by Cohen, indicating that an effect size or standardized mean difference of around 0.2 is considered a small effect, 0.5 a moderate effect, and 0.8 or higher a large effect (Schünemann et al. 2013). An effect size quantifies the difference between two groups. For example, in the case of a comparison between an intervention and a control group in an intervention study, an effect size of 0.8 means that the score of the average person in the intervention group is 0.8 standard deviations above the average person in the control group and hence exceeds the scores of 79% of the control group.

Another highly relevant method for determining clinical significance is the **NNT or number-needed-to-treat** to get benefit and the **NNH or number-needed-to-harm** or number needed to treat to get harm. The NNT is the number of patients that must be treated with the therapy or intervention for a duration equal to the study period, in order to have one additional person experience a beneficial outcome. Ideally, NNT would be small as this means that the new intervention is a lot better than the standard or control (a "perfect" NNT would be 1). NNH is the number of patients that are needed to be exposed to a risk factor before an additional patient is harmed by side effects of the treatment or intervention. Hence, NNT and NNH are meant to help clinicians balance the benefit and risks of a therapy or intervention for an individual patient (Mayer 2010).

Next to these important elements for clinicians to consider when using evidence, Figure 2 also clearly indicated that clinical decisions are a result of four factors, that is, available evidence, the clinical situation, the patients' preferences, and clinical experience. Most evidence produced by research studies is not straightforward. Research designs all have strengths and weaknesses. Also, studies often have a specific target population that might not correspond to the individual patient of a clinician. That individual patient might have different characteristics in terms of gender, age, socio-economics, pathophysiology, compliance, comorbidity, risk of adverse events or other. Hence, clinicians often need to make decisions with relative uncertain or not easily transferable evidence. EBP has been advocated as an approach in which an experienced clinician decides whether and how external evidence applies to a particular patient (Wiebe 2000). It is not cookbook medicine.

If the application of evidence were a simple process, there would not be so much variability in actual practice as there is now. Research studies from various domains have shown there are large variations in diagnostic and therapeutic approaches between physicians from the same and other disciplines. Additionally, sometimes research studies clearly show the benefits of certain treatment or lack thereof, while clinicians do not act upon that evidence. One example is the observation that palliative care physicians all over the world use anticholinergic medications for the treatment of a "death rattle" at the end of life, while several studies including a systematic Cochrane review showed that there is no evidence of benefit of this medication (Wee and Hillier 2008). Qualitative research in this area showed that other factors were at play (e.g., feeling pressured, relatives that were distressed by the sound) that could explain clinician behavior (Wee et al. 2008a; Hirsch et al. 2013; Visser et al. 2015).

There are multiple factors contributing to or influencing actions and decisions of physicians. The complexity of the clinical problems, the uncertainty of outcomes of certain decisions, the lack of high-quality evidence, the feeling of physicians that they "need to act" and do something for their patients, patient expectations, examples of peers, or changes in reimbursement schemes, are only a few factors causing variability in practice. Medical decision-making can be very complex. Hence, clinical expertise does have a major role to play in the EBP process.

To increase the likelihood that physicians will make the best possible decisions, we must

perform the best possible clinical research and improve the quality of the evidence, and at the same time train physicians in all parts of the EBP process, from evaluating to applying evidence.

Finally, the factor "patient preferences" in the decision-making process cannot be underestimated. As most clinical decisions might have both advantages and disadvantages for patients, patients and clinicians must discuss the different treatment options together to make joint and well-informed decisions (Adriaenssens et al. 2018). The process is called "shared decision-making." Optimal patient care results out of the optimal interaction between evidence-based medicine and patient-centered communication skills, that is, shared decision-making (Hoffmann et al. 2014). Without shared decision-making, authentic EBP cannot occur (Greenhalgh et al. 2014; Hoffmann et al. 2014). Over recent decades, this process of shared decision-making has gained considerable attention and research has shown how difficult it is to put into practice. Health-care professionals do not always have the necessary skills and competences and there is a lack of good tools to support this process in practice, also in palliative care.

3.5 Step 5: Evaluate Own Performance as Clinician

Clinicians should evaluate the results of applying the evidence to their patient or patient population. Evaluating one's own performance as a clinician was already recommended by Sackett early 1990s and remains very necessary today (Sackett et al. 1991). Questioning yourself and regularly monitoring whether you are asking answerable questions, how efficiently you search the literature using current technologies, whether you can efficiently and critically appraise the literature, and what are determinants in applying evidence, can help in remaining an active and lifelong learner. Today, a whole body of literature has evolved around quality monitoring and quality management, aimed at monitoring performance of clinicians or practices or services using quality indicators, quality circles, or other methods for continuous quality improvement.

4 A Critical Reflection on EBP

The evidence-based movement has made important contributions to improving the quality of medical care. Scientific evidence has received a much more central and explicit role in medicine, reducing uncertainty, subjectivity, and bias. Ineffective or even harmful care or treatment can be identified better and prevented. It also helps to identify domains that lack sufficient evidence and can prevent new technologies from being advocated before sufficiently proven. EBP has also led to a critical reflection about the care we offer patients and has made the generating and dissemination of knowledge considerably easier. Consequently, research methodologies and statistical methods are improving consistently (Dutch Council for Public Health and Society 2017).

Nevertheless, EBP has not been left without criticism. One of the critiques on EBP in general is that the EBP model has become too focused on a "top-down" approach which emphasized "populations, statistics, risk and spurious certainty." Consequently, there might be too little flexibility needed to provide real person-centered care, focusing on the individual needs of patients (Greenhalgh et al. 2014).

An important essay published in the *BMJ* in 2014 by Greenhalgh et al. argues that, although EBP has had many benefits, it has also had some negative unintended consequences. Some of the problems highlighted today concern: the influence of industry (drug and medical devises companies) on setting the research agenda (Adriaenssens et al. 2018); the volume of evidence (in particular clinical guidelines) which has become unmanageable (Aoun and Nekolaichuk 2014); statistically significant benefits which may be marginal in clinical practice (Banzi et al. 2010); a danger of care being management-driven (e.g., computerized decision-support systems, point of care prompts, or structured templates) instead of patient-centered (Banzi et al. 2011); and EBP guidelines that often map poorly to complex multi-morbidity (Bauça-Machado et al. 2017).

These authors suggest refocusing on providing useable evidence that can be combined with context and professional expertise so that individual

patients get optimal treatment. They advocate to return to "real EBM," that is, to the movement's founding principles, instead of rejecting EBM as a failed model: "to individualise evidence and share decisions through meaningful conversations in the context of a humanistic and professional clinician-patient relationship." Fig. 6 further explains "real EBM" as defined by these authors.

The importance of context in EBP has received progressively more attention by different organizations. The Dutch Council for Health and Society in the Netherlands has published a report in 2017 entitled "Without context, no proof: concerning the illusion of evidence-based practice in health care" (in Dutch). The Belgian Health Care Knowledge Centre has also highlighted the importance of context by adding a fourth dimension to the definition of the concept of EPB. "A fourth dimension, contextual factors (such as costs and availability of resources) is added as this is an element that affects the strength of a recommendation and can hamper implementation of a guideline." This is depicted in Fig. 5. The Centre states that "solely using scientific evidence in health care decision making without taking into account professional expertise, context and patient' preferences (called 'cookbook medicine') does not result in high quality healthcare provision" (Adriaenssens et al. 2018).

Greenhalgh et al. (2014), the Dutch Council for Health and Society, and the Belgian Health Care Knowledge Centre do not advise to fully abandon EBM, EBP, or the search for evidence. As stated by the Dutch Council for Health and Society, what is needed, is evidence in multiple forms. If daily reality of health and social care can be seen from multiple angles, the search for conclusive evidence is an illusion and would lead to over-simplification of good care. "The" evidence as a basis for good care is an illusion. To deliver good patient-centered care, external knowledge or evidence as such is not enough. Clinical expertise, local knowledge, knowledge from patients, and knowledge of the context – the circumstances of living, patient preferences, the care setting, are also of utmost importance. Care professionals should embrace uncertainty in evidence and take the context in which their patients live into account. Researchers should acknowledge that scientific evidence is always incomplete. Healthcare insurance companies, the government, and inspectors should also allow a more experimental approach in health care and value the ability of care professionals and care organizations to learn and improve via such experiments. The Council pleads for a context-based practice instead of pure evidence-based practice.

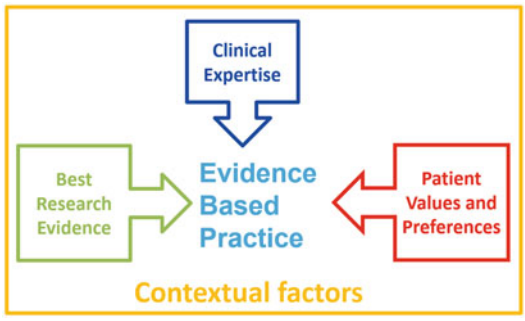

Fig. 5 Visualization of the concept of EBP including the importance of context. (From Adriaenssens et al. 2018, with permission (CC-BY-NC-ND license); no changes made)

5 A Critical Reflection on EPB in Palliative Care

In principle, the same issues addressed in EBP apply to palliative care, as this is one branch of medicine, although a highly complex one. Decisions concerning patients and families should be evidence-based or evidence-informed, depending on the evidence at hand. However, several authors in the field of palliative care have also criticized the EBM and EBP approach where RCTs are considered the gold standard. They indicate that while well-executed RCTs can minimize the different sources of bias via the use of universal and objective methodological criteria (e.g., via CONSORT guidelines, Moher 1998), conducting such high-quality research studies is very challenging in the context of palliative care – both ethically and methodologically. The population at hand as well as the complexity of the interventions in palliative care are both reasons that complicate doing high-quality RCTs. Visser et al. (2015)

Box 2: What is real evidence based medicine and how do we achieve it?

Real evidence based medicine:

- Makes the ethical care of the patient its top priority
- Demands individualised evidence in a format that clinicians and patients can understand
- Is characterised by expert judgment rather than mechanical rule following
- Shares decisions with patients through meaningful conversations
- Builds on a strong clinician-patient relationship and the human aspects of care
- Applies these principles at community level for evidence based public health

Actions to deliver real evidence based medicine

- Patients must demand better evidence, better presented, better explained, and applied in a more personalised way
- Clinical training must go beyond searching and critical appraisal to hone expert judgment and shared decision making skills
- Producers of evidence summaries, clinical guidelines, and decision support tools must take account of who will use them, for what purposes, and under what constraints
- Publishers must demand that studies meet usability standards as well as methodological ones
- Policy makers must resist the instrumental generation and use of "evidence" by vested interests
- Independent funders must increasingly shape the production, synthesis, and dissemination of high quality clinical and public health evidence
- The research agenda must become broader and more interdisciplinary, embracing the experience of illness, the psychology of evidence interpretation, the negotiation and sharing of evidence by clinicians and patients, and how to prevent harm from overdiagnosis

Fig. 6 Box 1 Real EBM. (Reproduced from Greenhalgh et al. 2014, with permission from BMJ Publishing Group Ltd)

highlight, for example, that recruitment is inherently difficult in palliative care because of the gatekeeping role of relatives or clinical staff which prevents studies from achieving adequate sample sizes. They also show that the high attrition rates are probably often caused by symptomatic deterioration of patients which is problematic for intention-to-treat analyses in RCTs that rely on completeness of data sets. Furthermore, in palliative care trials, interventions are often multi-componential targeting multiple problems and symptoms of patients and/or their families (physical, psychological, social, and/or spiritual) which makes it very difficult to identify one primary outcome and link outcomes clearly to the intervention components.

Visser et al. (2015) have highlighted the need for improving palliative care research not only by improving the quality of RCTs where possible but also to devote more attention to alternative research methodologies, including high-quality observational studies. Some important work outside of the field of palliative care (Benson and Hartz 2000; Concato et al. 2000) has shown that high-quality methodologically valid observational prospective studies with adequately large sample sizes can yield equivalent results to RCTs, challenging the hierarchy of evidence traditionally put forward in EBP. Based on an evaluation of the current literature, Visser et al. (2015) highlight that – although promising – currently the quality of observational studies is not sufficient enough to rival RCTs. Hence, both improving methodologies of trials as well as other study design will be of utmost importance in palliative care to ensure that clinical practice is informed by adequate levels of evidence. They also conclude that "the EBM model is likely to grow more flexible as the traditional unimodal top-down approach is replaced by the use of multiple diverse methodologies as a research tool kit. Such a mixed-method approach will be viewed not as a means by which to dodge the challenge of conducting methodologically rigorous work in palliative care. Instead, a multi-faceted approach can be regarded as a more valuable scheme with which to address the complex and subtle questions that define the objective of the palliative care research agenda" (cited from Visser et al. 2015).

6 Conclusion

EBP has enormously transformed clinicians' approach to practicing their profession. It was responsible for a true paradigm shift in medicine and improving the standards of treatment and care for all people. To ensure patients in palliative care receive the best possible care, decisions should be taken in conjunction with them, based on their preferences and wishes and the best available evidence on treatments and care. The research community in palliative care must strive to provide high-quality research, high-quality reviews, and high-quality guidelines of that research and ensure that clinicians can easily access and use the best available evidence at the point of care. To produce this evidence and considering the complexity and large diversity of the palliative care population at hand combined with the multicomponent nature of palliative care, there is a need for research groups and trial centers to work together across multiple disciplines – medical and social science disciplines, quantitative and qualitative research methods. The future of EBP lies in generating useable evidence that can be combined with context and professional expertise to provide individual patients optimal treatment and care.

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Part X

Public Health Approach in Palliative and End-of-Life Care

New Public Health Approaches to End-of-Life Care

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Libby Sallnow and Sally Paul

Contents

Abstract

The palliative and end-of-life care movement worldwide has been a success story in many respects. Palliative care services exist in many countries throughout the world and are increasingly integrated into mainstream health services. Despite these achievements, the movement continues to face challenges from demographic trends, changing patterns of illness, and social contexts of care, which suggest an increasing need for services. Questions have been raised regarding the appropriateness of building further services, as compared with new perspectives on care, which see communities and professionals working in partnership. These perspectives are collectively known as the new public health perspective and this chapter details the emergence of new public health perspectives in end-of-life care.

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_97

1 End-of-Life Care in Need of New Public Health Approaches

The end-of-life care movement worldwide has been a success story in many respects. Palliative care services exist in many countries throughout the world and are increasingly integrated into mainstream health services. The experiences of those dying in pain have been highlighted as a human rights issue at both national and global levels (Knaul et al. 2017), and the impact of early palliative care is increasingly recognized in certain disease groups (Temel et al. 2010).

Despite these achievements, the movement continues to face challenges from demographic trends, changing patterns of illness, and social contexts of care which suggest increasing need for services. Further to this, the movement is increasingly facing criticisms that the original vision of holistic care is being interpreted in a more restrictive manner, focusing on physical or psychological symptoms at the expense of social concerns. The proliferation of professionals in the discipline has led some to reflect that communities no longer feel confident or able to respond to end-of-life issues, depending increasingly on professional responses which both disempower people and place further demands on services.

One response to these concerns has been to redefine how end-of-life care is understood. Rather than holding it as a medical issue, under the remit of health and social care professionals, it should be reframed as a social experience. This then allows individuals, families, and communities to take an active role in the issues affecting them, working with professional services to meet the needs of the dying. This approach of working in partnership with communities is named the new public health approach to end-of-life care.

This chapter will begin by detailing the emergence of the new public health movement and the key documents that have shaped its development. It will go on to discuss the relevance of a new public health approach to end-of-life care, identifying key theoretical models that seek to develop and conceptualize this area of practice. It finishes by highlighting examples of new public health approaches to end-of-life care to illustrate the different ways in which this approach is being used in practice.

2 An Introduction to New Public Health

The new public health movement emerged in the later part of the twentieth century. While it emerged from and was built on the traditional or classical public health movement of centuries before, the movement was "new" in that it challenged and redefined certain components of the approach. New public health continued to endorse many aspects such as the role of policy in improving health and the importance of prevention of disease or ill-health, but it also represented a departure from classical public health, through its radical reframing of health as everyone's responsibility. This included identifying the importance of the social determinants of health alongside biomedical factors and the positioning of patients, carers, communities, and citizens as experts in their own health. New public health approaches have equity as their core focus and seek to bring healthy lives within everyone's reach. As a result they take a much broader view of the causes and solutions for health and well-being, going beyond medicine, biomedical approaches, and professional responses.

Fran Baum, in her book *The New Public Health* (2015), describes five innovative features of a new public health approach (see Box 1).

Box 1: Features of a new public health approach

1. Puts the pursuit of equity at the center of public health endeavors
2. Is based on the assumption that social and environmental factors are responsible for much ill-health
3. Argues for health-promoting health services that are based on a strong system of primary health care

(*continued*)

Box 1: (continued)

4. Stresses the role of all sectors in impacting on health and the importance of health in all policies
5. Stresses the importance of participation and involvement in all new public health endeavors

As the new public health approach was formalized, it galvanized a range of different approaches from preexisting global movements such as community development, behavioral, health education, and environmental approaches and indigenous and lay medicine. This has led to a diverse and inclusive field.

2.1 Key Documents that Have Shaped the New Public Health

A series of documents and declarations have helped define the field of new public health.

1) The so-called *Lalonde Report,* after the then ruling Canadian Health Minister, was published in 1974 (formally titled "A New Perspective on the Health of Canadians") and provided an important articulation of the broad range of factors, beyond the biomedical healthcare system, understood to influence and determine health. It recognized the role of environmental, political, and lifestyle factors and healthcare services, through the health field concept (Lalonde 1974).

2) The *Alma-Ata Declaration*, published by the World Health Organization (WHO) in 1978, positioned primary health care as participatory health care, in which people have both a right and a duty to participate. It provided a new model for affordable, sustainable, and universal primary health care (see Box 2).

3) The *Ottawa Charter for Health Promotion* (World Health Organisation 1986) (see Box 3) defined the new practice of health promotion as the process of enabling people to increase control over, and to improve, their health. While it has provided a framework for a new public health approach globally, there have been some criticisms voiced over the extent to which it incorporates the diversity of perspectives globally, focusing on individual rather than collective approaches to health (McPhail-Bell et al. 2013).

Box 2: An excerpt from the Alma-Ata Declaration (WHO 1978)

Primary health care is essential health care based on practical, scientifically sound and socially acceptable methods and technology made universally accessible to individuals and families in the community through their full participation and at a cost that the community and country can afford to maintain at every stage of their development in the spirit of self-reliance and self-determination.

Box 3: The Ottawa Charter for Health Promotion (WHO 1986): the five pillars

1. Building healthy public policy
2. Creating supportive environments
3. Strengthening community action
4. Developing personal skills
5. Reorienting health-care services toward prevention of illness and promotion of health

Subsequent documents from the WHO have further embedded this approach, including the *Millennium Development Goals* and the subsequent *Sustainable Development Goals* (Sachs 2012), but new public health approaches go beyond the WHO principles. Much grassroots community action can be considered under the umbrella term of new public health approaches. The balance of power between such local and informal initiatives and those supported by health-care organizations and institutions continues to inform, challenge, and redefine the field.

3 New Public Health Approaches and End-of-Life Care

The hospice and palliative care movement has made great strides in challenging the conditions in which the dying and their close family are cared for and supported. It is argued, however, that these movements have become predominantly a professional or service-based response, and this has led to over-professionalization of care and a disempowerment of communities in relation to these issues (Kellehear 2005). Further concerns have been raised regarding the inequity of care provided at the end of life (Dixon et al. 2015) or the international variation (Economist Intelligence Unit 2015). The predicted demographic changes, relating to rising numbers of older people and the prevalence of chronic illness, will place further stress on the system (Etkind et al. 2017).

For these reasons, alternative approaches to supporting death, dying, loss, and care can offer more holistic, empowering, and sustainable models of support. The new public health approach to end-of-life care integrates principles of health promotion, equity, social and environmental responses to ill-health, and professional/lay power sharing and partnerships. The broad natures of both new public health and end-of-life care have meant that a range of examples is in existence today. The two common terms used to describe these approaches are health-promoting palliative care and compassionate communities.

Health-promoting palliative care describes the application of the five pillars of health promotion to end-of-life care (Kellehear 1999). It aims to change the practice of end-of-life care and provides a structure for services to develop health-promoting practices. This model focuses heavily on the role of professional services, and the subsequent movement of compassionate communities moves beyond end-of-life care services to look at the role lay communities, schools, businesses, or councils play in end-of-life care.

One of the key principles of new public health is working with communities as partners, often termed community engagement and defined by the authors as:

> An umbrella terms for a process which enables communities to work together to understand, build capacity and address issues to improve their experience of end-of-life and bereavement and related wellbeing. It exists on a spectrum of engagement that extends from informing through to empowering, depending on a range of factors such as the degree of participation from the local community and the intention of the work. Community engagement activities in end-of-life care services go beyond working in the community to working with the community to improve the experiences of end-of-life care. (Sallnow and Paul 2015)

4 Current Practices in End-of-Life Care

Examples of new public health approaches to end-of-life care are developing around the world and represent a diverse set of approaches, shaped both in response to local need and the differing approaches contained within the new public health field. Such work includes, but is not limited to, mobilizing existing or facilitated community networks and/or resources; working with community organizations to influence perceptions of and responses to death and bereavement; awareness raising, education, and/or training activities around specific end-of-life issues; and policy reform (Sallnow et al. 2016). The significance of these activities for meaningful end-of-life care, and the challenge of applying a new way of thinking to this area of practice, has resulted in a number of frameworks that attempt to define and develop how new public health approaches to end-of-life care are conceptualized and how they are different to service delivery approaches.

4.1 The Theory: What Defines a New Public Health Project?

Allan Kellehear's (2005 p.156) "Big Seven Checklist" offers a guide to understanding "genuine" health-promoting palliative care activities (see Box 4). It highlights the significance of community ownership, collaboration, and participation in employing a health-promoting approach to end-of-life care. The checklist also identifies

the importance of developing activities that are based on early intervention and harm reduction that involves normalizing death, dying, and bereavement: proactively preparing individuals and communities for related experiences.

Box 4: The Big Seven Checklist

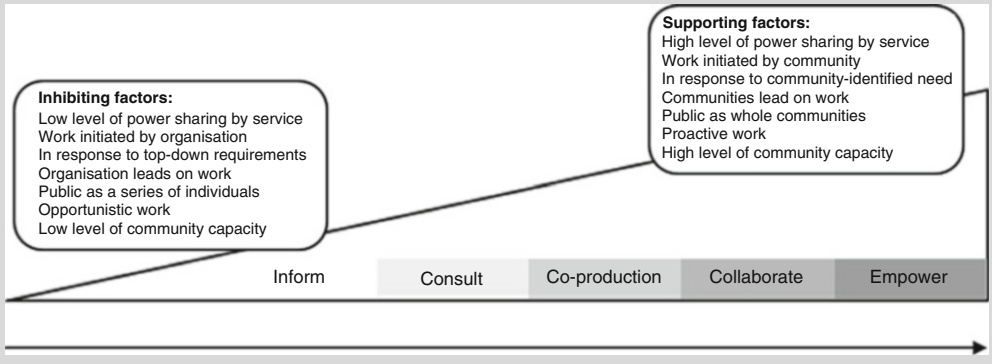
1. In what way does the project help prevent social difficulties around death, dying, loss, or care?
2. In what way do they harm-minimize difficulties we may not be able to prevent around death, dying, loss, or care?
3. In what ways can these activities be understood as early interventions along the journey of death, dying, loss, or care?
4. In what ways do these activities alter/change a setting or environment for the better in terms of our present or future responses to death, dying, loss, or care?
5. In what way are the proposed activities participatory – borne, partnered, and nurtured by community member?
6. How sustainable will the activities or programs be without your future input?
7. How can we evaluate their success of usefulness so that we can justify their presence, their funding, and their ongoing support?

The Spectrum for Community Engagement in End-of-Life Care (Sallnow and Paul 2015) offers a framework for end-of-life care service providers to both understand and develop new public health approaches (see Box 5). It employs a hierarchical model that represents five types of work along a continuum involving different levels of power sharing and participation. This extends from informing the people or communities that they work with to consulting with them, co-producing, collaborating, and finally empowering them. The spectrum thus distinguishes a new public health approach from more traditional forms of service provision by placing emphasis on the development of community capacity and resilience.

4.2 Practice: Examples of Existing New Public Health Approaches in End-of-Life Care

This section discusses four existing practice examples that are illustrative of new public health approaches to end-of-life care. It follows the earlier theoretical sections by exploring what these approaches look like in practice and how they have been understood and evaluated.

Box 5: The Spectrum for Community Engagement in End-of-Life Care: developing community capacity [EoLC – End-of-life care]. Reproduced with permission from Sallnow and Paul (2015)



4.2.1 Example 1: Compassionate Neighbours, London

The Compassionate Neighbours project recruits and trains local people to become Compassionate Neighbours. Compassionate Neighbours are local people who support those nearing the end of their lives in their own homes. The project focuses on supporting people to be good neighbors rather than training them in a new role. The aim is to support those at the end of life and their families through companionship, practical support, connecting people to their communities, or helping people to access services they need.

Recruitment is through a series of open days that culminate in a selection day, where participants select whether they would like to participate in the project and the project managers determine if there are any reasons they may not participate. Once enrolled in the project, participants complete a training course. This is either over 4 full days or over 2 weekends. Approximately 15 participants take part in each training program. At the end of the training program, a DBS (Disclosure and Barring Service) check is carried out. The project managers and Compassionate Neighbour then jointly consider the roles most appropriate for them. For some, they are matched with people in the community immediately, but for others, a different role within the project is selected. Not everyone begins with being matched to someone in the community; some participate in other aspects of the project, and some are never matched yet remain with the project. The focus is less on matching set numbers of people but instead on developing the capacity of members of the community to make their own contribution.

The project holds supportive and reflective monthly meetings for all Compassionate Neighbours. In these meetings, participants can reflect on their relationship with the person they are visiting but are also encouraged to reflect on themselves and their own personal development. These are based on a model of personal and group learning and are termed practice development meetings (PDM). In addition to these more formal modes of support, the project hosts a weekly coffee morning in a public space in the hospice open to all participants and the general public. These meetings allow people to come and learn about the project and for the Compassionate Neighbours to meet with each other and develop the network of peer support. Internal and external speakers come and speak about topics related to the project such as how to support someone with dementia or that can be of general relevance, such as managing fuel poverty.

The project has developed to have over 200 trained Compassionate Neighbours matched with over 90 people in the community at the time of writing and has won many prestigious national awards. It has two full-time members of staff coordinating the project and, although initially set up outside the traditional volunteer department, is working increasingly closely with it today.

The project has been the subject of a mixed methods evaluation (Sallnow et al. 2017). The study showed how participating in the project improved participants sense of well-being, connection, and feelings of loneliness. Interestingly, although those being visited at the end of life described these changes, the most significant changes were observed for the Compassionate Neighbours. Their membership of a large network, the time taken to develop new skills and make new friends, and the development of a sense of meaning and purpose were seen to have the most significant impact. These outcomes illustrate how this functioned as a new public health project, acting to prevent and reduce social isolation and disconnection in people before they reached the end of life. The outcomes for those training were seen as important as those receiving the care, illustrating how this sits distinctly from a service-based approach focusing only on outcomes for the recipient.

4.2.2 Example 2: Work with Schools, Central Scotland

Strathcarron Hospice, in Stirlingshire, Scotland, undertook an action research study to identify how hospice staff could work with schools in their catchment area. This was because the hospice catchment area covered 160 schools and received numerous ad hoc requests from schools for pre- and post-bereavement support for pupils,

education sessions relating to end-of-life care, and presentations on the role of the hospice due to local fundraising initiatives. The study therefore aimed to explore how the hospice could work with these schools in a more structured and meaningful way that involved advancing education and support around end-of-life and bereavement care. Through a process that involved working in partnership with staff, parents, and children aged 9 to 12, several practice developments were identified that were found to be useful for the school curriculum and the relationship between hospices and school communities (Paul et al. 2016). Four activities were subsequently co-created, piloted, and then delivered as part of normal service delivery at both the hospice and participating schools. These innovations include:

- The Resilience Project – an education program for all 9–12-year-olds that aims to introduce death as a normal part of the life cycle, develop an understanding of what happens to the body at death, nurture the skills and capacity of children to cope when someone dies, and support an awareness of other people's needs when someone dies and how to respond appropriately. The program is delivered over five core lessons but is adapted according to the needs, and questions, of each group of children.
- Bereavement training to school staff – a 2-hour free training session that is offered to all schools in the hospice catchment area. It seeks to assist staff to develop confidence and skills in engaging and supporting children experiencing bereavement while also dispel myths associated with hospice care and ensure that any referrals for specialist bereavement support are appropriate.
- Hospice information leaflets – children and hospice staff co-designed a leaflet that explains the role of the hospice in the community. This leaflet is included in all hospice fundraising materials that are sent to/used with schools so that school staff are able to communicate to children what the hospice does in an age-appropriate way.
- A Schools Bereavement Policy – a document sent to all schools that provides a framework for school staff on what to do if a child and/or staff member is bereaved. The policy seeks to support staff to feel more confident when dealing with bereavement experiences and where to access appropriate support and resources if needed.

Box 6: Role of the hospice in working with schools: a model for integrated practice. Reproduced with permission from Paul et al. (2016)

Role of hospice	Goal	Practice innovation(s)
Awareness raising	Dispel myths associated with hospice care, end-of-life care, and bereavement	Develop existing fundraising campaigns that focus on raising awareness of hospice care
Education and training	Increase awareness of childhood bereavement Develop capacity of school staff to manage childhood bereavement within the school setting and at home	Plan and deliver bereavement training for school staff
Leadership in death education and bereavement	Influence policy makers and/or management teams to establish death, dying, and bereavement affirming activities, policies, and procedures	Engage with school communities to raise awareness of palliative care issues Work with school staff to develop a death and life-affirming curriculum Work with school staff to develop bereavement policies and procedures

These practice innovations sit apart from the hospices previous work with schools as they do not involve the hospice delivering specific services but mobilizing those involved in caring for children to be actively involved in providing support and education around hospice, end-of-life, and bereavement care. The learning about what these activities means for hospices in working with school communities is outlined in Box 6.

4.2.3 Example 3: Compassionate City Charter

The Compassionate City Charter focuses on sectors of society outside traditional palliative care or even health and social care services. The reason for this is the potential hit-and-miss nature of services developed by discrete community interests or services, where some communities may be involved, while others are unaware of the projects. The Compassionate City Charter takes a civic approach by developing a program of work through local governments, mayor's offices, or other municipal agencies and engaging broadly with all the cultural, religious, commercial, or leisure organizations in a locality, both to engage with a broader part of the local community and also to explicitly situate issues around death and dying as outside the remit of health and social care. It then becomes everybody's business.

Kellehear (2016) has outlined the steps a local government should take to develop their local area as a Compassionate City (see Box 7).

Box 7: The Compassionate City Charter (Kellehear 2016)

Compassionate Cities are communities that recognize that all natural cycles of sickness and health, birth and death, and love and loss occur every day within the orbits of its institutions and regular activities. A Compassionate City is a community that recognizes that care for one another at times of crisis and loss is not simply a task solely for health and social services but is everyone's responsibility.

Compassionate Cities are communities that publicly encourage, facilitate, support, and celebrate care for one another during life's most testing moments and experiences, especially those pertaining to life-threatening and life-limiting illness, chronic disability, frail, ageing and dementia, death in childhood, grief and bereavement, and the trials and burdens of long-term care. Though local government strives to maintain and strengthen quality services for the most fragile and vulnerable in our midst, those persons are not the limits of our experience of fragility and vulnerability. Serious personal crises of illness, dying, death, and loss may visit any of us, at any time during the normal course of our lives. A Compassionate City is a community that squarely recognizes and addresses this social fact.

Through the auspices of the Mayor's office or equivalent body, a Compassionate City will – by public marketing and advertising, by the use of the city's network and influences, and by virtue of collaboration and cooperation, in partnership with social media and its own offices – develop and support the following *13 social changes* to the cities key institutions and activities:

1. Our schools will have annually reviewed policies or guidance documents for dying, death, loss, and care.
2. Our workplaces will have annually reviewed policies or guidance documents for dying, death, loss, and care.
3. Our trade unions will have annually reviewed policies or guidance documents for dying, death, loss, and care.
4. Our places of worship will have at least one dedicated group for end-of-life care support.
5. Our city's hospices and nursing homes will have a community development program involving local area citizens in end-of-life care activities and programs.
6. Our city's major museums and art galleries will hold annual exhibitions on the experiences of ageing, dying, death, loss, or care.
7. Our city will host an annual peacetime memorial parade representing the major sectors of human loss outside military campaigns –

cancer, motor neuron disease, AIDS, child loss, suicide survivors, animal companion loss, widowhood, industrial and vehicle accidents, the loss of emergency workers and all end-of-life care personnel, etc.

8. Our city will create an incentive scheme to celebrate and highlight the most creative compassionate organization, event, and individual/s. The scheme will take the form of an annual award administered by a committee drawn from the end-of-life care sector. A "Mayor's Prize" will recognize individual/s for that year who most exemplify the city's values of compassionate care.
9. Our city will publicly showcase, in print and in social media, our local government policies, services, funding opportunities, partnerships, and public events that address "our compassionate concerns" with living with ageing, life-threatening and life-limiting illness, loss and bereavement, and long-term caring. All end-of-life care-related services within the city limits will be encouraged to distribute this material or these web links including veterinarians and funeral organizations.
10. Our city will work with local social or print media to encourage an annual citywide short story or art competition that helps raise awareness of ageing, dying, death, loss, or caring.
11. All our compassionate policies and services, and in the policies and practices of our official compassionate partners and alliances, will demonstrate an understanding of how diversity shapes the experience of ageing, dying, death, loss, and care – through ethnic, religious, gendered, and sexual identity and through the social experiences of poverty, inequality, and disenfranchisement.
12. We will seek to encourage and to invite evidence that institutions for the homeless and the imprisoned have support plans in place for end-of-life care and loss and bereavement.
13. Our city will establish and review these targets and goals in the first 2 years and thereafter will add one more sector annually to our action plans for a Compassionate City – e.g., hospitals, further and higher education, charities, community and voluntary organizations, police and emergency services, and so on.

4.2.4 Example 4: To Absent Friends Festival, Scotland

To Absent Friends, a People's Festival of Storytelling and Remembrance is a Scotland-wide event that is held on the 1st–7th of November each year. The festival was initiated by the Scottish Partnership for Palliative Care, through the Good Life, Good Death, Good Grief Alliance, and aims to empower Scottish society to reassert control of death in their own lives by making it acceptable to share memories and stories of people who have died. The festival has a number of supporters but is not owned by one particular group, instead it seeks to provide an opportunity for individuals and groups to remember people who have died in whatever way is meaningful for them and their communities, in public or private.

Since the first festival in 2014, the range and breadth of activities have expanded and now occur across Scotland. Patterson et al. (2017) detail some of these activities that include:

- Public events that are open to all, such as concerts, storytelling, and poetry events
- Community events that are run by organizations for their own members and invitees, such as activities ran by local hospices, nursing homes, and charitable organizations that encourage the sharing of memories
- Private events that are held by individuals, families, and groups of friends, such as making memory boxes, lighting remembrance candles, and visiting cemeteries
- Online activities, such as using the festival website to dedicate music videos or leave messages on the wall of remembrance

The festival has been subject to an evaluation that identified its potential to engage people from a variety of social and economic communities (Scottish Partnership for Palliative Care 2015). This evaluation also identified that the success of the festival was related to local ownership of the

events. The time, knowledge, and skills of the Scottish Partnership for Palliative Care in growing the festival were also highlighted yet this time were viewed as necessary in supporting the promotion of activities that would, in turn, generate wider participation.

5 Summary

This chapter has explored the emergence of new public approaches to end-of-life care and their establishment as an integral component of end-of-life care for the future. The range of approaches that have evolved recognize the diversity of need that exists for individuals, families, communities, and society when faced with issues relating to death, dying, loss, and care: a new public health approach represents a broad inclusive model for meeting these needs collectively. Four practice examples have been provided that identify the breadth of the approach but by no means define the scope, as projects must be locally relevant and tailored. Such activities sit apart from traditional, clinical-based, service delivery approaches by working *with* communities as equal partners to identify and respond to their own end-of-life and bereavement needs.

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A Public Health Approach to Integrate Palliative Care into a Country's Health-Care System: Guidance as Provided by the WHO

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The following chapter is largely based by on the following publication by the WHO:

World Health Organization. Planning and Implementing Palliative Care Services: A Guide for Programme Managers. World Health Organization. 2016.

The full report can be downloaded for free at: apps.who.int/iris/bitstream/10665/250584/1/9789241565417-eng.pdf

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
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Abstract

Many people across the globe are in need of quality palliative care (PC), of which a majority live in low- and middle-income countries. However, many still see their needs unmet. It is estimated that only 14% of people in need of PC actually receive it. To improve access to PC as a core component of health systems, the WHO developed evidence-based tools on how to integrate PC into national health systems, across disease groups and levels of care. The current chapter provides an overview of this WHO Public Health Approach to Palliative Care, and discusses the seven components that were set out as a practical guidance for policy makers and program managers at national or subnational level to plan and implement PC services integrated into existing healthcare services. The components discussed are: (1) the development of appropriate PC policies, (2) the scaling up and integration of PC into the healthcare system, (3) the improvement of pain relief medicines access, (4) the strengthening of human resources for PC, (5) the establishment of palliative care services, (6) the setting of standards for evaluating PC services, and (7) the costing of PC services.

1 The Need for Palliative Care Globally

Every year, an estimated 20 million people globally are in need of palliative care in the last year of their life, with even more requiring palliative care in their preceding years (Connor and Bermedo 2014). Of these people in need, 78% live in low- and middle-income countries. For children, 98% of those needing palliative care live in low- and middle-income countries, with almost half of them living in Africa. For these children, the evidence of models and outcomes of care is very scarce (Harding et al. 2014a). In 2014, it was estimated that only 14% of people needing palliative care at the end of life actually receive it. An analysis of global palliative care provision found that 33% of countries had no known activity (Connor and Bermedo 2014). In recent years the field of global health has begun to address the underdeveloped field of palliative care, with growing evidence of need, models, and outcomes that are appropriate for local health systems (Harding and Higginson 2014).

With other organizations, the WHO sees access to palliative care as a fundamental right. In 2014, the first ever global resolution on palliative care, WHA 67.19, called upon WHO and member states to improve access to palliative care as a core component of health systems, with an emphasis on primary health care and community-/home-based care. Member states have requested WHO to develop evidence-based tools on integrating palliative care into national health systems, across disease groups and levels of care. This has been further strengthened by the WHO universal health coverage (UHC) policy which "means that all people have access to the health services they need (prevention, promotion, treatment, rehabilitation and palliative care) without the risk of financial hardship when paying for them" (World Health Organization 2018a). The current chapter provides an overview of the approach and practical guidance suggested by the WHO for policy-makers or program managers at national or subnational level to plan and implement palliative care services, integrated into existing health-care services. It is a condensed version of the WHO document "Planning and Implementing Palliative Care Services: A Guide for Programme Managers" (World Health Organization 2016). In proposing the approaches, the WHO has paid specific attention to feasibility for low- and middle-income settings.

2 Definitions

The World Health Organization has defined palliative care as an approach that improves the quality of life of patients (adults and children) and their families who are facing problems associated with life-threatening illness (World Health Organization 2018b). It prevents and relieves suffering through the early identification, correct assessment, and treatment of pain and other problems. Palliative care is the prevention and relief of suffering of any kind – physical, psychological, social, or spiritual – experienced by adults and children living with life-limiting health problems. It promotes dignity, quality of life, and adjustment to progressive illnesses, using best available evidence.

Palliative care for children represents a special field in relation to adult palliative care. Palliative care for children is the active total care of the child's body, mind, and spirit and also involves giving support to the family. It begins when illness is diagnosed and continues regardless of whether or not a child receives treatment directed at the disease.

Primary palliative care refers to the core elements of palliative care (e.g., aligning treatment with a patient's preferences, basic symptom management) that are provided by all physicians and health-care workers caring for chronically or terminally ill patients.

Specialist or specialized palliative care refers to palliative care provided by health-care professionals or teams that mostly care for chronically or terminally ill patients, are specialized in addressing more complex palliative care needs (e.g., negotiating a difficult family meeting, addressing hidden existential distress, and managing refractory symptoms), and have received specific training for these skills (Quill and Abernethy 2013).

3 Core Aspects of the WHO Public Health Approach for Palliative Care

What constitutes a comprehensive public health strategy?

The published strategy builds on the WHO Public Health Strategy pioneered in the 1990s (Stjernswärd et al. 2007). The strategy assumes a responsibility for national health systems to include palliative care in the continuum of care for people with serious chronic, life-limiting health problems, linking it to prevention, early detection, and treatment programs. A good palliative care system is one that is integrated into primary health care, community- and home-based care, but also into informal care, such as care provided by family and community volunteers. Integrated palliative care implies that specialist palliative care is just one component of palliative care service delivery. All health-care providers are to be trained in pain management and the needs of patients with life-threatening illness.

A comprehensive approach to strengthening palliative care requires addressing **seven essential components:**

1. The development of appropriate (national) palliative care *policies*
2. *Scaling up and integration* of palliative care into the health-care system
3. Improving access to *medicines* for pain relief (especially oral morphine) and to palliative care
4. Strengthening *human resources* for palliative care (i.e., education of policy-makers, health-care workers, and the public)
5. Establishing palliative care *services* in accordance with the principles of universal health coverage
6. Setting standards and *evaluating* palliative care services
7. *Costing* palliative care services

All these components of the comprehensive approach are addressed below, with a more detailed elaboration on how to develop policies, establish services, and integrate palliative care into the health-care system.

3.1 Component 1: Developing a Palliative Care Policy (Including Assessment of the Current Situation)

A first essential element of a comprehensive approach is to develop appropriate palliative care policies. A palliative care policy can take many forms. Whether it is a stand-alone policy, part of a national health plan, or an element of a national NCD, HIV/AIDS, or cancer control strategy, the principles remain the same.

A national palliative care policy should seek to address the following elements:

- Service delivery through a continuum of care (through primary health care, community- and home-based care, and specialist palliative care services)
- Strategies to provide palliative care to all patients in need (e.g., noncommunicable diseases, HIV/AIDs, tuberculosis, older adults, children) and with attention to reaching vulnerable groups (e.g., poor, ethnic minorities, people living in institutions)
- Defining the government–civil society interface in establishment and delivery of palliative care
- Universal coverage of palliative care, through financing and insurance mechanisms
- Ensuring support for carers and families (social protection)
- Identification and allocation of resources for palliative care
- Development of national standards and mechanisms to improve quality of palliative care (see also component 6)
- Setting up a monitoring of palliative care need, access, and quality (e.g., by identifying indicators), at national and subnational levels (see also component 6)

When planning the policy, it is important to involve partners who can provide helpful input, assistance, and maybe funding:

- The Ministry of Health, but other ministries may also become involved.
- Health workers and their professional bodies.
- Social workers (or their organizations).
- NGOs.
- Academic institutions.
- National ethics committees.
- Funding bodies (including potentially private-sector groups).
- International partners should also be considered (especially the WHO country office, but also representatives of other United Nations agencies, international NGOs working on palliative care, and international technical experts).

Development of a palliative care policy takes a step-by-step approach, in order to make sure that all concerns are taken into account and that there is sufficient support and a firm legal basis. Figure 1 provides an example of what this stepwise process is likely to involve.

Ideally, developing a palliative care policy should begin with an assessment of the current situation and a description of the population in need for palliative care. A needs assessment survey can be adapted to the different levels of existing information in countries. It is important to consider factors such as the following:

- *The policy situation related to palliative care:* Has palliative care been included in any major health policy documents (e.g., national health strategies, national cancer control plans, HIV plans, healthy aging strategies)?
- *Availability and coverage of existing palliative care services:* Where are palliative care services currently delivered (e.g., types of patients, in which geographical areas, at what cost)? What dimensions of care are provided? How many patients currently receive care?
- *Current availability of palliative medicines:* Are all essential palliative care medications for adults (World Health Organization 2015a) and children (World Health Organization 2015b) available in the country, including oral morphine and liquid formulations? What is the availability and affordability of opioids

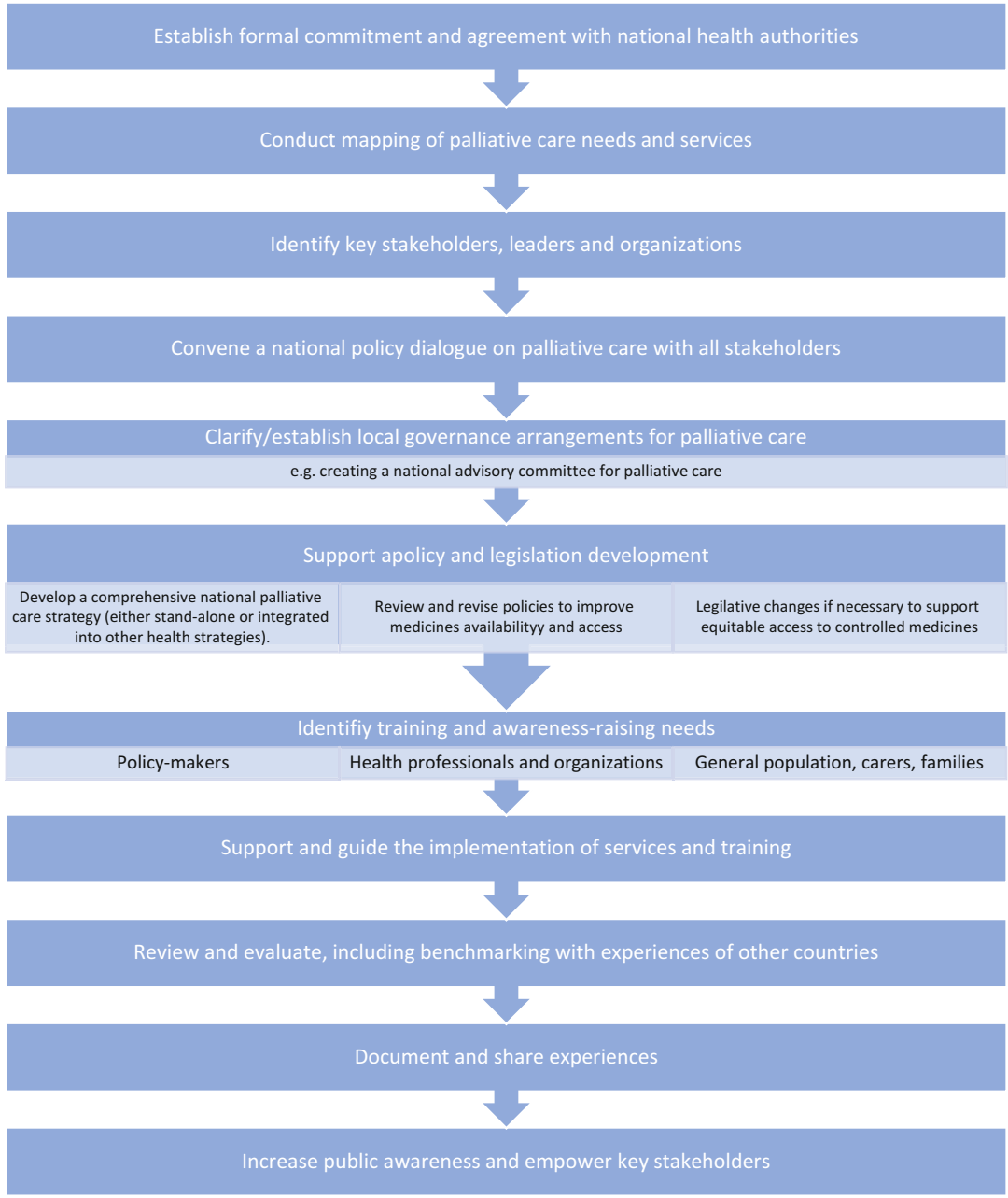

Fig. 1 Example of a stepwise process for developing palliative care strategies and programs

for pain relief and what restrictions are in place? However, evaluation of innovative programs to roll out opioids such as the Ugandan program (Merriman and Harding 2010) found that following enactment of policies to enable opioid availability, supply problems persisted due to unwillingness to prescribe (Logie and Harding 2005).

- *Quantitative estimate of the need for palliative care:* Several approaches to determining the

number of persons needing palliative care can be used (see Box 1 below). The health workforce and the number of inpatient beds/services needed to meet the need also need to be estimated.

- *Qualitative assessment*, e.g., interviews with patients and their families to identify any unmet needs for care as well as strengths, weaknesses, and barriers of the current system. This allows evaluating the capacity of key services (e.g., primary care, hospitals) for providing palliative care and identifying settings that can help in implementing actions decided upon.

Box 1 Useful Methods for Calculating Population Need for Palliative Care

There are a number of ways to estimate the numbers of people in a population who are likely to need palliative care at any one time, and several approaches have been proposed (Higginson et al. 2007; Murtagh et al. 2014):

- *Estimates based on disease prevalence*: The WHO has used a method (based on prevalence of pain) for estimating the proportion of people with various diseases who require palliative care in the last year of their lives (Connor and Bermedo 2014). This method can be used for adults and children. The need for palliative care at the end of life should be doubled to account for patients needing palliative care prior to the last year of life.
- *Estimates based on mortality*: Death registration data, where there is reliable reporting, can give good estimates of the population-based need for palliative care without the need for symptom or hospital activity data. Methods used in 14 middle- to high-income countries estimate that 38–74% of those who die need palliative care (Morin et al. 2017).

3.2 Component 2: Developing a Strategy to Gradually Scale Up and Integrate Palliative Care into the Health-Care System

Based on the needs assessment, a plan will be developed for scaling up coverage of palliative care services in the population. The WHO advises to plot a timeline that projects the growth in what percentage of need is being met every year. The plan clearly identifies where the need is greatest geographically and where resources already exist.

Again, there is not one single approach to expanding coverage: expanding from population centers to rural areas, from regional centers to other centers, from private to public providers, and from states or districts to national strategies are all possible scaling up strategies.

In the absence of any system of palliative care, a stepwise approach to introducing a palliative care program is advised covering policy actions, health-care financing, service delivery, workforce development, access to medicines, and information and research.

These strategies must take into account the WHO building blocks of health systems, which in palliative care take into account finance (to ensure services are part of the mainstream health system), workforce (training in palliative care), governance (to ensure that opioid restrictions are well adhered to), information systems (to understand outcomes of care), and access to essential medicines (which is a common problem at all stages of the WHO pain ladder) (Harding et al. 2014b).

3.3 Component 3: Improving Access to Medicines for Pain Relief and Palliative Care

The national medicine policy needs to use the concept of essential medicines. This will help to set priorities for the health-care system, promote equity and sustainability in the pharmaceutical sector, and provide a framework for identifying national goals and commitments.

Table 1 WHO model list of essential medicines for palliative care (extract from the detailed list, limited to only the drug types; for details see the published WHO strategy document World Health Organization 2015b)

		General	Children
Non-opioids and non-steroidal anti-inflammatory medicines (NSAIMs)	Acetylsalicylic acid	X	
	Ibuprofen	X	X
	Paracetamol	X	X
Opioid analgesics	Codeine	X	
	Morphine (alternatives limited to hydromorphone and oxycodone)	X	X
Medicines for other common symptoms in palliative care	Amitriptyline	X	X
	Cyclizine	X	X
	Dexamethasone	X	X
	Diazepam	X	X
	Docusate sodium	X	X
	Fluoxetine	X	X
	Haloperidol	X	
	Hyoscine butylbromide	X	
	Hyoscine hydrobromide	X	X
	Lactulose	X	X
	Loperamide	X	
	Metoclopramide	X	
	Midazolam	X	X
	Ondansetron	X	X
	Senna	X	X

Source: Adapted from World Health Organization 2015b

To determine what are the essential medicines, the WHO has published model lists of essential medicines for palliative care in adults and in children (see Table 1). They include medicines for pain relief and for the most common symptoms in palliative care. From these model lists, countries, regions, or districts can propose a list of essential medicines that is in line with their own needs (cfr. component 1) and resources. When an essential medicine list is finalized, it should be made widely available. The intended use, legitimacy, and authority of the list should be clear to all.

A next step is access to the medicines for those in need. The vast majority of patients with palliative care needs do not have access to essential medicines. Countries should, therefore, implement strategic plans to ensure access to many medications, including internationally controlled medications. The WHO has published guidelines to help countries to develop and implement a policy to make these medicines available to all those who need it (World Health Organization 2015a).

Continuing barriers to opioid availability for medical use in, for instance, sub-Saharan Africa include overly restrictive controlled medicines' laws; use of stigmatizing language in key documents; inaccurate actual opioid consumption estimation practices; knowledge gaps in the distribution, storage, and prescription of opioids; critical shortage of prescribers; and high out-of-pocket financial expenditures for patients against a backdrop of high levels of poverty (Namisango et al. 2017).

3.4 Component 4: Strengthening Human Resources for Palliative Care

The fourth component of the comprehensive strategy is concerned with training and education. Increasing the skills and awareness of palliative care among the health workforce is critical to improving access to and quality of palliative care. While specialist training in palliative care is

important, a basic training in palliative care principles and good pain management should also be implemented for all health professionals by integrating it into their training. Because most practicing health professionals have received limited or no training in palliative care in their preservice training, strategies should also include in-service training.

Because much of the care for dying persons and those with advanced chronic conditions with palliative care needs will occur in the community and in various health-care settings (see Fig. 2) and will include health professionals who are generalists and not specialist practitioners, palliative care training in primary care and community care is essential. This training should include a focus on increasing the ability for primary care professionals to identify people potentially in need of palliative care.

The WHO strategies to strengthen human resources for palliative care assume that different health workers are able to perform palliative care tasks safely and effectively (see Table 2). The level of skills, and hence the level of training required for different types of health providers as suggested by the WHO, can be as follows:

- *Expert palliative care skills* for specialist palliative care professionals who will work in specialized palliative care units and will help to train others
- *Advanced palliative care skills* for health-care professionals seeing a large number of patients with advanced illnesses – e.g., cancer, HIV/AIDS, dementia
- *Core palliative care skills* for all health-care professionals – e.g., doctors, nurses, pharmacists, social workers, psychologists (including trainees and practicing professionals)

Ensuring that core tasks and skills are built requires training to various health-care professionals and to informal carers:

- *All palliative care providers* have a responsibility for communication and smooth information transfer and need training in management of both physical and emotional problems, as well as in communication.
- *Community health workers and other community workers dedicated to palliative care* have a range of tasks related to assisting other members of the palliative care team as well as giving guidance and support to the patient and family members, e.g., including developing an individualized home-based care plan for each patient, routinely conducting comprehensive assessments of palliative care needs, answering questions and providing information, providing treatments and instructing the family in this task, training the patient and family in care and comfort-giving

Fig. 2 Where palliative care is provided. (Source: adapted from Kumar and Numpeli 2005 and Government of India 2014)

Table 2 Trained health workers are able to perform palliative care tasks safely and effectively

	Medical doctor	Non-physician clinician	Nurse	Community health worker
Pain management				
Conduct pain assessment(s)	x	x	x	x
Treat mild, moderate, and severe pain using chronic pain management guidelines, including oral morphine	x	x	x	
Teach the patient and caregiver how to give pain medicine, including oral morphine	x	x	x	x
Prevent, recognize, and treat the side effects of pain medications	x	x	x	
Advise on non-pharmacological methods of controlling pain	x	x	x	x
Treat extreme, nonresponsive pain appropriately, including through the use of steroids where indicated	x	x		
Symptom management				
Manage other common symptoms (weight loss, nausea, fever, diarrhea, trouble sleeping, anxiety, etc.)	x	x	x	
Psychosocial support and end-of-life care				
Counseling, psychosocial and spiritual support	x	x	x	x
Support for the patient at end of life	x	x	x	x
Support for caregivers, family members, and children	x	x	x	x
Supervision				
Supervise non-physician clinicians, nurses, and community health workers in above activities	x			
Supervise nurses and community health workers in above activities	x	x		
Supervise community health workers in above activities	x	x	x	

Source: WHO guidelines on task shifting (Task shifting: rational redistribution of tasks among health workforce teams 2008)

procedures, and checking that they are being carried out.

- *Staff nurses at primary, secondary, and tertiary care facilities* have a range of supervisory, coordination, and teaching roles, provide specialist nursing procedures such as care of lymphedema and stoma, and ensure documentation of home care.
- *Physicians and authorized prescribers at primary and secondary care facilities* are able to provide management of severe symptoms, prescribe medicines, and train and advise staff, patients, and families.
- *Providers at tertiary care level (including the hospital)* are skilled to provide inpatient care for patients with intractable pain and other symptoms, including, e.g., radiotherapy and other treatments available only at this level. They are able to maintain patients pain-free.
- *Family* has to understand the nature and prognosis of the disease and recommended treatment. It is the health worker's role to ensure this, to involve the family in joint decision-making, and to guide the family in best practices of palliative care. Both family and other informal carers can be taught to provide home-based care.

Finally, an effort should also be made in educating the public and policy-makers to make sure that they understand what it is, who can use it, and how to benefit from it. This will increase the chance that people who need palliative care will ask for it and access it. One strategy includes involvement of the media to disseminate information of educational value while avoiding sensationalism.

3.5 Component 5: Establishing Palliative Care Services

Establishing and implementing palliative care services is a next core component of the comprehensive strategy. Before establishing palliative care services, it is good to determine the minimum tasks of palliative care services.

3.5.1 Minimum Tasks of Services

Palliative care services can be provided in any health-care setting and also in patients' homes and should at a minimum:

- Identify patients who could benefit from palliative care.
- Assess and reassess patients for physical, emotional, social, and spiritual distress, and (re) assess family members for emotional, social, or spiritual distress.
- Relieve pain and other distressing physical symptoms.
- Address spiritual, psychological, and social needs.
- Care for families and caregivers.
- Clarify the patient's values and determine culturally appropriate goals of care.

The essential practices for palliative care include physical care, psychological/emotional/spiritual care, care planning and coordination, and communication.

(i) *Identifying who could benefit from palliative care and assessing and reassessing needs*

First, a system of timely identification of palliative care needs to become a feature of all health-care settings. Pain that disrupts daily life activities, breathlessness at rest, or functional decline can, for instance, be clinical indicators that result in further palliative care assessment. A multidimensional assessment of physical, emotional, social, spiritual, and cultural needs, values, and preferences of both patients and families is then needed. This can be done with validated short screening instruments such as the Edmonton Symptom Assessment Scale (ESAS) and the Palliative Outcome Score (POS) as adapted by the African Palliative Care Association (African POS). As needs can change, assessments should be repeated regularly throughout the course of the disease.

(ii) *Relieving pain and other symptoms*

Palliative care services need to treat pain and other symptoms experienced by adults and children and should aim to maintain or improve the quality of life and optimize physical and cognitive function throughout the course of illness. This requires (1) treatment of the underlying causes of symptoms (respecting a balance between expected benefit and burden from the intervention), pharmacological (see list of essential medicines above) and/or non-pharmacological (e.g., mouth or skin care, lymphatic drainage, physiotherapy) treatment of any symptom, and attention to each patient's values and needs. The patient and/or family caregivers, as appropriate, should be involved in decision-making about the treatment plan. A key task for low- and middle-income countries is to ensure that the relief of pain and symptoms is evidenced – it is not enough to develop and deliver services; their outcomes must be proven at the individual and facility level. This has been successfully achieved in sub-Saharan Africa (Defilippi and Downing 2013).

(iii) *Addressing spiritual, psychological, and social needs*

Palliative care services pay attention to the psychological, emotional, social, and financial well-being of patients and family members. Bereavement support is also a core component of palliative care. In low- and middle-income countries, spiritual concerns may be the greatest contributing factor to quality of life in advanced illness (Selman et al. 2011), and caring for a family member can push poor families into greater poverty (Streid et al. 2014).

Another core task for palliative care services is to support family caregivers. This includes assessing their needs as they too often have

unmet needs and problems including, for instance, physical and psychological morbidity and social isolation.

3.5.2 Setting Up Services

Palliative care services can be established in a number of different ways. There is no single best starting point, and the approaches suggested by the WHO need to be seen as complementary and depending on capacity and context and taking into account the country's social and health system context. However, in all cases, it is important to assess which services are already providing palliative care, including in the non-governmental sector, and to build on these existing resources.

Depending on the local situation, a country may, for instance, decide to begin by:

1. Setting up a palliative home-care service or integrating palliative home care into existing home-care services
2. Establishing palliative care in a community setting
3. Integrating palliative care services into a district or general hospital
4. Establishing a palliative care service for children, including neonates
5. Setting up a stand-alone palliative care center or hospice
6. Taking an integrated approach in a district

Table 3 provides an overview of different categories of palliative care services. The WHO manual provides a guideline for establishing each of these services.

Setting Up a Palliative Home-Care Service or Integrating Palliative Home Care into Existing Home-Care Services

Home-based palliative care provides care to people with chronic, life-limiting health problems such as cancer; advanced cardiac, renal, and respiratory diseases; HIV/AIDS; and chronic neurological disorders, in the home in which the patient lives. It is best delivered by a multidisciplinary team trained in palliative care, including doctors, nurses, community health workers, and volunteers. A basic home-based palliative care service can be set up quite simple. The minimum essential requirements for a home-care service are listed in Table 4.

Establishing Palliative Care in a Community Setting

Community-based palliative care services are those offered at a community health center or that are run with community participation. Community-based palliative care services can be a way to achieve significant coverage of services for patients with chronic, life-limiting health problems. Wherever possible, this should be initiated in collaboration with the local health authorities and should follow the planning processes used in the health system. Typically these services are provided by both health-care professionals and community health workers/volunteers (Table 5).

Table 3 Categories of palliative care services

		Palliative care		
	Palliative care approach	Specialist support for general palliative care		Specialist palliative care
Acute care	Hospital	Volunteer hospice service	Hospital palliative care support team	Palliative care unit
Long-term care	Nursing home, residential home		Home palliative care teams	Inpatient hospice
Home care	General practitioners, community nursing teams			Home palliative care teams, day-care center

Source: EAPC (Radbruch et al. 2009) adapted from (Nemeth and Rottenhofer 2004)

Table 4 Minimum requirements for a home-based palliative care service

Basic infrastructure	Central meeting point
	Storage facilities (including for controlled drugs)
	Transport for team and home-care kit
	Method of communication (e.g., mobile telephone)
Personnel	Doctor
	Nurse
	Volunteers or community health workers
Home-care kit	Medications (including morphine)
	Equipment
	Documentation
Finance	Salaries for team members
	Transportation/vehicle hire
	Rental for room/storage facility
	Communication and printing
	Medication and equipment costs

Table 5 Key human resources required for a community-based palliative care service

	Tasks	Suggested minimum training
Community volunteers/health workers		
Untrained sensitized volunteers	Provide support to the palliative care service (e.g., transport, food for patients, fund-raising)	Sensitization course (approx. 2 h) covering basics of palliative care, home care, communication
Trained volunteers	Contribute to patient home care, offering:	Basic palliative care course for volunteers (approx. 16 h theory plus 4 home visit days) covering communication skills, emotional support, patient assessment, nursing care, home care, basics of symptom management, reporting to higher level
	Emotional support	
	Basic nursing tasks	
	Help with mobility	
	Reporting of uncontrolled distress to higher level	
Community health workers	Contribute to patient home care, offering:	Basic palliative care course for community health workers (approx. 3–6 h) covering communication skills, emotional support, patient assessment, reporting to higher level
	Emotional support	
	Basic nursing chores	
	Help with mobility	
	Reporting of uncontrolled distress to higher level	
Health-care professionals		
Nurses	Key professionals in the team, providing nurse-led home care and/or care at CHCs	Staff nurses with mid-level training in palliative care supported by nurses or auxiliary nurses with basic foundation training in palliative care (3 months/400 h)
Doctors	Provide medical support and supervision for nurses and CHCs, home visits, and outpatient and inpatient care	Physicians with training in palliative care

Source: Adapted from (Guidelines for developing palliative care services 2009)

Integrating Palliative Care Services into a Regional or General Hospital

In sub-Saharan Africa, 38–46% of patients at a national referral hospital were found to have life-limiting illness (Lewington et al. 2012; Jacinto et al. 2015). All hospitals involved in the treatment of patients with cancer should have a palliative care service, and this can enable improvements in costs and outcomes for patients and families in low- and middle-income countries (Desrosiers et al. 2014). Any hospital that caters for people with other chronic diseases – such as

Table 6 Minimum staffing required for a hospital-based palliative care service

	Role	Capacity/skills required	Position	Availability
Doctor (required)	Team manager/ member	Training in palliative care and communication skills. As a minimum, a course with a theoretical component and at least 10 days practical. Ideally a specialist qualification in palliative care	Regular staff	Full-time or part-time, depending on workload
Nurses (required)	Team member	Training in palliative care and communication skills. As a minimum, a course with a theoretical component and at least 10 days practical. Ideally a more specialized qualification in palliative care	Regular staff	Full-time
Psychologists or counselors (recommended)	Team member	Trained counselor with orientation to special needs in palliative care	Regular/ visiting	Full-time
Auxiliary nurses/ palliative nursing aides	Team member	Assisting staff nurses in clinical work	Regular staff	Full-time
Pharmacist	Team member		Regular staff	Part-time
Social workers (recommended)	Team member	Trained social worker with orientation to special needs in palliative care	Regular/ visiting	Full-time/part-time
Volunteers (recommended)	Additional support to the team	Specific to their role	Visiting	Part-time

Source: Adapted from (Guidelines for developing palliative care services 2009)

HIV/AIDS, chronic respiratory diseases, heart failure, and chronic renal diseases – should also consider a palliative care service. The on-site availability of various specialities and diagnostic procedures makes the care more comprehensive and makes it easier to control symptoms. Hospital-based palliative care also facilitates the discussion of the patient's values, diagnosis, prognosis, and agreement about the goals of care (Table 6).

Establishing a Palliative Care Service for Children, Including Neonates

Palliative care for children includes physical, emotional, spiritual, and social care; it also takes into account the developmental needs from neonate to young adult. The family (including siblings and the extended family) is seen as the unit of care. Although palliative care for persons of any age has many similarities, palliative care for children represents a special area of care. It involves active total care of the child's body, mind, and spirit and also involves giving support to the family. It begins when illness is diagnosed and continues regardless of whether or not the child receives treatment directed at the disease. The role of the health providers is to both evaluate and alleviate a child's physical, psychological, and social distress (Table 7).

Setting Up a Stand-Alone Palliative Care Center or Hospice

A stand-alone palliative care center or hospice may have several roles and functions. When planning to set up such a center, it is important to be clear which function it will have and, if more than one function is envisaged, in what order they should be established. The basic elements of palliative care should be present – medical, nursing, psychological, social, and spiritual support – but the level of care depends on local resources, the availability and capabilities of staff, and their training. Depending on the target group of patients, the care provided may need to include financial support and basic necessities – such as food, utilities, mobile telephone and travel subsidy, and the lending of equipment (Table 8).

Taking an Integrated Approach in a Region

There is no one-size-fits-all public health approach to integrating palliative care into

Table 7 Ideal health workforce for a pediatric palliative care service

	Role	Competencies	Position	Availability
Doctor with pediatric knowledge or pediatrician	Team member and as consultant/attending physician	Palliative care for children; 10-day course includes theory and practical experience	Regular staff	Part-time, as required
		Communication skills with children and families		
		Understanding of childhood development and children's rights		
Registered nurses – preferably with pediatric experience and knowledge	Team members/ coordinator	Palliative care for children; 10-day course includes theory and practical experience	Regular staff	Full-time
		Communication skills with children and families		
		Understanding of childhood development and children's rights		
Staff and auxiliary nurses	Team members	Palliative care for children; 10-day course includes theory and practical experience	Regular staff	Full-time
		Communication skills with children and families		
		Understanding of childhood development and		
		Children's rights		
		Nutrition		
Social worker	Team member for psychosocial care, with access to social security/grants where available	Palliative care for children; 10-day course includes theory and practical experience	Regular staff – not all countries have access to social workers and may use a trained counselor or child psychologist	Full- or part-time
		Communication skills with children and families		
		Understanding of childhood development and children's rights		
Teacher	Team member	Palliative care for children; 10-day course includes theory and practical experience	Regular staff	Full- or part-time
		Communication skills with children and families		
		Understanding of childhood development and children's rights		

(*continued*)

Table 7 (continued)

	Role	Competencies	Position	Availability
Chaplain/spiritual care worker	Team member	Palliative care for children; 10-day course includes theory and practical experience	Ideally regular staff; often a volunteer	Part-time
		Communication skills with children and families		
		Understanding of childhood development and children's rights		
Care workers/ community caregivers for home care and day care	Team members	30-day course on all aspects of palliative care, pediatric care, childhood development and play, and children's rights	Regular staff	Full-time
Occupational therapist/ physiotherapist/ nutritional therapist/speech, play, music therapists	Team members	Introduction to pediatric palliative care; 5-day course	Ad hoc consultants or volunteers	Part-time
Child psychologist	Team member	Introduction to pediatric palliative care; 5-day course	Ad hoc consultant	Part-time
Neonatologist	Consultant or team member depending on the focus of the program and number of neonates cared for	Palliative care for children; 10-day course includes theory and practical experience	Consultant/advisor	Part-time
		Communication skills with children and families		
		Understanding of childhood development and children's rights		

Source: WHO Planning and implementing palliative care services (World Health Organization 2016)

different levels of care or types of services as much depends on services already existing. Nevertheless, there are a number of general principles for success:

- The approach must acknowledge the resources and structures that a health system in an area has at its disposal and respect its values.
- The approach must be dynamic and responsive to the needs of the area.
- It should be based on co-production and co-development of services set in a context of shared knowledge about palliative care.
- Palliative care is not to be seen as a medical approach that belongs only to health providers; it is an approach everyone needs to embrace for effective working in a health-care area.

Palliative care integration requires different steps: invitation, initiation, innovation, and implementation.

Step 1: Invitation
This step requires:

Table 8 Different roles and functions of a stand-alone palliative care center or hospice

Role or function	Advantages	Disadvantages
Hospice home-care service	Can be a very cost-effective service, serving the most patients with the least resources	Less convenient for teaching and training except on a one-to-one basis
	Needs little space – only office space with workstations and storage space for medications and equipment	Difficult for donors to see the service and how their donations make a difference
	Most patients prefer to stay in their own homes; many may not be fit to travel to seek health care	Volunteers do not have a center to meet, as they are scattered, working with patients at their homes
		May be difficult for staff to travel to visit patients in challenging localities or at night
Inpatient hospice service	The environment can be controlled and adjusted to provide hospitable, respectful, and individualized care	Highly skilled medical and nursing care, if provided, is the most expensive form of palliative care, costing as much or possibly more than hospital care
	Patients and families can be given intensive care and support at a level not possible in a hospital, whether it is physical care of the patient or psychosocial care of both patient and family	Patients may prefer to be cared for or to die in their own homes and may not wish to be at a hospice
	With both patients and staff present in the same place, training and education is facilitated	Because of distance, cost, or convenience, it may not be practical for families to visit often
	Donors have a clear view of the effect of their donations	If many deaths occur at a hospice, patients may become unsettled. The hospice may be labeled as a death house
	Volunteers may congregate and have a better sense of belonging	
	It is easier to do community outreach as there is a place where people can meet	
Hospice day-care service	Patients can stay at their own homes and still receive specialized care at a hospice	Transportation often has to be provided unless the family can bring the patient
		Specialized transport (e.g., ambulances with wheelchair facilities or stair crawls) may be needed
	The hospice day care may provide custodial care for the patient during the day when family members are at work, thus enabling the patient to stay at home, at least until such time as the patient is unable to travel	Travel is constrained by travel time as much as by distance
	A good place to deploy volunteers and engage the community	Patients may be exhausted by the time they reach the day-care center
		Group activities may not suit all patients
Education center	Patients are concentrated in one location, providing enough clinical material for teaching	The patient's and family's privacy must be safeguarded
	Groups of trainees may be accommodated if proper facilities are available	Requirement for clinical staff to do teaching necessitates a reduction in their workload
	Requirement for clinical staff to do teaching will drive their own learning and raise standards	Having positions for trained teaching staff involves more costs
Research center	An academic culture is good for attracting staff of high caliber	Research requires considerable investment in time and money. Most clinicians are not trained in research and need to be trained. Time must be reserved for research, and trained staff must be dedicated to doing it

Source: WHO Planning and implementing palliative care services (World Health Organization 2016)

1. Engaging political leadership. Regional health-care bodies are in most cases government entities, structured as part of local and national government. Therefore engaging with the political leadership of a region is an important process.
2. Advocating about palliative care: sustained advocacy about palliative care that is open and explicit, non-threatening and positive.
3. Providing information about need: evidence of need will be required, i.e., informed data that illustrate the local burden of disease, end-of-life care requirements, and inpatient, outpatient, discharge, and follow-up processes. Political leadership needs to understand the current and foreseeable problems if need is not addressed. Those who can best inform leaders of the need are the staff of hospitals, health centers and clinics, persons living with non-curable illnesses, their caregivers, local faith communities, educators, and local businesses – all of whom interact directly or indirectly with individuals who need care. Data are often available through health information systems, hospital and clinic records, records from community health workers and volunteers, NGOs, and private services. However, such data are often neither standardized nor accessible to those who can use it most effectively.

   There are a number of ways to estimate the numbers of people in a population who are likely to need palliative care at any one time (see ▶ Chap. 5, "Development of Palliative Care: Past, Present, and Future").

Step 2: Initiation

Once an invitation (however broad or wide) to develop an integrated approach has been established, initiation of the approach can begin. This requires:

1. Wide stakeholder engagement, including with isolated centers of care. Bypassing existing institutions which have delivered specific care in isolation from the rest of the health service rarely contributes to effective integration. Recognizing the strengths of these individual centers and the challenges they face allows them to become stakeholders in the larger conversation.
2. Making a business case for developing an integrated approach to palliative care by showing how the integrated approach will demonstrate effectiveness and efficiency. Gaps and barriers in services must also be identified (e.g., beliefs about death, views on dying, geographical distance).

Step 3: Innovation

Having created the awareness and the openness to begin developing changes in services, opportunities need to be found to develop and trial new ways of delivering care. Some districts have engaged local businesses to run competitions in schools and companies to elicit innovative ideas on new ways of developing and delivering services and ways of engaging all community members in understanding palliative care.

Step 4: Implementation

Key success factors are likely to be:

- Senior management agrees that palliative care is part of the role of all health workers, rather than seeing palliative care as a speciality that requires separate health workers.
- Palliative care is embedded in the health-care continuum, making it an essential component of primary care. It is seen as a normal health-care activity rather than a specialist one.
- Opportunities in the national palliative care context (e.g., training, financing, legislation, regulation of drugs) are used to build ownership of them at regional level.
- The infrastructure for delivery is in place. This usually does not mean setting up new services but rather uniting separate services and systems to become part of the whole. The system enables services to be in the right place at the right time, supported by people with the right skills and the right resources to care.

3.6 Component 6: Setting Standards and Evaluating Palliative Care Services

All providers of palliative care should be committed to continuous improvement of the quality of their services. Data collected from quality indicators are a primary source of information for improving services. When possible, palliative care services should be able to compare their quality indicator results with other similar services. Services can be compared with similar initiatives in other locations, which will provide the technical basis for political decisions about the development of the service, including the provision of further funding and support. Both the African Palliative Care Association and the Hospice Palliative Care Association of South Africa have developed standards that have been widely taken up and offer useful templates (African Palliative Care Association 2018).

Evaluation of national/regional programs allows monitoring to progress toward the predefined program goals and the targets of different phases, enables comparisons between different population groups, and provides an opportunity for continuous quality improvement interventions in critical areas. Populations with disproportionately high risk factors can be given specific attention.

3.7 Component 7: Costing Palliative Care Services

To cost palliative care services, both direct costs and indirect costs can be determined. The total annual budget, cost per day, cost per patient per month, cost per inpatient day, cost per inpatient episode of care, or cost per home or clinic visit needs to be presented. The highest costs are related to personnel costs, unlike in other health-care services in which the costs of treatments are higher.

The total costs can be compared with the expected sources of funding. Additionally it may be worthwhile comparing the costs to the possible reduction in health-care costs by the establishment of palliative care services. By reducing avoidable hospitalization, emergency department presentations, and unnecessary treatments, palliative care can save health-care resources and costs while providing a better quality of life (Smith et al. 2014).

4 Conclusion

The WHO has developed a comprehensive public health approach to integrate palliative care into a national health-care system that provides policy-makers or program managers at national or subnational level with practical guidance. The seven components of this approach need to be addressed: (1) developing a palliative care policy, (2) scaling up and integrating palliative care into the health-care system, (3) improving access to medicines for pain relief and palliative care, (4) training and education those who hold a stake in palliative care, (5) establishing and implementing palliative care services, (6) setting quality standards for palliative care services and evaluating these, and (7) costing the palliative care services.

The WHO insists that there is no one-size-fits-all approach. A country's specific context needs to be acknowledged and respected. Countries may, for instance, differ in needs, prevailing views and values, availability of resources, basic health-care characteristics, and services already existing. Low- and middle-income countries have an even greater need to deliver cost-effective services that are developed to meet prevailing health conditions, fit within cultural preferences and practices, and are feasible within existing health systems. Therefore, the WHO palliative care public health strategy requires local evidence to inform development of services (Harding et al. 2013).

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Part XI

Financial Aspects and Cost-Effectiveness in Palliative Care

Measuring Cost-Effectiveness in Palliative Care

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Charles Normand and Peter May

Contents

Abstract

Resources for health care will always be scarce and choices have to be made within palliative care as well as between palliative care and other services. Good choices are based on good evidence on value for money. In principle, we can compare the benefits of all health care interventions using the quality-adjusted life year (QALY) measure. However, there are multiple reasons to question the fitness for purpose of QALY analyses in evaluating palliative and end-of-life care. Tools are needed that measure and value services against the objectives of care, that take account of the wider group of beneficiaries and that value good processes as well as outcomes. Measuring costs and cost-effects in this field faces additional obstacles. Studies estimating the effect of palliative care on costs have identified substantive variation by intervention timing and comorbidity count. A critical challenge is posed by the complexity and heterogeneity of the interventions and populations under assessment.

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_101

1 Introduction: What Is the Purpose of Cost-Effectiveness Analysis?

There is a simple logic to cost-effectiveness analysis. We cannot individually or collectively provide all possible health and social care services (just as few of us are able to buy all housing and holidays we would like), so the best strategy is to provide those services that yield the best value for the resources used. This involves assessing the costs and benefits of all potentially useful services. In our normal lives, we choose to use our resources on goods and services that provide us with the greatest benefits. Similarly, collectively in principle, we should give priority to those services that give the best return. Priorities should be set in order of the ratio of benefits to costs (since this rule provides the highest gains for any level of spending). In principle, it does not matter who the payer is – we should not choose to buy ourselves any services that are not worth the cost, insurance should not cover services that are poor value for money, governments should only fund services where benefits exceed the costs, and for any given budget, any decision-maker should prioritize those choices that provide the greatest value.

To make this a reality, we need evidence on the cost-effectiveness of different services. However, since not all individuals will benefit equally from health-care interventions, it does not always make sense in general to describe a service as being cost-effective or not cost-effective. What we really need evidence on is the cost-effectiveness of each intervention for each type of person and each circumstance. The capacity to benefit from treatment may depend on factors such as the presence or absence of disability and comorbidity and the availability of family support, lifestyle choices and habits, goals, or objectives of the individual. Clearly this heterogeneity in the wants and needs of patients (and their families) poses significant challenges for the application of cost-effectiveness analysis to services for older people and for people with complex needs. These contextual issues are compounded by some of the measurement issues discussed in this chapter.

The use of cost-effectiveness analysis needs evidence, but it also needs mechanisms by which this evidence can be fairly and efficiently used. Even discussing rationing in health care can be controversial, but the reality is that care is rationed in all countries. It may be rationed by ability to pay out of pocket, by insurance status, or by the local availability of services, but one way or another there are some limits to what is provided to at least some people in the population. Since in most cases at least some of the cost of care is paid by third parties (e.g., government agencies or insurance companies), much of the care provided is free or subsidized *at the point of use*. If something is provided free, then naturally people will want it even if it is poor value for money – economists call this problem "moral hazard." From the point of view of the service users, the question is whether the value to them of the service is higher than the cost to them. There are very good reasons for removing financial barriers to accessing some health care – indeed evidence shows that high user fees deter people from using high value as well as low value care, but an inevitable consequence of providing care without charges is that people will choose to use services that are poor value for money in their case.

We see this in the case of some new drugs, which have only a small extra effect on health but a very high cost. Those with insurance and who therefore may pay nothing will naturally want it – for them there is a gain and no apparent cost. Since every dollar spent for little gain cannot be spent on services that provide more benefit, in principle it is desirable to limit use of services that are poor value. Insurance companies limit the coverage of services or in some cases require patients to make a co-payment to limit use. Rationing by government (or government agencies) is sometimes done on the basis of specifying coverage limits, sometimes also by the use of co-payments, and sometimes simply by unavailability of services and long waiting times. Ideally the decision on what should be available for whom should be made on the basis of evidence on cost-effectiveness.

In some services, particularly those aimed at treating a single health problem, the measurement

of costs and benefits can be relatively straight forward – we have the trials that have shown improved survival or better health, and this can be compared to the cost. Cataract surgery usually cures vision problems for many years. Emergency cardiology services can prevent deaths and extend life. Hip replacements can restore mobility and reduce pain.

Since the 1970s, a consensus has developed around two dimensions of effectiveness – longer life and better "health-related quality of life" (HRQoL). Using data from various sources and surveys, these two dimensions have been combined into a single measure – the quality-adjusted life year (QALY) (Weinstein et al. 2009). Effectiveness of an intervention is measured by the difference between QALYs for those treated (the number of years of life, adjusted to account for HRQoL) and the number of QALYs for those who did not receive the treatment.

It has been argued that this approach has the advantage that the same measures can be applied regardless of the type of treatment and the health problem being treated (Williams 1991). *In principle*, the benefits of a new cancer drug can be compared to those of cataract surgery, and hip replacements can be compared to coronary angioplasty. Life-extending treatments can be compared with ones that reduce disability. In this sense, the approach compares benefits on a "level playing field." There are many new drugs (and many existing drugs), and we can compare the evidence on costs and effectiveness, typically in terms of cost per QALY. While the evidence on effectiveness is not always perfect (e.g., drug trials do not always include older patients so there may be some uncertainty about effects), there is often a reasonable basis for judging if a new product is good enough to justify the cost. The results of cost-effectiveness studies are widely used in setting health-care priorities and for decisions to reimburse new treatments.

It is hard to argue against this approach where the health problems being addressed are simple, the treatments make a difference that can readily be measured, and the effectiveness is easily characterized in terms of extra years of life and improvements in HRQoL with a predictable duration. While there are vigorous intellectual debates about how quality of life is best measured, and how to take account of the timing of costs and benefits, in the context of simple problems and treatments with well-calibrated effects, there is much to recommend the use of these metrics. Equally, it is obvious that where the needs of patients are complex, where evidence on effects of treatment is often lacking or of poor quality, and where the context of patient and carer needs is very varied, it is more difficult to apply this approach (Normand 2009).

2 What Are the Goals in Palliative Care and How Can We Assess Cost-Effectiveness?

What makes cost-effectiveness studies in palliative care difficult is first, that the objectives of treatment tend to be complicated, focusing on both the patient and the wider family and friends and covering domains that are outside what is conventionally considered to be HRQoL; second, the degree to which objectives are met is not easily measured using simple metrics; third, it is hard to characterize the timing of benefits of palliative care since they occur not only at time of delivery but also in anticipation and in the memory of this period in someone's life; fourth, palliative care is often delivered alongside a range of other interventions so it can be difficult to identify the unique costs or unique contribution of palliative care. As will be discussed below, these problems generate significant challenges in the measurement of costs and benefits and can make it difficult to compare the cost-effectiveness of palliative care and other health and social care.

It is now recognized that palliative care is not end-of-life care (although may be of particular importance near the end of life) and is not necessarily an alternative to services with a disease-modifying or curative intent. In many ways, this is a false dichotomy, since good control of symptoms may require disease-modifying treatments and good control of symptoms may be life-extending. Palliative care is concerned with optimal management of symptoms and the best

achievable quality of life, and this inevitably bring a focus both on disease and its effects and on wider psychological, social, and spiritual needs of patients and their carers.

There is often a trade-off between the different goals – some people may choose to live with more pain if that allows them to be more alert, and sometimes people will prefer pathways of care that reduce stress on family and informal carers. There may be a choice between different probabilistic outcomes, for example, a very small chance of much longer life, and a statistically longer life expectancy but one where the longest possible survival is quite short. There remains a popular belief that this is commonly the choice, but evidence in general suggests that good symptom management does not shorten life and in some instances may offer survival advantages. The more important point is that there are legitimate choices to be made between different care pathways, and it is quite legitimate to choose different balances of disease-modifying and more direct symptom management interventions.

There are particular problems in people wanting optimal experiences of care – it is not only the services that are used that are valued but also their availability, the linkages, and the processes that people encounter. In many cases, the experience of the processes is as important as the content of care – patients do not expect palliative care professionals to have all the answers but do value evidence of availability, caring, and engagement. In studies of patient and family preferences, a common theme is being able to navigate the access to appropriate care and being free of the frequent system failures that make it difficult to get necessary support (Douglas et al. 2005). People value the services they use, but also value availability of services that do not in fact use, but which are likely to play a crucial role in achieving the optimal pathway should the need arise. Put simply, it is a big enough challenge to have multiple health problems and to be approaching the end of life, and people simply do not want the additional challenge of confronting a complex and apparently hostile care environment.

The implication is that we need to understand the goals of patients and their carers and assess effectiveness against these (possibly complex) goals. Since the objectives are not simply to live longer or to have better (narrowly defined) HRQoL, there is a need to include a wider range of benefits and to include benefits to a wider range of people. In addition, two particular issues have become apparent in assessing effectiveness (Johnston 2017). First, it is not only what is delivered but also how it is delivered that can matter. Second, to a significant extent, people are interested in the whole experience of care when faced with life-limiting disease.

3 Measuring Effectiveness and Benefits in Palliative Care

Studies that have attempted to apply the QALY framework in palliative care have typically found that the measured benefits are small, but when asked, people put a high value on the effects of the services. This is not surprising. Palliative care does not normally contribute long periods of additional survival, and QALYs tend to be driven by achievement of longer life. It is also unsurprising given that QALYs measure only some of the intended quality of life and quality of experience benefits – those that conform to the domains typically included in HRQoL. QALYs typically use quality of life tools that focus on ability to perform activities of daily living and pain. While pain is clearly relevant to palliative care objectives, interventions may not focus strongly on improving mobility and self-care skills. QALYs also ignore benefits to families, friends, and other carers. Similar problems have been found when these measures have been attempted in other areas of complex care, such as in mental health – simple quality of life measurement tools do not measure some relevant dimensions and do not measure others very well (Chisholm D et al. 1997).

There are ongoing debates about how to deal with this problem (Williams 1996; Hughes 2005; Round 2012; NICE 2013; Normand 2012). One suggested approach has been to give extra weighting to benefits that are measured near the end of life – in essence to say that a day or a year is intrinsically more valuable if it is near the end.

This has the effect of making it more likely that palliative care interventions will be deemed to be cost-effective, and as a result more resources might become available. However, it does little to tackle the underlying measurement issues. In particular, it is not likely that this approach will be very helpful in looking at the *relative* cost-effectiveness of different palliative care services, since the tools used remain insensitive to important objectives of care, so inherently they will fail to identify more or less useful care.

Other approaches have used different types of measure that aim to include dimensions of benefits that go beyond those captured in QALYs and include benefits to families and carers as well as patients. This is more promising in that it specifically addresses the underlying measurement issue. A number of scales relating specifically to palliative care have been developed (such as the POS and IPOS), and these help to give a focus on the declared objectives in palliative care, although they were not specifically designed for use in economic evaluation (Dzingina et al. 2017). Other measures, such as ICECAP, aim to be more generic and can in principle be applied in a range of disease and treatment contexts and have versions of the measure that are aimed at carers (Huynh et al. 2017). In principle, the advantages of these developments are that benefits in palliative care can be compared to those of other services, especially other services that aim to tackle complex needs.

A further approach has been to look at the preferences of those using the services (e.g., using discrete choice experiments Malhotra et al. 2015) and to assess the extent to which services delivered achieve these objectives. Some interesting findings have come from this (relatively underdeveloped) body of work. One is that the quality of the process can be very important. People want to know that they can get access when needed *even if they do not in fact use the service*. Difficulty in accessing and navigating the care system is strongly disliked even when the services are in other ways appropriate and effective. At what is often a very stressful time for patients and carers, the additional stress of complex and poorly coordinated care delivery, financial obstacles, and unintended barriers to access increase the stress and reduce the benefits.

There is also some evidence that people can only cope with a certain amount of information and choices and will tend to deal initially only with the most important issues. Economists call this having lexicographic preferences. For example, while there may be high value given to recreational activities and support to improve appearance, these are only valued when people are assured access to good symptom management and support for basic needs. In effect people like to ensure that their more basic needs are being met well before they engage with the issues of their other wants.

There are particular issues with regard to the role of informal carers. Patients are keen to avoid excessive burdens (both financial and caring) on carers and may choose a trajectory of care that suits them less well but suits the carers better. In addition, there is now some evidence that links better care experiences with better bereavement experiences for families and carers, so that some benefits of good palliative care should be measured after the death occurs (Addington-Hall and O'Callaghan 2009; Gelfman et al. 2008). In terms of achieving the best possible bereavement trajectory, good quality experiences of end-of-life care has a key role.

One reason for low QALY scores in palliative care, and some judgments that it is not cost-effective, is that the time over which benefits can be enjoyed is often short. The logic is simple. While cataract surgery or angioplasty may affect health and quality of life for many years, palliative care may affect outcomes only for days or weeks. When asked to value palliative care, patients and families tend to emphasize its importance and substantial benefits, but the short time limits any QALY gain. Even a very large increase in quality of life from 40% to 90% will only generate 0.125 QALYs over 3 months. Even if QALYs are weighted at the end of life (as discussed above), it is unlikely that the measured effectiveness will be large over a short period. One possible argument is that in fact the benefits are enjoyed not only at the time but also before and after the end-of-life period – the knowledge of good care at the

end of life may provide reassurance in preceding years, and good care may reduce stress and sadness in bereaved relatives. A more radical approach is to question if in fact units of time can simply be added up. Evidence from economic psychology suggests that they cannot. The work of Daniel Kahneman suggests that people value whole experiences, and a longer experience is not necessarily valued more highly than a shorter one with some better features (Kahneman 2011). There is, as yet, no definitive evidence in the context of palliative care, but this understanding does suggest that new approaches to measuring cost-effectiveness of palliative care near the end of life should try to value the whole experience and not to assume that we can add up the value of packages of time that have specified quality and value.

In summary, while debates continue about the best ways to measure effectiveness in palliative care, and the different innovations are continuing to develop new approaches, it is clear that the nature of the objectives in palliative care, the context in which care is provided, and the wide range of potential beneficiaries make conventional economic evaluation metrics inadequate, and a broader range of tools is needed. This inevitably leads to problems of comparability with cost-effectiveness studies in some other fields of health care. Since all services are in some sense competing for the limited pool of resources, it brings some disadvantages to palliative care if it is not feasible to measure effectiveness in the same ways as those for other elements of care.

4 Measuring Palliative Care Activities and Costs

While there are important conceptual and practical difficulties in measuring palliative care activities and costs, the body of high-quality evidence is growing, and some important results have emerged. The key issues in measurement have been the fact that palliative care is often delivered by a range of specialist and generalist professionals, that palliative care is not always distinct from care with some disease-modifying intent, and that interventions in one setting can affect services and costs in other settings (or importantly to families and informal carers).

Palliative care professional skills are scarce, and in many cases, the best strategy is to use these to encourage other care professionals to adopt a palliative care approach. Time is spent on training and education activities as well as direct advice to care staff, and this can be difficult to record and very difficult to link to specific care of individual patients or families. In general, this important role of palliative care does not get fully recorded, and overall the activity and costs are therefore underestimated.

Palliative care is often provided by teams, and in many cases, team include people with skills across other aspects of medicine and care. From the perspective of estimating volumes of activity and costs of care, it is not always clear where the boundary lies between palliative care costs and other costs. This problem is compounded by the fact that there is no simple boundary between what is and what is not best classified as palliative care.

A more serious difficulty in assessing costs in palliative care comes from the fact that palliative care services in one setting may significantly affect activity and costs in another. When specialist palliative care teams provide consultation in hospital, this affects the pattern of services during that hospital stay but may also affect the care provided and costs after discharge from hospital and may affect the likelihood and the services provided in future hospital admissions. If an intervention is successful in reducing hospital stays and admissions, this reduces hospital costs but may increase costs of community health services and may increase costs to families. Economists call this "cost shifting," since what is happening decreases cost to one payer but may increase them to another. In principle the only way to avoid this problem is to estimate the patterns of services and costs in all settings (including costs to families), ideally till the end of life. The cost of an intervention is therefore the amount spent on it plus any increase in costs elsewhere as a consequence, minus any savings in costs elsewhere.

5 Assembling Evidence on Cost-Effectiveness of Palliative Care

There are good reasons to focus on costs of palliative care in hospital settings, and the effects of interventions on hospital costs, since typically this is the setting in which costs of care are highest. Palliative care interventions can lead to decisions not to receive treatments that, given the overall circumstances, are not likely to be useful. There is good and growing evidence that timely palliative care consultations for patients admitted to hospital with life-limiting disease generally lead to fall in the cost of the stay by reducing expensive surgical and pharmacological treatments (and resulting intensive and high dependency care) (May et al. 2014a). This is (unsurprisingly) particularly the case where the patient has several comorbidities and is therefore unlikely to benefit from intensively treating one disease (May et al. 2016a) (see Example 2). For some groups of patients, it has also been shown that future costs in total are lower following a hospital consultation and that this change in treatment usually improves the experience of patients and families (Bausewein et al. 2011) and can be associated with longer survival (Temel et al. 2010).

The obvious conclusion from this evidence is that palliative care consultations can be effectively free or even have a negative cost, since the total cost (including the cost of the consultation) is lower. Any service with zero or negative costs is inevitably cost-effective if it does some good or at least does no harm. While the objective of this type of intervention is not limited to lowering cost, where it does reduce cost, it can actually release rather than use health-care resources and should have the highest priority. Ongoing studies are seeking to understand where palliative care consultations are most likely to bring gains at no cost, but the current evidence suggests that this is where patients are most frail and have many chronic conditions (May et al. 2018).

While cost-saving services (which at least do no harm) are always cost-effective, there is some evidence that people who receive more palliative care will often have higher overall cost, and better outcomes, and then the question is whether the additional gains outweigh the additional costs. Better outcomes include a lower risk of dying in an acute hospital, improved patient quality of life and symptom management, and better experiences of family and carers. Differences in reported costs are usually small, so the better experiences and outcomes are likely to be considered good value.

6 Conclusion: The Importance of Measuring Cost-Effectiveness in Palliative Care

This chapter has outlined the serious difficulties in measuring benefits and costs in palliative care. The problems in cost estimation are largely technical, and the evidence base on costs of palliative care and effects of other costs is developing well. The problems in measuring effectiveness and benefits are less tractable. On one hand, there is a strong case for trying to present evidence on the cost-effectiveness of palliative care that is compatible and comparable to that presented for other types of treatment. On the other hand, this may be largely pointless, since palliative care outcomes will almost certainly look weak even when there is evidence that they are highly valued by service users. If the measurement tools are not fit for purpose, then they will not provide a robust basis for choices.

But as has been argued at the start of the chapter, resources for health care will always be scarce, and choices have to be made within palliative care as well as between palliative care and other services, and good choices are based on good evidence on value for money. To some extent, the measures used in the standard cost-effectiveness analysis of many other services are not fit for purpose. They have been shown to be insensitive in areas such as mental health and may often be inappropriate when applied to a wider range of services used by people with complex needs. Since more than half of all health-care encounters are for people with two or more chronic conditions, it is likely that the issues that are clearly seen in palliative care cost-effectiveness studies apply

more widely. Increasingly the needs are complex, the choices may differ between seemingly similar individuals, and the goals of care can be varied and personal. Tools are needed that will measure and value services against the objectives of care, that take account of the wider group of beneficiaries, and that value good processes as well as (simply measured) good outcomes.

Example 1 Importance of Cost-Effectiveness Evidence: The Case of Ireland

Adapted from: May et al. (2014b).

In 2001, Ireland became one of the first countries in the world to publish a dedicated national policy on palliative care (National Advisory Committee on Palliative Care 2001). The policy recommended comprehensive national provision of specialist-led care, free at the point of use, nationwide. There was broad support for the policy among political leaders and society: palliative care in certain regions of Ireland dates back to the nineteenth century, and the Irish Hospice Foundation, founded in 1986, is active and high profile in promoting high-quality end-of-life care.

Even in this supportive environment, the policy document was extremely ambitious. The estimated annual cost of comprehensive national provision in 2001 was €144 million, requiring more than a three-fold increase in the existing budget of €44 million. Additional to this was the one-off construction costs of new inpatient hospices and other capital facilities in regions that had not enjoyed historical political and volunteer support, and so had limited capacity in palliative care.

Moreover, there was no ring-fenced budget to fund the policy. Rather, funding was to be secured from the general health budget. The 2001 policy coincided with unusually large increases in that budget. Competition for these new resources was fierce after two decades of recessionary spending cuts. The international literature on the economics of palliative care was small and of variable quality, and in the face of competing demands, policymakers in the Irish health service found the relevant evidence on cost-effectiveness to be wanting (May et al. 2014b; Murray 2009).

Significant increases in palliative care spending were observed following publication of the policy, reaching €76 million in 2007 before the start of the Great Recession. But these increases were consistent with funding increases across the Irish health system at the time (Fig. 1).

(*continued*)

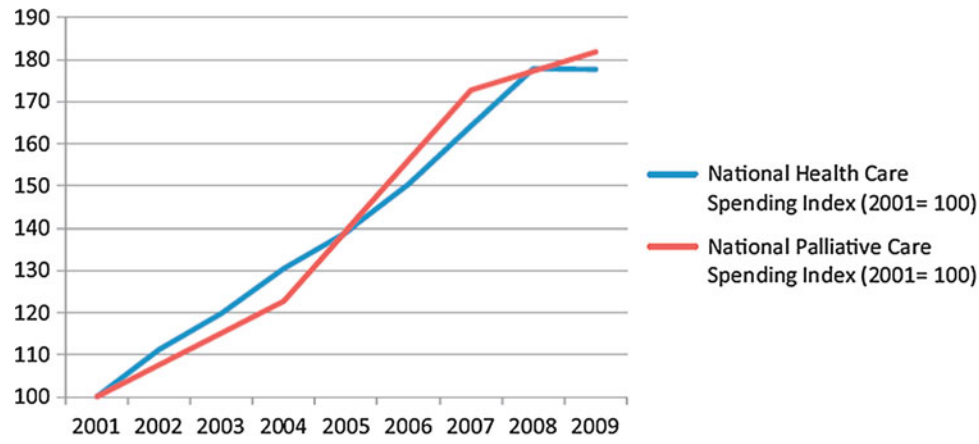

Fig. 1 Health care and palliative care budgets in Ireland (2001–2009)

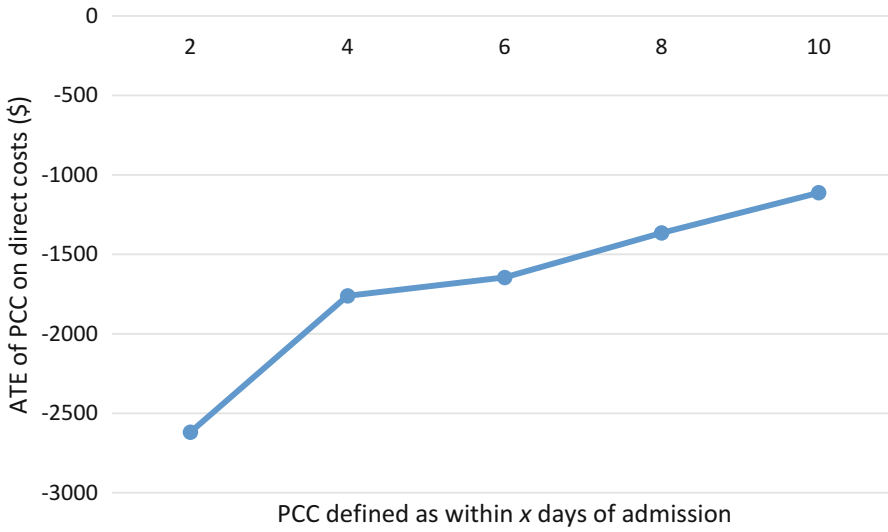

Fig. 2 Estimated impact of PCC on direct costs ($), by time from admission to PCC consult. ATE: Estimated average treatment effect for PCC compared to UC only. For detailed methods and results see (May et al. 2015) or contact authors. Results are robust to myriad sensitivity analyses, details from authors

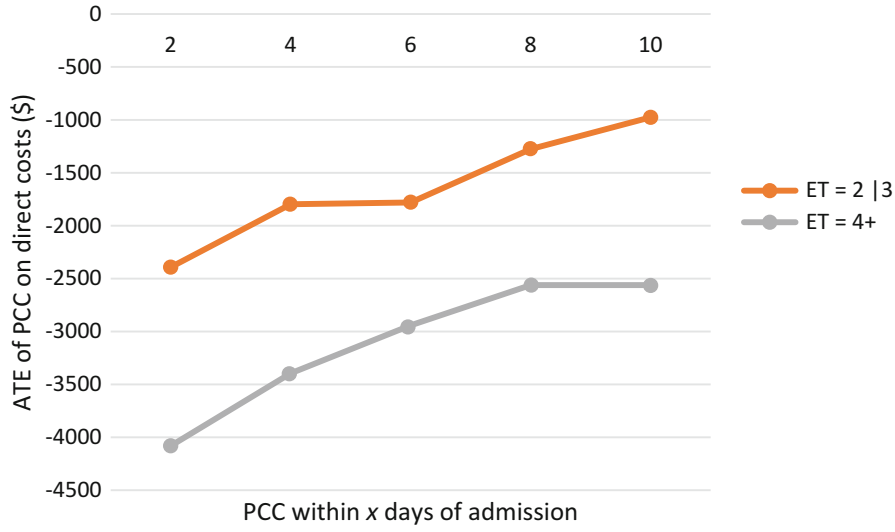

Fig. 3 Estimated impact of PCC on direct costs ($), by time from admission to PCC consult & comorbidity count. ATE: Estimated average treatment effect for PCC compared to UC only. ET: Elixhauser total of comorbidities (Elixhauser et al. 1998). Results are robust to myriad sensitivity analyses, details from authors. Copyrighted and published by Project HOPE/Health Affairs as (May et al. 2016a). The published article is archived and available online at www.healthaffairs.org/. See (May et al. 2016a) or contact authors for details. Results are robust to myriad sensitivity analyses, details from authors

A high-profile, widely embraced palliative care policy at a time of budgetary increase was insufficient to secure palliative care priority status or to realize the ambition of universal provision. Cost-effectiveness evidence was also essential to convince policymakers that new resources would yield most value in palliative care, and this evidence did not exist.

Other factors included a lack of readiness of underserved areas to avail of available funding. There was competition not only between palliative care and other areas of the health service but also within palliative care between different regions of the country. Historically well-served areas were most likely to have representation at the table when policies were being developed and decisions made about funding allocation. Underserved areas did not have the structures and processes, established and well-positioned advocates, and communication networks to seek and implement programs of funding.

Subsequently during years of austerity, the emphasis of policy debate shifted away from "ethics" (i.e., a case for universal palliative care provision to manage pain and symptom burden, and to ensure a good death for all) and towards "economics" (i.e., a case based on the cost-effectiveness of services) (Murray 2011). However, to an economist there is no such distinction. In both times of austerity and surplus, available healthcare budgets must be allocated to those services that provide the greatest value.

Despite enormous strides in the last 10 years (May et al. 2017a; Smith et al. 2014), palliative care requires further evidence to meet this standard and so ensure the widest possible access to appropriate care for the seriously ill.

Example 2 Complexity: Key to Cost-Effectiveness in Palliative Care

In Example 1, we highlighted the importance of economic evidence on palliative care in order to secure funding in competition with other healthcare services. Another important dimension is the allocation of available resources *within* palliative care.

Palliative care is widely recognized as an inherently multifaceted concept – accessed in a wide range of settings, provided by a wide range of professionals, and benefitting a wide range of patients with different diagnoses, prognoses, symptoms, and needs. As such, it stands to reason that different models of care will have different impacts for different populations in different circumstances. Understanding these dynamics is particularly important in the context of staff shortages (Spetz et al. 2016): Palliative care staff are a scarce resource and must be used where they have the greatest impact. Recent evidence from a study of hospital-based palliative care consultation (PCC) teams for adult inpatients has provided new and provoking insights into *when* and *for whom* palliative care is most impactful (May et al. 2015, 2016a, b, 2017b, c).

The results of the timing enquiry are presented in Fig. 2 (May et al. 2015). When the treatment group is restricted to those who received palliative care within two days of admission, there is an estimated $2619 cost-saving associated with PCC. Moving rightwards along the x-axis eases the definition of treatment to include later consults and the estimated cost-saving effect lessens in magnitude and statistical significance. The authors' conclusion, that early palliative care consultation is associated with larger cost-saving effect all things being equal, has been confirmed in follow-up studies (May et al. 2017c; May and Normand 2016).

The results of the multimorbidity enquiry are presented in Fig. 3 (May et al.

(*continued*)

2016a). For a subsample of patients with 2–3 comorbidities, PCC within 2 days is estimated to save $2392 in direct hospital costs. For a subsample with four or more comorbidities, the equivalent estimate is significantly larger: $4081. This disparity remains for other definitions of the intervention along the x-axis: as later consults are included in the treatment group, the estimated cost-saving effect diminishes in each subsample; the estimated effect for the 4+ comorbidities group is always larger than the 2–3 comorbidities group.

From these results the authors infer that, contingent on some basic assumptions about how outcomes for patients and their families are impacted by the intervention, palliative care is more cost-effective for patients with a higher illness burden. More research is required to pick apart the associations and causal relationships, but it is hypothesized that palliative care is more effective for people with more serious conditions because palliative care fundamentally reflects complex decision-making and is an approach more appropriate in more complex cases than a single-disease-focused alternative.

As the field of palliative care looks to grapple with the challenges of cost-effectiveness in the field, a critical factor is going to be complexity and heterogeneity of everything: differences among complex patient groups; differences between interventions in terms of timing, settings, and skill mix; and differences in how those interventions effect those populations.

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Financial Aspects of Inpatient Palliative Care

99

Peter May and R. Sean Morrison

Contents

Abstract

The economics of hospital inpatient palliative care is a subject of significant policy interest internationally. Older people, and particularly those with multiple serious chronic conditions, account disproportionately for hospital admissions (McCusker et al. 2003), and up to half of recorded deaths worldwide occur in hospital (Bekelman et al. 2016; Broad et al. 2013). Hospitalization costs represent the main component of end-of-life costs across healthcare settings (Simoens et al. 2010a). Economic studies of palliative care for adult hospital inpatients suggest that persons who receive palliative care have lower costs and earlier discharge than matched patients who receive usual care only, as well as improved outcomes. Additionally, palliative care's effect is larger when provided earlier (raising questions of when palliative care should be introduced in the trajectory of illness for people both inside and outside the hospital) and is also larger for adults with higher numbers of comorbidities (suggesting that complex interdisciplinary interventions are more effective for complex clinical cases, an insight with major potential policy relevance worldwide).

Further economic evaluations of palliative care beyond the hospital silo to evaluate

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_102

impacts across whole trajectories of care are needed. Only then will policymakers have the full story on the costs and benefits of complex care for those with complex illness.

1 Introduction

The economics of hospital inpatient palliative care is a subject of significant policy interest internationally. Older people, and particularly those with multiple serious chronic conditions, account disproportionately for hospital admissions (McCusker et al. 2003), and up to half of recorded deaths worldwide occur in hospital (Bekelman et al. 2016; Broad et al. 2013). Hospitalization costs represent the main component of end-of-life costs across healthcare settings (Simoens et al. 2010a).

Thus, hospital care for people with palliative care needs raises major resource allocation concerns. In the United Kingdom's National Health Service, an estimated fifth of hospital bed days are accounted for by end-of-life care (Hatziandreu et al. 2008). In the United States, the 49% of Medicare beneficiaries with persistently high utilization in the last year of life are more likely to visit hospital and receive high-intensity treatments during these stays (Davis et al. 2016). Also in the United States, where spiraling cost of cancer care is a particular threat to the long-term viability of the healthcare system (Smith and Hillner 2011), a third of direct medical cancer costs are incurred in hospital (American Cancer Society 2015). In some cases, high hospital costs reflect appropriate treatment choices, but in many cases these represent avoidable admissions, overtreatment, and delayed discharge (Teno et al. 2013). Palliative care is one mechanism by which inappropriate high hospital costs may be mitigated with improved decision-making by clinicians and their families.

In turn, this poses questions of funding and organizing hospital palliative care provision itself. Multiple models termed "palliative care" are observable internationally. The most common is the interdisciplinary consultation (PCC) team, led by a specialist physician with nurse, social worker, and allied health supports (Morrison 2013; Davies and Higginson 2004). Dedicated units (PCU) where palliative care clinicians lead treatment rather than consulting in are also observable, particularly at large hospitals in the United States (Smith et al. 2012), and there is growing interest in evaluating the impact of palliative care expertise among generalist staff given that not all people with serious and life-limiting illness can or should receive specialist care (Radbruch and Payne 2010). While it is common for palliative care proponents to argue for improved use of budgets within overall healthcare systems, it is also essential resources within palliative care are allocated appropriately, including optimal allocation of hospital palliative care staff.

2 Early Evidence from the United States

The first economic studies of hospital inpatient palliative care were reported in the early 2000s in the United States, where cost-savings were reported from both the PCC (Penrod et al. 2006; Ciemins et al. 2007; Bendaly et al. 2008; Hanson et al. 2008; Morrison et al. 2008) and PCU (Smith et al. 2003) models of care. These early studies played a critical role in the development of palliative care in that country due to an artifact of the system: American hospitals are reimbursed a fixed sum according to diagnosis-related group (DRG), meaning that where an intervention lowers cost of admission, it in turn increases a hospital's profit margin on that admission. It has been estimated that an average hospital in the United States saves $3 million a year through having a palliative care program (Morrison et al. 2011), a significant factor in the prodigious growth of such programs over the last 20 years: 67% of hospitals with 50 beds or more had palliative care programs in 2015, compared to 15% in 1998 (Dumanovsky et al. 2015). There is now almost universal access in large (300+ bed) US hospitals, although access remains associated with geographical region (Dumanovsky et al. 2015).

In 2014, a review of the economic evidence on PCC found a total of ten studies, all from the United States (May et al. 2014). These ten were substantively consistent, reporting similar findings (a pattern of cost-saving in the 5–25%

Table 1 Summary of strategies that control for LOS in analysis of treatment effect on hospital utilization outcomes using observational data

Use of LOS	Definition – potential justifications	Potential problems	Examples from PC cost literature
I. Covariate	LOS employed as an independent variable/ predictor in regression analysis	Use of LOS as a covariate risks introducing endogeneity into analysis, since LOS is not an independent predictor of resource consumption or cost. Rather, it is associated with both treatment (long hospital stay suggests clinical complexity) and outcome (LOS and other utilization data are typically closely correlated), thus undermining estimation of the causal relationship of interest (Amporfu 2010; Garrido et al. 2012)	Whitford et al. (2014)
	Covariate intended to control for:		
	Unobserved heterogeneity, including hard-to-capture clinical complexity. LOS may be a useful proxy for complexity		
	Uneven accumulation of costs, higher costs being accrued early in hospitalization		
II. Sample parameter	Short- and/or long-stay outliers trimmed from sample	Defining a sample ex ante by a factor that is associated with both treatment and outcome risks biasing results and obscuring true treatment effect (Garrido 2014; Imbens 2004). Where propensity score matching is used[a], ex ante trimming is antithetical to the research framework, which aims to estimate a counterfactual using baseline data (Rubin 2007). LOS is not known at admission so evidence of treatment efficacy for a patient group defined by LOS is of limited practical use	McCarthy et al. (2015)
			Morrison et al. (2008)
	Sample parameter(s) intended to control for:		Starks et al. (2013)
	Unobserved heterogeneity, including clinical complexity. LOS outliers may be unrepresentative of the study sample in ways that are hard to capture – removing LOS outliers attempts to make the sample more homogenous		
	Outliers skewing distribution of utilization data such as LOS and cost, distorting and disguising treatment effects		
III. Outcome denominator	Average daily cost (the ratio of total cost to LOS) employed as primary outcome of interest	Estimated effect on average daily costs is of limited practical value because this is a ratio and not overall resource use: a treatment that reduces daily cost by 10% but increases LOS by 50% (thus increasing total cost) is not necessarily delivering desirable clinical or financial outcomes (Weinstein et al. 1996). Per diem ratios change systematically with LOS and must be interpreted carefully (Ishak et al. 2012). If LOS differs between treatment and comparison groups then daily cost (total cost/LOS) is a fundamentally different outcome to total cost	Ciemins et al. (2007)
	Outcome denominator intended to:		
	Indirectly limit impact of unobserved heterogeneity for which LOS is a proxy by accounting for long LOS		Penrod et al. (2010)
	Reduce skew and leptokurtosis common to healthcare utilization data distributions		
	Address specific stakeholders, e.g., a hospital reimbursed a fixed daily rate, who may prioritize average daily cost over total cost		

First published in May et al. (2016) in Health Services Research (May et al. 2016) and reprinted with thanks

[a]All examples cited in this table also used propensity scores to account for observed confounders, with the exception of Ciemins, who used DRG matching to account for observed differences

range, no significant impact on length of stay (LOS), cost-savings accruing through reduced intensity of stay) and limitations (nine of the ten were retrospective cohort studies with no original data collection, outcome measurement, or follow-up past discharge). Important methodological advances were observable across this literature. In particular, later studies had widely used advanced techniques to managing confounding (propensity scoring (Garrido 2014) or instrumental variable (Penrod et al. 2009)) where earlier studies had used simple matching approaches raising concerns about bias (Starks et al. 2009). Later studies had also used nonlinear modeling (e.g., generalized linear models (Manning et al. 2005)) to manage the distinct distributional properties of healthcare utilization data, where earlier studies had not adequately addressed important statistical issues such as the retransformation problem (Jones 2010; Manning 1998).

At the same time, an important limitation was also identified in the most robust of these studies. Common practice had been to control for LOS in analyses either as a covariate in regression, by removing LOS outliers ex ante or by estimating effect on daily cost instead of cost of admission. A summary of these strategies is provided in Table 1. The key thinking behind LOS controls was that in a field where observational designs (and those relying on routine data collection specifically) dominate, unobserved heterogeneity is a substantial concern. In particular, multiple investigators cite the risk that those receiving palliative care are significantly sicker in ways that matching techniques cannot control for, and since sicker people stay longer in hospital, controlling for LOS may indirectly control for illness burden.

However, these approaches also had a number of important weaknesses (also detailed in Table 1) (May et al. 2016). First, defining the analytic sample by LOS has an endogeneity problem: LOS is not a baseline factor but an outcome that itself may be impacted by the intervention under evaluation. Second, such results are not useful for policy or practice because LOS is not known at hospital admission. Third, since policymakers are most interested in the high-cost multimorbid minority who drive healthcare utilization, analyses that exclude complex long-stay outliers are excluding the priority population.

Nevertheless, multiple investigators had found that controlling for LOS markedly improved the performance and accuracy of their treatment effect estimates. This raised the question of which baseline factors are systematically associated with hospital length of stay. Using such factors to characterize and balance treatment groups, and more accurately define the intervention, would improve economic evidence for policy and practice as well as informing future methods in the field.

3 The Importance of Timing

Following identification of the problems summarized in Table 1, investigators on a new prospective study estimated the effect of PCC on costs for the whole sample and when LOS outliers were removed. They found results consistent with prior studies: PCC was associated with lower cost of hospital admission when the 5% of patients who stayed longer than 20 days were removed from the analysis, but when outliers were retained, no association was observable within the whole sample (Table 2). In Table 2, palliative care does not appear effective for a sample of adults with advanced cancer; it does appear effective for those who are discharged within 20 days. However, as summarized in the previous section, these findings are neither reliable nor useful – this cannot inform policy or practice.

They therefore devised two potential hypotheses for *baseline* factors systematically associated with hospital length of stay:

H1: Timing of first consultation. Longer-stay patients by definition have scope to accrue more days and costs in hospital prior to receiving the intervention, utilization that is included in the outcome of interest but that the exposure (receipt of palliative care) cannot impact. Therefore earlier interventions may be more cost-effective than later ones, *ceteris paribus*.

H2: Illness burden of patients. Longer-stay patients have on average more comorbidities and other health problems, potentially creating

Table 2 Estimated effect of PCC on cost of hospital admission, for the whole sample and the 95% of shortest stayers

Sample definition	UC (*n*=)	PCC (*n*=)	All (*n*=)	Estimated incremental effect (95% CI)	*P* value	Implied saving
LOS<=20 days	705	263	968	**−1165 (−2321 to −8)**	**0.04**	**13%**
All	734	286	1020	−117 (−1780 to +1546)	0.89	1%

UC usual care only. Estimates derived using propensity scores and generalized linear model with a gamma distribution and a log link, see May et al. (2016) or contact authors for details. Implied saving is calculated as estimated incremental effect/mean cost for UC patients. Results are robust to myriad sensitivity analyses, details from authors

Table 3 Estimated effect of PCC on cost of hospital admission, where definition of treatment is defined by timing after admission

Treatment defined as within _____ days of hospital admission	UC (*n*=)	PCC (*n*=)	All (*n*=)	Estimated incremental effect (95% CI)	*P* value	Implied saving
Any time	734	286	1020	−117 (−1780 to +1546)	0.89	1%
20	742	278	1020	−902 (−2201 to +397)	0.17	10%
10	750	270	1020	−1062 (−2339 to +214)	0.10	12%
6	767	253	1020	**−1664 (−2939 to −389)**	**0.01**	**19%**
2	811	209	1020	**−2719 (−3917 to −1521)**	**<0.01**	**30%**

UC usual care only. Estimates derived using propensity scores and generalized linear model with a gamma distribution and a log link. For full details see May et al. (2015) or contact authors. Results are robust to myriad sensitivity analyses, details from authors

a situation where a complex class incur intractably high costs that cannot be meaningfully altered by different decision-making via the PCC team (and this complexity cannot be controlled for using baseline data, only by also controlling for LOS).

Using data from a prospective multi-site cohort study of PCC for adults with advanced cancer in the United States, investigators examined H1 by altering the definition of "receiving palliative care" according to time to first consult after admission. Where prior studies had put in the treatment group all patients who received palliative care at any time during their index admission, the treatment group was instead variously defined as receiving PCC within 2, 6, 10, and 20 days of admission. The results revealed a systematic association (Table 3).

The top row of Table 3 is the same as in Table 2: There is no association between PCC at any time during the admission and cost of care. As we move down the table, later consults are excluded from the treatment group, and the estimated cost-saving effect grows. Palliative care within 2 days of admission is associated with a large and statistically significant cost-saving effect.

Follow-up work has since confirmed H1: Long-stay patients by definition have greater scope to accrue more costs prior to receiving the intervention, costs included in the outcome of interest but that the treatment cannot impact. Interventions are more cost-effective than later ones, *ceteris paribus* (May and Normand 2016). Controlling for intervention timing, instead of patient LOS, delivers results that are more robust and useful.

Palliative care for hospital inpatients therefore appears to be what economists call a dominant strategy: Patients who receive palliative care have lower costs and earlier discharge than matched patients who receive usual care only, and noneconomic literature suggests they also experience improved outcomes (Higginson et al. 2003).

4 New Insights from "Early" Palliative Care Economics

The development of timing-sensitive methods in economic analysis of hospital palliative care has led to a series of new insights for the field.

First, and most obviously, the importance of identifying patients with palliative care needs promptly following admission and ensuring early engagement. The association between timing and cost-effect is not linear: costs are accrued disproportionately in the early phase of a hospital admission (Ishak et al. 2012) and treatment decisions in that phase will likely result in some level of pathway dependency (Mierendorf and Gidvani 2014). Clearly this is a concern of the hospital palliative care field more widely – numerous checklists are available to identify new admissions with relevant needs, and much thought is given to improving engagement with primary physicians and their teams – but it is worth remembering that this kind of early engagement is also critical to realizing economic benefits. For the same reasons, palliative care late in an admission does not significantly reduce total cost of admission (although it appears to reduce costs from the point that it is administered) (May et al. 2017a). Palliative care any time in a hospital admission is not a strategy with notable economic benefits, even if it may have clinical ones. Precisely how "early" a consultation has to be following admission to reduce costs is methodologically complex and is yet to be definitively examined.

Second, contrary to Hypothesis 2 (above), patients with a higher illness burden were not associated with a lower cost-saving effect. Rather, the reverse turns out to be true. Follow-up analysis with the same data revealed that the estimated cost-effect of PCC was larger for patients with higher numbers of comorbidities (see also "Example 2" in ▶ Chap. 98, "Measuring Cost-Effectiveness in Palliative Care") (Maynard and Lynn 2016). A subsequent analysis showed that comorbidities and complications are the key drivers of hospital utilization in this sample, and so the increased effect of PCC for those sicker patients represents a key dynamic to improving cost-effectiveness of services to this high-priority population (May et al. 2017b). These are potentially influential discoveries – if complex interdisciplinary decision-making such as palliative care is more cost-effective for the most costly and complex patients, perhaps because management of symptoms and prescribing is more important for patients with multiple diseases, then palliative care ought to be targeted to that high-need population for whom the difference is greatest.

Third, where early studies found no consistent association between palliative care and hospital length of stay, evaluations incorporating intervention timing have found that early palliative care following admission does have a significant effect (May et al. 2017a). Researchers estimated that approximately two thirds of observed cost-savings from receiving a palliative care consult within 2 days of admission accrued through earlier discharge and only one third through reduced intensity of that stay. This finding is important not only in deepening our understanding of how palliative care "works" in reducing hospital costs but also in raising new research questions – notably, what happens to seriously ill people after they are discharged from hospital? Are these cost-savings in fact shifted onto patients and their families?

5 Future Research: Beyond the Hospital Silo and Beyond the United States

The significant contribution of studies to date notwithstanding the balance of evidence remains overwhelmingly in the United States, although exceptions are observable (Simoens et al. 2010b; Hwang et al. 2013). Both inside and outside that country, there remains a large and important research agenda in economics of hospital palliative care in the coming years:

- **Different models of patient care:** evidence to date has heavily emphasized PCC teams, but cost studies of PCUs, where specialist palliative care staff are the primary physicians with responsibility for directing care, have also reported cost-savings (Smith et al. 2003; Eti et al. 2014). Recently a comparison of the PCC and PCU models found that the latter are consistently more cost-saving than the former (Fig. 1) (May et al. 2017c). This difference is hypothesized to arise because consultations are

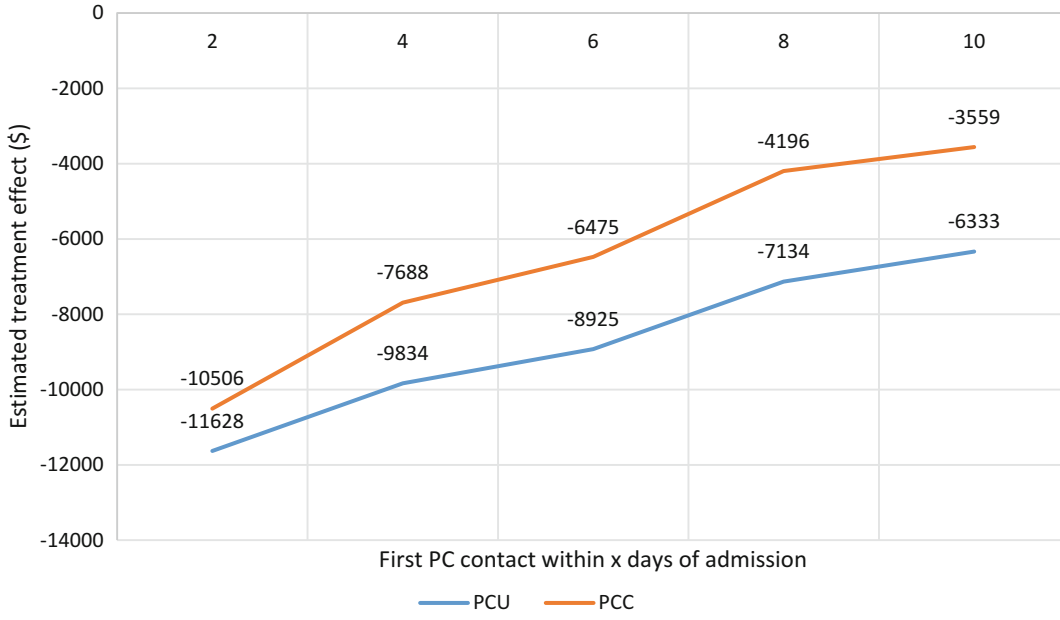

Fig. 1 Estimated treatment effect of PCC and PCU on direct hospital costs compared to UC only, by intervention timing. Each data point represents the ATE of the intervention compared to UC only where first PC interaction was within x days and x is given on the x axis. All ATEs in Fig. 2 are statistically significant ($p < 0.005$). First published as May et al. (2017c) in Journal of Pain and Symptom Management and reprinted with thanks

independent assessments, whereas PCU staff have more complete control over care, including medications and their dosages. This distinction deserves further examination. For example, should hospitals consider placing palliative care teams in direct charge of patient care from the moment of admission as happens with other specialisms in life-limiting illness? One possible location where palliative care staff could take a more prominent role earlier is the emergency department (ED): Many admissions of people with life-limiting illness occur through the ED (Mierendorf and Gidvani 2014; Latham and Ackroyd-Stolarz 2014), yet palliative care integration with the ED is often poor (Kistler et al. 2015; Quest et al. 2011; Elsayem et al. 2016; Grudzen et al. 2012).

- **Planning and education.** Staffing for hospital palliative care teams is found internationally to be underresourced (Spetz et al. 2016; Centeno et al. 2013). And the long-term projected growth of palliative care need is well-known (Etkind et al. 2017). Economic studies that demonstrate improved outcomes at lower costs (or modest increases) for these priority populations can contribute to the long-term planning of training for specialist palliative care staff. Additionally it is worth noting that studies to date exclusively focus on models of care that are led by specialist physicians. But it is surely also plausible that improving palliative care skills and capacity among non-palliative care staff could also yield economic benefits and studies of upskilling and education could be very informative to this set of questions.
- **Interdisciplinarity and complexity.** The recent discovery that palliative care is not ineffective but rather most cost-effective for people with more comorbidities (conditional on some basic assumptions about outcomes) invites further inquiry. This knowledge, which has demonstrable policy and practice relevance, is most plausibly explained by palliative care having its greatest impact in complex situations where disease-specific treatments are ill-equipped to address patient needs. For example, in the setting of multiple chronic conditions or serious illness, the application of

medications to adequately treat each condition may result in polypharmacy and enhancement of side-effects rather than appropriate treatment. Who, then, benefits most from palliative care? There are seven life-limiting illnesses typically observed in the literature: cancer; cardiovascular disease; respiratory, kidney, or liver failure; AIDS/HIV; and selected neurodegenerative conditions including dementia. Is palliative care more effective for some conditions than others? For different combinations of these? For specific primary diagnoses and other comorbidities such as complicated diabetes? At what point in the different disease trajectories are these benefits most realized? The inherent complexities of the population and the decision-making imply an almost infinite combination of important dynamics to be examined.

- **Beyond the hospital silo.** Hospitalizations for seriously ill people are a popular source of policy interest for the reasons cited at the start of this chapter: hospitals are the highest cost environment in which to receive care, many hospital admissions are avoidable or unnecessarily long, and many people die in hospital around the world. Nevertheless hospital admissions represent singular episodes – high-intensity care typically in response to adverse events. As populations age and people live longer with multiple serious conditions, hospital inpatient admissions will become less and less representative of the illness trajectory. Economic studies must broaden their scope to include but not be limited to hospital inpatient admissions, so as to establish when interventions are beneficial across the trajectory, when hospital-based care is optimal and when it is better substituted with care outside of institutions, and how the relationship between reported cost-savings and reported improvements in outcomes is best understood.

6 Conclusion

Economic studies of palliative care for adult hospital inpatients appear as a dominant strategy: persons who receive palliative care have lower costs and earlier discharge than matched patients who receive usual care only, as well as improved outcomes. Significant methodological progress has also been made, which future investigations can benefit from.

The findings from this literature have learnings for the field of palliative care more widely. In particular, palliative care's effect is larger when provided earlier (raising questions of when palliative care should be introduced in the trajectory of illness for people both inside and outside the hospital) and is also larger for adults with higher numbers of comorbidities (suggesting that complex interdisciplinary interventions are more effective for complex clinical cases, an insight with major potential policy relevance worldwide).

At the same time, significant limitations to this evidence remain. In particular investigators must look to take evaluations beyond the hospital silo to evaluate impacts across whole trajectories of care. Only then will policymakers have the full story on the costs and benefits of complex care for those with complex illness.

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Financial Aspects of Outpatient Palliative Care

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_103

Abstract

Community-based palliative care has become the focus of palliative care's growth and opportunity. Twelve of the largest randomized control trials on palliative care are community-based and result in equal or greater survival, positive satisfaction from patients and caregivers, and equal or less cost. Surprisingly, sometimes the business case is the easiest to make (Cassel et al. 2015). With health care financing that embraces value-based programs, such as serious-illness care models, shared savings, bundled payments, and global budget revenues, community-based palliative care shows great promise and may be part of the solution to provide better care for patients at an affordable cost. Some key obstacles include a shortage of practitioners and the necessity to perform as a public health system instead of a revenue-generating center. We provide examples of some successful programs that are reproducible.

1 Introduction

Studies from the United States, United Kingdom, and Canada suggest that most people prefer to both be cared for and die at home (Gomes et al. 2013a; Bell et al. 2009; Higginson and Sen-Gupta 2000). However, only a minority of deaths occur at home (Cohen et al. 2010). In the US in 2007, 24% of deaths occurred at home among those aged 65 years and older (Teno et al. 2013; Statistics 2010). In the UK in 2010, 21% of deaths occurred at home (Gomes et al. 2012). In Canada, from 1994 to 2004, 30% of deaths occurred at home (Wilson et al. 2009). In addition, the rapid rise of concurrent palliative care alongside disease-directed therapies for diseases like cancer and multiple sclerosis – where people may live a long time and not die – has made many programs retool for chronic ongoing care.

Varied initiatives in outpatient palliative care have focused on aligning care with people's preferences, improving clinical outcomes during and after treatment and increasing the proportion of people dying at home by decreasing hospital admissions near the end of life. In light of these trends and using a system-level international perspective, this chapter aims to explore what goes into the business planning for outpatient palliative care services.

This chapter describes research surrounding both "outpatient" (that is, clinic-based) and "home-based" palliative care. Clinic-based services may be associated with large health care systems. Home-based palliative care involves caring for seriously ill patients where they live, including private homes, nursing homes, and assisted living facilities. Both types of care may utilize telemedicine. Outpatient clinic-based and home-based palliative cares are sometimes referred to as Community-Based Palliative Care (CBPC).

CBPC developed differently in different countries. While it is outside the purview of this chapter to detail the development in each

country, we will briefly list a few key points. In the USA, CBPC developed on a site-by-site basis, which largely reflects the health care system in that country. End-of -life care was and continues to be predominantly funded by the Medicare Hospice Benefit, which promotes community-based hospice models that rely on home care (Bull et al. 2012). In Canada, CBPC had a more organic development, and while palliative care services and availability vary widely across the country, various provincial initiatives (e.g., the Ontario Palliative Care Network) are working to standardize palliative care and improve access. In the UK, palliative care services were developed similar to the USA, in a haphazard manner, site by site, often as a feature of charities. Since the NHS Cancer Plan 2000 (https://www.thh.nhs.uk/documents/_Departments/Cancer/NHSCancerPlan.pdf) along with end of life (EOL) strategy in 2008, there has been a more systematic attempt to figure out the regional needs, led by the National Council for Palliative Care. The Royal College of Physicians has set target numbers of consultant palliative care physicians to per capita population. This will help identify under-resourced and recognize where there is a greater need for physicians.

In this chapter, we first present a literature review of the research in the finances of CBPC. Second, we provide case studies of organizations that have been successful in their implementation of outpatient and/or home-based palliative care. Third, we provide suggestions and a blueprint for steps to take to create a sustainable and replicable outpatient and/or home-based palliative care program.

2 Literature Review

When reviewing the literature, it is important to note that it is challenging to compare across programs and jurisdictions. As acknowledged by Gomes et al. in their 2014 systematic review of the effectiveness of home-based palliative care, what constitutes "home palliative care" varies – be it physician- or nurse practitioner-provided; daily, weekly, or monthly visits; the extent of care that can be provided in the home. Also, importantly, the comparator of "usual care" varies across setting. In the above systematic review, usual care included community care, that is, primary or specialist care at home, outpatient clinics or in nursing homes, and in some instances hospice care (Gomes et al. 2013b).

Others have noted that the existing cost effectiveness and costs savings research on CBPC have certain limitations, including ambiguous currency and cost information, and limited statistical information (e.g., t-test results, confidence intervals, ranges, and disaggregated data) (https://www.thh.nhs.uk/documents/_Departments/Cancer/NHSCancerPlan.pdf). In addition to the above-noted challenges, Davis et al.'s systematic review of trials featuring early integration of outpatient and home-based palliative care found that studies typically had high attrition rates, lack of mention regarding whether participants were blinded, infrequent power calculations, and minimal use of intention-to-treat analysis (Davis et al. 2015). Both reviews noted that many studies in this field do not incorporate family nonmedical factors, including productivity impacts (e.g., patients/caregivers taking time off work as a result of illness or caregiving), use of life savings to cover medical expenditures, and food and transportation. Similarly, a systematic review on the financial impact of caring for family members of patients receiving palliative care found that there is limited research on the financial burden of caregivers; however, the few available studies suggest the financial costs are substantial and result in caregiver burden (Gardiner et al. 2014).

3 Symptom Management in Home-Based Palliative Care

Gomes et al.'s recent Cochrane Systematic Review on home-based palliative care demonstrated that, compared to usual care, home-based palliative care increased the odds of dying at home (from their meta-analysis: odds ratio (OR) 2.21, 95%CI 1.31 to 3.71; $Z = 2.98$, P value $= 0.003$), and small but statistically significant benefits of

reducing symptom burden for patients (https://www.thh.nhs.uk/documents/_Departments/Cancer/NHSCancerPlan.pdf). Davis et al.'s systematic review of trials featuring early integration of outpatient and home-based palliative found that most studies demonstrated improvement in depression and quality of life, decreased caregiver burden, and better maintenance of caregiver quality of life; however, they also noted that some trials demonstrate symptoms and quality of life did not improve (Gomes et al. 2013b). Sarmento et al. conducted a meta-ethnography to attempt to identify what components of home-based palliative care leads to these positive outcomes. The two overarching themes that emerged were that the 24/7 availability of home-based palliative care helped patients and families feel they had sufficient access to services, and that effective communication and symptom control made patients and their caregivers feel secure (Sarmento et al. 2017).

To our knowledge, only one trial has shown worse symptoms. Hoek et al. (2017) randomized 74 Dutch patients to weekly palliative care telemedicine sessions or "care as usual" without mandated palliative care consultations. In the intervention group, the Total Distress Score and anxiety scores (but not depression) were significantly worse at week 12. Their explanation was that the telemedicine allowed the patients to give excess attention to symptoms and suffering, and that the usual care had good palliative care as standard. But for the most part, these programs seemed to, according to the qualitative literature, allow patients and family caregivers to focus on living life and preparing for death at home, rather than dedicating time to the medical components of care (Gardiner et al. 2014).

There are specific examples of how concurrent palliative care improves symptoms. The UCSF outpatient team did an observational study of the outpatient cancer program that saw 266 patients at least twice. The only symptom that did not improve was nausea, but pain, depression, anxiety, quality of life, and spiritual wellbeing all improved clinically and statistically ($p < 0.002$ for all) (Bischoff et al. 2013). With US Oncology, Muir and colleagues embedded a palliative care advance practice or doctor or both (but not a social worker or chaplain) in oncology offices (Muir et al. 2010). The symptom burden was reduced by 21%, with ESAS scores falling from 49.3 to 39 (a meaningful difference). Oncology providers ranked satisfaction with the new PC service at 9/10, and consultation requests increased 87%, a doubling per oncology provider. The PC service saved the practice over 4 weeks of time, or 170 min per referral, used time-based billing by the PC group to calculate; this would allow the practice to see 121 new patients. Hospice length of stay, a marker of quality care, increased from 15 days to 24 days with palliative care consultation ($p < 0.001$) (Scheffey et al. 2014). In addition, opioid prescribing practices improved when palliative care saw the patient, with extended release analgesic prescriptions rising from 45% to 73% and pain scores dropping by 2/10 (Muir et al. 2013). The billing revenues from the palliative care providers paid their salaries, but the average half day session for a doctor and advance practice nurse included four new and six to eight follow-up visits in a half-day session, productivity which can be hard to sustain as a fulltime practice (Alesi et al. 2011).

3.1 Cost Effectiveness of Home-Based Palliative Care (United States)

While there is good penetration of inpatient palliative care programs in US hospitals, there are fewer outpatient palliative care programs. The total number of outpatient palliative care programs is not known but likely the current capacity in CBPC is inadequate to meet the current need (Bull et al. 2012; Kerr et al. 2015). To date, there have been some studies on the costs/benefits of home-based palliative care, but there is discordance in their findings. Overall, the aforementioned *Cochrane Review* of home palliative care services for adults with advanced illness and their caregivers deemed the evidence inconclusive regarding the cost effectiveness of this intervention as compared to hospital-based palliative care (6 studies). Similarly, Davis et al.'s systematic review of early integration of outpatient and

home-based palliative care found that there is mixed evidence on whether these services reduce hospital length of stay and number of hospitalizations, as well as reduce costs. They suggest that the inconclusive nature of these results may stem from large variability in studies; standard deviations are often larger than the means suggesting lack of precision, skewed economic data, and heavy influence of outliers. Further, patient populations are often comprised of those with diverse primary diagnoses. Rabow et al.'s systematic review of outpatient palliative care interventions found that the evidence suggestions these programs reduce health care utilization. They suggest that while the delivery of outpatient palliative care is communication-rich, and staffing intensive, the program's ability to reduce overall health care utilization balances out the costs of delivery, especially in integrated health systems (e.g., accountable care organizations) (Rabow et al. 2013).

There are a few notable studies that examined the cost effectiveness of particular home-based and outpatient palliative care programs. One of the most cited cost-effectiveness studies is Brumley et al.'s work from Kaiser-Permanente in 2007 that entailed a randomized control trial in Hawaii and Colorado comparing home-based palliative care to usual care (Brumley et al. 2007). This study found that overall costs of care for those enrolled in the home-based palliative care program were 33% less than those receiving standard care ($P = 0.03$). Further, the average cost per day incurred by palliative care recipients (USD$95.30) was significantly lower than that of usual care group members (USD$212.80) ($P = 0.02$). This study and a similar one for inpatients convinced Kaiser-Permanente to adopt the palliative care interdisciplinary team in all their major markets.

Bookbinder et al. found a home-based palliative care model involving a nurse practitioner and social worker connected to a palliative care home team did not generate enough annual revenue from patient billings to offset the nurse practitioner's salary costs; however, a model of a nurse practitioner linked to a hospice program led to an increase in hospital referrals thereby generating sufficient revenue to support the nurse practitioner (Bookbinder et al. 2011). Indeed, an early study of outpatient palliative care practices suggested that billing revenue covers less than half of program budgets (Rabow et al. 2010).

Cassel et al. examined the cost impact of a concurrent care home-based program designed for individuals with advanced chronic illness found that, compared to a propensity-matched usual care control group, patients in the intervention group had less hospital use (mean hospital days per month of 0.69 (SD 1.84) vs. 2.62 (SD 3.44), p 0.001) and lower hospital costs (mean per month costs of $984 (SD $2,776) vs. $5,195 (SD $7,353), $p < 0.02$). In addition, overall, the cost of care in the last 6 months of life remained relatively the same in the intervention group ($1,550 4 months before death, $3,711 in the final month), compared to a significant increase in the control group ($2,631 4 months before death, $17,006 in the final month). The numbers included were for patients with a primary diagnosis of cancer. This home-based palliative program included in-home medical consultation, ongoing evidence-based prognostication of further survival, caregiver support, and advance health care planning (Brian Cassel et al. 2016).

Kerr et al. compared the costs of a community-based outpatient palliative care program featuring a hospice-private payer partnership to propensity-score matched control group, and found that outpatients costs were significantly lower for the intervention group at 2 weeks, 1 month, and 3 months, no difference at 6 months, and significantly higher at 1 year and 2 years (Kerr et al. 2014). Lustbader et al., examined the effect of a home-based palliative care program within an Accountable Care Organization, compared to usual care. The study found that the cost per patient during the final 3 months of life was $12,000 lower in the intervention compared to control group ($20,420 vs. $32,420; $p = 0.0002$). This decrease resulted from a 35% reduction in Medicare Part A ($16,892 vs. $26,171; $p = 0.0037$), and a 37% reduction in Medicare Part B ($3,114 vs. $4,913; $p = 0.0008$). The intervention group also resulted in a 34% reduction in hospital admissions, a 35%

increase in hospice enrollment, and a 240% increase in median hospice length of stay, compared to usual care (Lustbader et al. 2017).

Pouliot found that, in a pre-post study evaluating the impact of a home-based palliative care program, patients experienced decreased emergency department visits and inpatient hospital admissions (Pouliot et al. 2017).

In the study of concurrent palliative care embedded in oncologists offices described above, the practice was self-sustaining but may be difficult to sustain (Alesi et al. 2011). In our own practice (RR and TJS), billing revenues will cover at least half the salary (our arrangement with the institution) if the provider sees four patients; a busy practitioner see two new patients and four to six return visit patients in a half-day session and comes close to covering full salary.

It is important to recognize the importance of early versus late referral at their cancer in changing end of life practice patterns. At the UCSF Cancer Center, only 32% of decedents were referred to palliative care, with 68% referred less than 90 days before death (Scibetta et al. 2016). If the patients were referred 3 months before death, the health system saved $5198 due to fewer end of life hospital days with lower inpatient care costs ($19,067 vs. $25,754, $p < 0.01$), while outpatient costs were no different.

Besides the timing of referrals, the number of outpatient visits plays a role in reducing aggressive care at the end of life and resultant expenses. As shown in Fig. 1, as the number of visits increased, less aggressive care near the end of life was provided (less chemotherapy in the last month of life; fewer emergency visits, admissions, and Intensive Care Unit admissions) (Jang et al. 2015).

3.2 Cost Effectiveness of Home-Based Palliative Care (Canada)

Most figures from Canadian studies are 5–10 years old; therefore, there is a need for an updated cost-effectiveness analysis comparing home-based palliative care to hospital-based palliative care. Of note, while all hospital-based services are covered under public health insurance in Canada; home care and community care are only partially covered, depending on the province. For example, patients and families in Ontario cover 25–50% of the total costs (Dumont et al. 2009).

While models of palliative care exist across Canada, there are disparities and gaps in access across regions. One study compared costs of 6 months in a palliative care program in an urban versus rural setting and found that the total cost per patient was $26,652 in urban areas (with families covering 20.8% of the costs), while $31,018 in rural areas (with families covering 21.9% of the costs) (Dumont et al. 2015). Notably, these figures reflect inpatient, outpatient, and home-based palliative care, aggregated. Urban families tended to cover more costs related to formal home care, while rural families tended to cover more costs related to prescription medication,

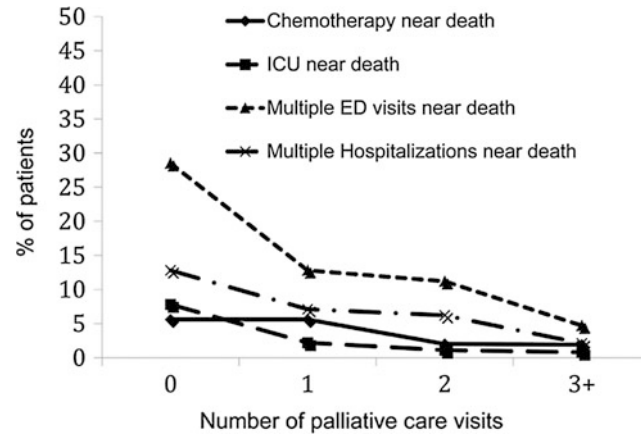

Fig. 1 Relationship between number of palliative care visits and end of life aggressive care

out-of-pocket costs, and transportation (Jang et al. 2015). There have also been province-based studies accessing disparities. In Quebec, where home-based palliative care services are provided by the Public Local Community-Based Health Care Service providers (Locaux de Services Communautaires [CLSC]), one study found large variation in delivery of these services to patients with cancer (Gagnon et al. 2015). Of the 53,316 cancer patients included in the study (representing patients with cancer who died in Quebec between 2003–2006), 52.1% received home visits during the 90 days before death, and of those, 72.5% received three visits or more.

The models of home-based palliative care programs have shifted over time. One study documented changing trends in services models from 2005 to 2015 in Ontario and found that the propensity and intensity to use home-based physician visits and personal support workers increased, while propensity and intensity of nurse visits deceased (Sun et al. 2017).

Regarding the cost effectiveness of these services, several studies have captured the impact of certain models of care on system costs. Klinger et al. tested a model of home-based palliative hospice care in Ontario (Klinger et al. 2013). The study found the average costs were approximately CAD$117.95 per patient day or a total of CAD$17,112.19 per patient over the 15-month study period. These findings are roughly equivalent to the Ontario Auditor General's reporting that the average per day palliative care costs in the last month of a patient's life is under CAD$100/day for home-based palliative care. Alternatively, the average costs of other palliative services were CAD$1,100 per day in an acute-care hospital bed, CAD$630 to $770 per day in a bed in a palliative-care unit, and CAD$460 per day in a hospice bed. There is incongruence regarding these costs. A 2010 report estimated that it costs approximately CAD$4,700 per client annually to provide palliative care in the home as compared to CAD$19,000 for acute care annually. A piloted palliative home care service that ran in Ontario from 2000 to 2001 cost CAD$5,586 per patient for a year. From a system perspective, a 2013 study in Ontario projected that expanding in-home palliative care to those currently not receiving such services (approximately 45,000 people per year) can avoid CAD$191 million to CAD$385 million in health care costs. Shifting just 10% of patients at end of life from acute care to home care would save CAD$9 million a year.

A study of palliative care costs in the last 5 years of life among patients in Halifax, Montreal, Winnipeg, Edmonton, and Victoria found that the mean total cost of outpatient palliative care increased by 70% from the first to the last month of life, and the mean total cost of home care was 4.5 times higher during the last month of life compared to 5 months before death. While costs for transportation gradually increased, costs of prescription medications decreased from the fifth to the second last month of life, and costs of medical equipment increased from the fifth to the third month but then decreased from the third to the last month before death (Dumont et al. 2010).

Few Canadian studies have accessed the costs of home-based palliative care from a societal perspective, which considers third-party insurance payments, travelling expenses, caregiving time devoted to patients and missed time from work and leisure. Yu et al. investigated the differences in societal costs of end-of-life care associated with hospital and home deaths, and found that there was no significant differences in total societal costs; however, the higher hospitalization costs for hospital death patients were ultimately equivalent to the unpaid caregiver time and outpatients service costs for home death patients (Yu et al. 2015) Diving deeper into the distribution of societal costs, Dumont et al.'s study of resources utilization during the palliative phase of care in five regions in Canada found that the costs across inpatient hospital care stays, home care, and informal caregiving time were paid for 71.3% by the public health care system, 26.6% by the family, 1.6% by not-for-profit organizations, and 0.5% by other payers. The majority of costs supported by the family were attributable to caregiving time (66.3%), followed by out-of-pocket costs (17.0%), home medical equipment or aids (6.7%), and home care (4.4%) (Dumont et al. 2009).

Further investigating the source of these non-public system expenses, Chai et al. interviewed 169 caregivers of patients receiving home-based palliative care as well as abstracted data on health care utilization of patients. This study determined that the average monthly cost per patient for these services over the last 12 months of the patient's life was CAD$14,924 per patient (2011 Canadian dollars), which broke down into 77% unpaid caregiving cost (i.e., caregiver time lost from market labor and leisure) (CAD$11,334), 21% publicly financed health care costs (i.e., costs incurred by the public sector in the organization and delivery of home-based palliative care services) (CAD$3,211), 2% privately financed costs (i.e., out-of-pocket costs for expenditures on consultations with clinicians, travel expenses, private insurance plans supplementing public insurance) (CAD$379). The study also found that the magnitude of costs increased exponentially over the last 12 months of life. A previous study by the same group found that the mean monthly cost per patient for services over the last 12 months of life was CAD$24,549 (2008 Canadian dollars), which broke down into 70% unpaid caregiving cost ($17,184), 26% publicly financed health care costs (CAD$6,396), 4% privately financed costs (CAD$870) (Guerriere et al. 2010).

3.3 Cost Effectiveness of Home-Based Palliative Care (Australia)

A systematic review and meta-analysis of the impact of community specialist palliative care services found the evidence to be inconclusive regarding whether the impact these services have on home deaths, symptoms, and costs. Importantly, none of the studies in this review found a significant effect in favor of an alternative intervention (Luckett et al. 2013). Kralik et al. compared home-based palliative care service utilization among patient with cancer and non-cancer conditions and found that patients with cancer were referred earlier, patients with non-cancer conditions were higher users of home-based palliative care services over a longer period of time (Kralik and Anderson 2008). An Australian home-based palliative care model was found to cost AUD$3,489 per patient, which was largely offset by lower mean inpatient care costs (AUD$2,450), resulting in a net incremental cost of AUD$1001 per patient (McCaffrey et al. 2013).

4 Highlighting of Organizations that Have Been Successful in Their Implementation of Outpatient Palliative Care

4.1 Johns Hopkins Medicine Palliative Care Program (Baltimore, USA)

Palliative care delivery at Johns Hopkins began at the Sidney Kimmel Comprehensive Cancer Centre (SKCCC) with outpatient palliative care, which was run primarily by pharmacy for cancer patients for three half days a week. Once two fulltime palliative care providers joined the hospital, physicians co-led the clinic with pharmacy, and the program also included access to a psychology nurse liaison, social workers (to address psychosocial issues and hospice referrals), and one chaplain. Often there were palliative care fellows staffing the clinic for half the year along with pharmacy residents and pharmacy students. The number of outpatient visits that were billed increased from 200 to over 1000/year from 2011 to 2016.

In 2013, the program developed a half day clinic for non-oncology patients, including those with severe neurological disorders, mitochondrial diseases, chronic obstructive pulmonary disorder (COPD), pulmonary hypertension, and cirrhosis. Due to funding, this clinic for non-oncology patients is only provided by a palliative care physician and an additional palliative care fellow for half the year. The program consults with all patients prior to left ventricular assist device (LVAD) and heart transplant, and periodically sees patients with pulmonary hypertension, heart failure, and liver disease in embedded clinics with the respective teams. Across inpatient and outpatient services, the program uses the modified

Memorial Symptom Assessment Scale Condensed (MSAS-C) for symptom assessments, spiritual, psycho-social assessments, as well as engages in prognosis evaluation after speaking with specialists. Over half of the patients in the program are primarily referred to receive symptom management; the remaining patients primarily are referred for either goals of care discussions and/or evaluation for hospice.

We have recently estimated the total impact of the palliative care program on the health center, and 2016 activity should save the institution nearly five million dollars (Isenberg et al. 2017) (Fig. 2).

With the increased acceptance of palliative care at Johns Hopkins Medicine among providers, coupled with increased institutional buy-in and more and more accountable care organizations, the program is in the process of developing home-based palliative care with an already established geriatric home-based care program, JHome. This multiprogram collaboration involves stakeholders from home care, geriatrics, pharmacy,

Financial impact	Cases/year projected 2016	Financial impact per case	Contribution ($/year)	5 year total contribution
IP PCU margin (1)			$100,000	$500,000
IP PCU cost $1595 savings/transfer (2)	154	$1,595	$245,630	$1,228,150
PC IP consult cost savings per case, $2,374 for patients discharged alive (3)	1355	$2,374	$3,216,770	$16,083,850
PC IP consult cost savings per case, $6,871 for decedents, 11% died (4)	167	$6,871	$1,147,457	$5,737,285
JHFAU vetted savings			***$4,709,857***	***$23,549,285***
Early PC OP consult cost savings per case. $5198/case – if seen 3 months before death compared to near death	297	$5,198	$245,630	$34,355,000
Hospice referrals cost savings per case, $4348/case; assumes half of the actual savings of $8697 in the last year[i]	800	$4,348	$3,478,400	$17,392,000
Professional fees, 50% collection rate			$500,000	$2,500,000
Improvement in HCAHPS (2% of Medicare reimbursement in 2017).			?	
Increased ICU bed availability leading to revenue			?	
Reduction in 30 day readmissions			?	
Goodwill; impact on disparities ; charitable contributions			?	
Total impact			**$13,643,744**	**$101,345,570**

PC palliative care; IP inpatient; PCU palliative care unit; JHFAU Johns Hopkins Fiscal Analysis Unit; HCAHPS Hospital Consumer Assessment of Healthcare Providers and Systems

Fig. 2 Financial impact of the palliative care program on the health system, projected to 2016

business development, and the hospital's financial analysis unit.

The outpatient program has encountered some challenges, in particular approximately 25% of outpatient visits are no shows. To address this issue, one of the program's administrative assistants calls patients 2 days before scheduled visits to confirm attendance. This process has decreased no show rates by approximately 25%. The program sees over 1000 patients/year with 468 unique medical record number visits, which are either new visits and/or patients who have not been seen in a year. They have half day clinics for patients with cancer 3 days per week and a half day clinic for patients who have non-cancer diagnoses. Outpatient palliative care program accounts for 14% of the total program work Relative Value Units (wRVUs). The program expects each provider to meet wRVU goals and to cover at least half their salaries and benefits, with the hospital absorbing the rest.

It is critical to bill and collect appropriately for professional fees or the program will not succeed. We show two "Levels of Care" billed by two practitioners who saw patients of similar severity. Provider one – based on chart review and time spent with the patient – is not billing enough to cover his/her salary. Note that provider B documented her time consuming, difficult medical decision-making visit in subsequent visits with the 99233 code (Fig. 3a, b).

The Harry J. Duffey Family endowed the Palliative Care Program at the cancer center, which has now spread across all disciplines. There is an endowed annual lecture on "Hope" and an endowed professorship in Neuromodulation with emphasis on Scrambler Therapy (Majithia et al. 2016). A memorial service is held yearly at the cancer center, and one for all the patients who have died on the Osler Medical Service. Scholarly activities have included the updating of the national clinical practice guidelines in

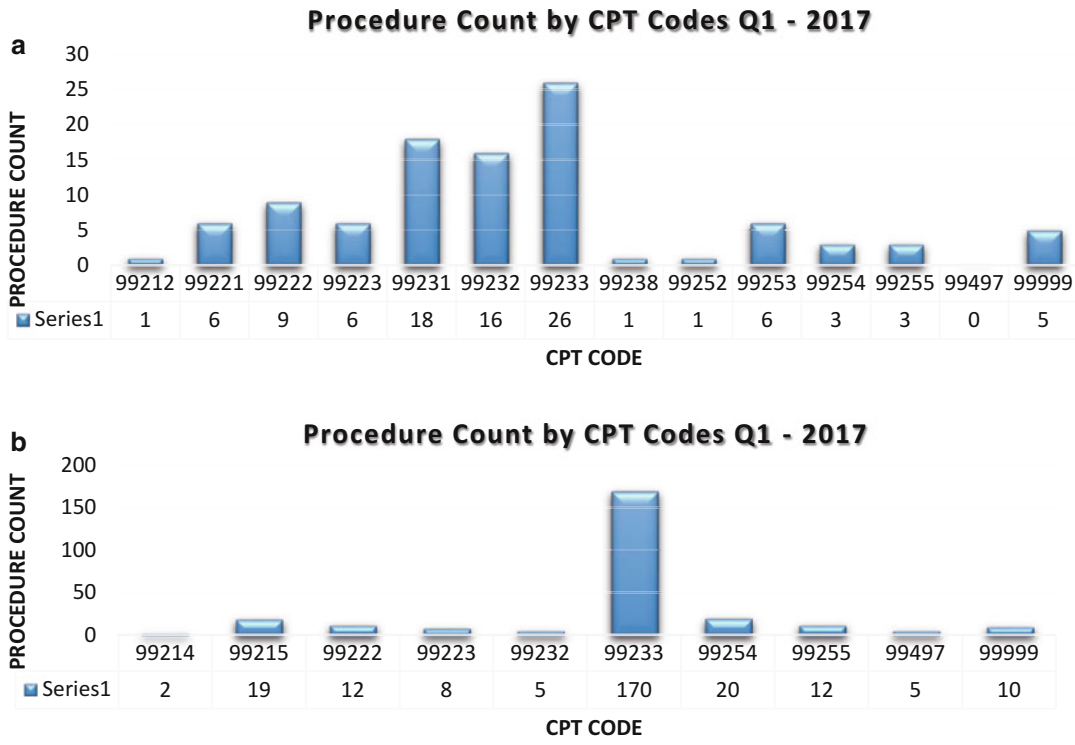

Fig. 3 (**a**) Different billing codes from two providers who gave the same service. (**b**) Different billing codes representative of the actual work performed

palliative care (Ferrell et al. 2017; Levy et al. 2016); communication in the neonatal intensive care unit; neuromodulation for relief of pain from cancer, HIV, post-mastectomy syndrome; integration of palliative care with hospitalist work; and one widely accepted play ("Life Support") presented locally and at the national meeting.

4.2 The Symptom Management Service at the Helen Diller Family Comprehensive Cancer Center, UCSF (San Francisco, CA)

The Symptom Management Service (SMS) is the clinic-based palliative care program at UCSF's comprehensive cancer center. The SMS provides comanagement with the oncology teams. The majority of referrals are for pain and depression. Approximately, 60% of patients in the SMS have metastatic disease. The SMS was launched in 2005 in Genito-Urinary Oncology with a single half-day clinic staffed by a palliative care physicians and social worker. In 2008, the SMS was available to patients throughout the cancer center. Currently, the SMS has grown to offer 25 half-day clinics weekly across both cancer center campuses. In 2017, the SMS had 605 new patients and 1,436 follow up visits. The program includes physicians (1.9 FTE total across 7 physicians), a nurse practitioner (1.0 FTE), a nurse (1.0 FTE), a program coordinator (1.0 FTE), a practice manager (0.5 FTE), and a chaplain (0.2 FTE). Among SMS staff, physicians are supported from clinical billing revenue. All other staff are supported by the medical center. Social workers are shared with the cancer center programs, as are psychologists and nutritionists. The SMS trains palliative care fellows, oncology fellows, medical residents, medical students, nursing students, and pharmacy residents. SMS clinics are primarily stand-alone but with an expanding number if embedded clinics, including in Breast Oncology and Gastrointestinal Oncology.

The SMS primarily has served patients with solid tumors (the top referring programs are Breast, GI, and GU oncology) but is currently expanding with 2 half-days embedded in the Bone Marrow Transplant Clinic (at yet a third UCSF campus). The SMS program includes annual memorial services at two cancer center campuses, a video legacy project for patients, cancer center awards to leading faculty and staff, and a campus-wide lecture series. The SMS oversees inpatient palliative care services at the affiliated cancer hospital. At UCSF, in addition to outpatient palliative care for cancer patients provided by the SMS, inpatient palliative care is available at the main university hospital; there is a home-based palliative care service for UCSF patients in San Francisco county, and an outpatient palliative care clinic for non-cancer patients will be launching soon.

SMS research has demonstrated improved clinical outcomes in nearly all symptoms assessed and persistence of benefit over more than 80 days (Bischoff et al. 2013). Patients have similar improvement regardless of gender, age, ethnicity, disease stage, disease progression, and concurrent oncologic treatments. In another study, clinician and financial outcomes were explored among UCSF patients who died of cancer. Patients who received palliative care early (in the SMS, prior to 90 days before death) had improved end-of-life outcomes, health care utilization, and total costs compared to patients who received palliative care late (within 90 days of death, primarily from inpatient palliative care consultation).

4.3 Temmy Latner Centre for Palliative Care at Sinai Health System (Toronto, Canada)

The Temmy Latner Centre for Palliative Care (TLCPC) is a department in Sinai Health System (Toronto) that began in 1989, initially providing both hospital and home-based care with a team comprised of one physician, a clinical nurse specialist, social worker, and two chaplains. Co-founded by Dr. Larry Librach and Dr. Frank Ferris, the program is the first and largest organized home palliative care program in Ontario (Temmy Latner Centre for Palliative Care 2015).

As of 2015, the program has 21 physicians on staff (17 in the Home-Care program and 6 in the In-Hospital Care Program), 2 full-time equivalent (FTE) coordinators, and 3.8 FTE staff (Seow et al. 2013). The program receives referrals from physicians across the Greater Toronto Area. As of 2017, the program includes: a home-based palliative care program serving residents of the Greater Toronto Area, a 32-bed inpatient palliative care unit, and inpatient consultation services within the Sinai Health System. The home-based care program partners with community agencies (i.e., Community Care Access Centres) to provide multidisciplinary palliative care in the home, and there is a physician available to patients 24 h a day, 7 days a week. In addition to the care it provides, the clinicians in the program assist with education providers at Mount Sinai Hospital, as well as providing training in palliative care to all medical students and many postgraduate medical trainees in many specialties at the University of Toronto.

Seow et al. evaluated the effectiveness of the home-based palliative care program comparing 676 patients who received home-based care from TLCPC from April 2009–March 2011, to a comparison group of patients matched on demographics and primary diagnoses. The study found that compared to the control group, TLCPC patients had a 30% (relative risk = 0.70) lower risk of being in the hospital in the last 2 weeks of life, a 35% (RR = 0.66) lower risk of dying in the hospital, a 53% (RR = 0.47) lower risk of visiting an Emergency Department in the last 2 weeks of life, and a three times (RR = 3.02) greater risk of dying someplace outside of the hospital (Seow et al. 2013) A study of patients in this program found that the average monthly cost for these services over the last 12 months of the patient's life was CAD$14,924 per patient (2011 Canadian dollars), which broke down into 77% unpaid caregiving cost (i.e., caregiver time lost from market labor and leisure) (CAD$11,334), 21% publicly financed health care costs (i.e., costs incurred by the public sector in the organization and delivery of home-based palliative care services) (CAD$3,211), 2% privately financed costs (i.e., out-of-pocket costs for expenditures on consultations with clinicians, travel expenses, private insurance plans supplementing public insurance) (CAD$379) (Chai et al. 2014).

4.4 Outpatient Specialist Palliative Care Clinic, Scarborough, North Yorkshire, England

The specialist palliative care clinic in Scarborough via Scarborough General Hospital (SGH) serves a population of about 220,000 across a mixed urban-rural setting. This program is associated with Hull York Medical School and is in partnership with Saint Catherine's Hospice. The hospice is an independent charity and gets 70% of its funds from the community donors. The rest is provided by the NHS. Patients have access to lymphedema clinic, complementary therapy, and those in the area have access to bereavement services. They have a community specialist palliative care nurse advisory service including a neurology palliative nurse specialist. In addition, they provide an out of hours phone advice service for patients and relatives and non-palliative care health care professionals which also acts as a liaison point for those at home who may need a medical visit from the GP out of hours service. Patients do not need to be otherwise known to the hospice to be registered for this service. They have an active education center which seeks to upskill non-palliative care clinicians who do the bulk of generalist palliative care, including running 2-day advanced communication skills courses. Palliative care providers are employed by the hospice and NHS Trust and work together as one team across all the settings – hospital, community, and hospice. This ensures continuity of care in all settings. There is excellent integration with oncology, cardiology, movement disorder clinic, neurology, and respiratory medicine. The group uses a needs-based model rather than a prognosis-based model in all aspects of the service. In the UK, the term end-of-life indicates someone with a prognosis of 6–12 months.

5 Blueprint of How to Make Outpatient Palliative Care Sustainable and Replicable

From our clinical experiences, the following are key tips that can help to create and/or enhance outpatient and home-based palliative care delivery: 1. Train your team in standardized care that includes goals of care discussions. This means to acknowledge barriers to engaging in these conversations, convince all providers to engage in Advance Care Planning (ACP) such that the difficult discussions are had, and add communication prompts (e.g., communication checklist or even a temporary tattoo (Leong et al. 2016)). The prompts can be built into your electronic medical record system. Use systematic way to assess systems such as a spiritual distress scale, a symptom assessment scale like the Edmonton Symptom Assessment Scale (ESAS). Train all providers in how to complete (and then measure, for program impact) other possible outcomes like the Physician Orders for Life Sustaining Treatment (POLST) completion, hospice referrals, and readmissions.

Second, obtain buy-in from leadership and administrators by asking them what matters most and measuring your impact on it. One qualitative study interviewed clinical and operations leaders at local, regional, and national levels in the US Veterans Health Administration (VHA) to gauge organizational factors that were potentially influencing the adoption of outpatient care in chronic illness. Participants perceived outpatient palliative care as a lower priority for them because there are not sufficient performance measures to gauge improvement nor incentivize update of palliative care. Participants expressed that their buy-in would be increased if were demonstrated to them that the costs of the program offset health service utilization costs, and that issues regarding staffing and space requirements were being sufficiently addressed. Participants were also concerned that palliative care be done as complimentary to other forms of care, to ensure that clinicians did not feel threatened by the palliative care team; building clinician trust and buy-in is perceived as integral, as well as clarifying the roles and responsibilities of outpatient palliative care and primary/specialty care for disease management in advanced chronic illness (Bekelman et al. 2016).

Third, do not be isolated; interface with the larger organization. It is important to align the patient-centered symptom management goals of outpatient and home-based palliative care with the organization's financial interests, as it may enable more budgetary, political, or operational support (Cassel et al. 2015). Promote the program to providers in the institution to help increase referrals to the program. To do so, it is important to build relationships with providers, as well as educate providers about palliative care processes (e.g., what is involved, how to refer).

Fourth, make the referral and consult process as easy as possible. Make sure the process is as streamlined as possible. Remember to ALWAYS send a letter to the referring doctor to close the loop. It usually takes 3 min in EPIC or Cerner. When interacting to a patient's other providers in the organization, engage in conversations about prognosis – make sure you obtain permission to discuss prognosis from the involved surgeon or oncologist, as well as the patient.

Fifth, consider with whom to partner. Existing inpatient programs may be convinced to enhance outpatient palliative care programs through the consideration that they help to prevent overutilization of the costliest health care services, which typically get provided at end-of-life. These programs also help to prevent readmissions and 30-day mortality admissions, which many hospitals in the USA and elsewhere are penalized for in-payment models. The business case is often the easiest to make! Other potential partners include: local meals on wheels program, hospital bed supplier, and personal support worker (i.e., home health aides, community health worker) agencies.

Sixth, make sure your own team is interdisciplinary as that is where much of the evidence of beneficial impact lies, not with individual palliative care providers (Ferrell et al. 2016). At the team level, give team members feedback and performance reviews based on evidence like

Fig. 3 above; budget time and finances for travel; monitor team burnout; and facilitate team building exercises (e.g., the group at Hopkins has a bi-monthly palliative care movie night. As you see more complex and difficult patients, develop strategies for dealing with complex patients. Some hints include the following (Text Box 1).

Text Box 1: Dealing with Difficult Families or Patients

- Build rapport – ask about joys (e.g., family)
- Address symptoms first – always the easy place to start
- Set expectations
- Figure out their goal
- Involvement with case management, social workers, and other supportive staff
- Notes – show data as to why you are making a recommendation
- Discuss coping strategies
- If family/caregiver is present, ask how they are coping too
- See regularly – monthly
- Email between visits
- Collaborate with specialists about care

Billing, income, and costs are crucial to long-term institutional support. Go after professional fees as appropriate, and in the USA, use the new Advance Care Planning codes which encourage physicians to document and bill for ACP discussions. Remember, though that while savings are system wide and might accrue to the ICUs, neurology, and home care, the costs are localized and usually come from one cost center. Plug in to national/regional groups like Center to Advance Palliative Care (CAPC) for knowledge sharing and collaborations. Use the Center to Advance Palliative Care (CAPC) office and home-based program design toolkits. They provide all the information and tools you need to launch office and home-based palliative care programs.

Bull et al. synthesized and identified five key barriers to outpatient palliative care (Bull et al. 2012). While these five are specific to the USA, many of them translate to other settings.

1. Large scale organizational challenges may hinder services delivery (e.g., differences in provider subspecialization, operational challenges, and lack of sufficient palliative care-trained providers to deliver services).
2. Limited funding to cover the costs of outpatient palliative care. For example, in the USA, Medicare covers palliative care for people with clear terminal diagnoses but not for people with chronic conditions. In Canada, reimbursements for home-based visits do not adequately compensate for the time that providers may spend visiting with patients in their home and travelling to the homes.
3. There is a lack of a gold-standard business model for outpatient palliative care, which means that each organization offering the services must create a business case for senior leadership to justify the incorporation of the program.
4. The fragmentation of care across settings (i.e., from inpatient to outpatient care) can result in difficult coordinating outpatient palliative care post-discharge. Further, as patients with palliative care needs often have multiple providers, it becomes challenges for outpatient palliative care to coordinate services and reduce redundancies with more acute care specialists.
5. There is a shortage of palliative care-trained physicians, nurse practitioners, and other health professionals, which results in few providers able to deliver outpatient or home-based services, let alone inpatient services.

To aid success, consider process changes that can help to reduce financial losses that may impede the success of programs. For example, Bull et al.'s use of Quality Assessment and Performance Improvement Cycles allowed them to identify challenges and inefficiencies in the Four Season's palliative care outpatient programs, develop strategies to overcome various barriers, institute said strategies and ultimately decrease financial losses by 40% (Kamal et al. 2011a, b) (Text Box 2).

Text Box 2: Ways to Improve Efficiency and the Bottom Line

- Do daily or weekly rounds for home-based patients (via teleconference) as needed to trouble-shoot
- Standardize the palliative care visit combining best practice components of care, identified by the National Quality Forum
  - For scheduling, 1 h for new patients, half hour for follow-ups
  - Keep an additional slot open for urgent appointments to avoid emergency rooms visits.
- Standardize data collection using established, validated data collection tools, and regularly aggregate and analyze the data. Bull and colleagues developed the Quality Data Collection Tool (QDACT), in partnership with colleagues at Duke University Medical Center. Use templates, Smart Phrases, and anything else that makes you more efficient.
- Increase referrals to palliative care by reaching out to providers across the health care system and other facilities
- Engage in several initiatives to increase referrals from palliative care to hospice (e.g., using quality metrics to track referrals, educating providers about referral process)
- Mentor providers to hone skills in palliative care delivery
- Introduce incentives to increase provider productivity and satisfaction (e.g., use of a nonfinancial bonus, extra paid time off, for providers who meet performance targets)
- Work to build a culture of accountability with regular performance reviews and sharing of team success
- Increase workforce to reduce provider strain and burnout
- Ensure that coding and billing are accurate by checking the billing, and engaging in education sessions

Text Box 2: Ways to Improve Efficiency and the Bottom Line (continued)

- Ensure that leadership time is best spent, and introduce administrators to perform administrative tasks, so that providers can focus on clinical work
- Clarify job expectations for providers and try to offload some of their non-clinical work to administrative staff

6 Conclusion

Community-based palliative care has become the focus of palliative care's growth and opportunity. Twelve of the largest randomized control trials on palliative care are community-based and result in equal or greater survival, positive satisfaction from patients and caregivers, and equal or less cost. Surprisingly, sometimes the business case is the easiest to make (Cassel et al. 2015). With health care financing that embraces value-based programs such as shared savings, bundled payments, global budget revenues, community-based palliative care shows great promise and may be part of the solution to provide better care for patients at a cost we can afford.

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Serious Illness and Out-of-Pocket Spending

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Yolanda W. H. Penders and Aline de Vleminck

Contents

Abstract

The last years of life are one of the most costly periods in terms of formal healthcare provision, often attributed to a high amount of critical care, hospital admissions, and care home stays. Some of these costs are borne directly by the patient and their family carers: out-of-pocket costs. Out-of-pockets costs include insurance premiums, deductibles, and all costs for services not covered by health insurance or government-funded healthcare. Specifically for the last phase of life, research has

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5_104

focused on insurer costs rather than out-of-pocket costs. The ability to design policy solutions is contingent on understanding the total societal costs, including both formal and out-of-pocket costs. While both the likelihood of out-of-pocket costs and the amount differ across healthcare systems and countries, they can have potentially serious consequences for patients and families, from refusing treatment to bankruptcy.

In this chapter, we discuss the distribution of costs in different health care systems and how different types of health care systems can have an effect on out-of-pocket costs. Next, we discuss how certain diseases (such as cancer or Alzheimer's disease) or vulnerable groups (people with a low income) may be particularly associated with higher out-of-pocket costs. Last, we review the impact of palliative care on out-of-pocket costs. We show how specialized palliative care can have a positive but limited impact on out-of-pocket costs and cannot on its own alleviate all out-of-pocket costs associated with serious illness.

1 Introduction

Being ill can be expensive. Even in systems where healthcare is accessible to and affordable for all, the consequences of serious illness can have far-reaching financial implications. In this chapter, we will examine the out-of-pocket costs that people with a serious illness or in the last phase of life may expect; how these costs are related to health care system and diagnosis; what the impact of these costs is on patients and families; and how specialized palliative care and the aging population may impact out-of-pocket costs.

2 What Are the Costs Associated with Serious Illness?

When considering the costs of healthcare, our first thought is often the direct costs of care: costs of treatment and medication, devices and supports such as wheelchairs, labor costs of healthcare professionals, and care in an institutional setting such as a nursing home. Serious illness, whether it is chronic or acute, often requires a great deal of care throughout the disease trajectory and particularly in the last phase of life. Indeed, much of the high cost of end-of-life care lies in the high amount of critical care, hospital admissions, and stays in a long-term care facility that people at the end of life require (Emanuel et al. 2002; Polder et al. 2006; Fassbender et al. 2009; Langton et al. 2014).

Beyond these direct costs of care, however, is a layer of secondary costs not quite so visible: opportunity costs in the healthcare system – the time and money spent on one patient cannot be spent on another – as well as lost income and economic activity on the part of the patient. There is also an impact on informal carers, whose caregiving activities are unpaid labor for the benefit of the patient. Informal carers may lose part of their income as a result of both the expenses of caring for the patient and time off from work that may be required. Caregivers also may be in more need of physical or mental healthcare themselves as a result of their caregiving activity. Finally, there are funeral costs that occur after death, as well as potential continued costs for next of kin associated with complex grief.

Thus, total costs can be divided into costs borne by the government or health insurance companies, so-called formal costs, and costs borne directly by the patient and their family carers that are not reimbursed through health insurance, so-called out-of-pocket costs. Out-of-pocket costs include insurance premiums, deductibles, plus all costs for services not covered by health insurance or government-funded healthcare – including many of the indirect costs mentioned above. Taken together, the sum total of all costs associated with serious illness and end-of-life care is referred to as the societal costs. Depending on the healthcare system and personal situation of the patient, out-of-pocket costs can be negligible or a reason for financial ruin. The financial burden of terminal illness can in this way contribute to the stress and psychological burden of patients and their families.

Given the complexity of the costs associated with terminal illness and end-of-life care,

quantifying these costs is not an easy task. Most research in this area focuses on formal costs, which are easier to measure through governmental and insurance records. It is this type of study that is often cited to support claims that palliative care can be more cost-effective than regular care. The impact of palliative care on out-of-pocket cost can often only be determined indirectly. A 2014 systematic review found that the main focus of studies investigating the costs of palliative care was on formal or direct costs, with little focus on informal or out-of-pocket costs (Smith et al. 2014).

3 Distribution of Costs in Different Healthcare Systems

It is practically impossible to compare the proportion of formal coverage and out-of-pocket spending between healthcare systems in a straightforward manner. Apart from the complexity of measuring costs of care mentioned previously, such a comparison must also take into account things like insurance premiums and means-tested pricing or reimbursement schemes. However, there are certain patterns distinguishable in costs based on the type of healthcare system used in different countries. A classic division of healthcare systems is in the following four groups:

3.1 Beveridge Model

In countries employing the Beveridge model of healthcare, so named after William Beveridge who designed Britain's National Health Service, all healthcare is provided and financed by the government without out-of-pocket payments. This system may also be called a "single payer national health service model" (not to be confused with national health insurance/single payer models, where all residents of a country have mandatory health insurance). Examples of such countries are the United Kingdom and Denmark. People living in a country that employs the Beveridge model never pay out-of-pocket for care, unless they choose private treatment that is not covered by the government (e.g., elective plastic surgery or alternative medicine). Whereas costs to patients are minimized, in actual practice, patients in countries employing the Beveridge model often experience long wait times for medical services as budgeted resources rarely meet the population's actual needs. For example, in the UK, while the NHS has established a general maximum waiting time of 18 weeks for a nonurgent referral, this target had not been met since 2016 (Care Quality Commission 2018). In addition, the indirect costs of care, such as loss of income by the patient and informal carers, are not necessarily covered in such a system.

3.2 The Bismarck Model

The Bismarck model, named after Prussian chancellor Otto von Bismarck, is based on three principles: (1) The government is responsible for universal access to healthcare, (2) health policy is implemented by the smallest political and administrative units in society, and (3) elected officials negotiate the terms of medical care and reflect the interest of different medical professions. Health insurance in a Bismarck model is financed through payroll taxes and all residents are required to have health insurance. Insurance providers cannot refuse clients. This system may also be called a "nonprofit sickness fund" system or a "social insurance model." Examples of such countries are Germany, Switzerland, and Japan. While clinics and hospitals in the Bismarck model may be private and for-profit, the government enforces strict financial control, reducing the costs per capita.

3.3 The National Health Insurance/ Single Payer Model

In countries that use a single payer model, medical care is privately run but paid for by a government-run insurance program that all residents pay into. Examples of such countries are Canada and South Korea. The NHI system can be seen as a combination of the Beveridge (because government-paid) and Bismarck (because privately run) models. The government can decide which treatments and

forms of care they will pay for. Like the Beveridge model, a downside of this system is the potentially long waiting lists.

3.4 Out-of-Pocket Model

In some countries, there is no formal healthcare system. All healthcare is paid for by the patients, sometimes with intervention from nongovernmental organizations, and no systematic insurance or reimbursement scheme exists. This system may also be called a "market-driven system." Many low-income countries fall in this category. In such countries, all costs are carried by the patient and care can quickly become unaffordable. People may not seek medical attention until very late in the disease trajectory, at which point curative or life-prolonging treatments may no longer be an option and intensive care is needed. Care for the dying outside the formal healthcare system may be dependent largely on next-of-kin or religious or charity organizations.

3.5 Other

Finally, there are countries that use none of these healthcare systems, while other countries use a combination of systems. The United States of America, one of the most expensive healthcare system in the world costing more than 17% of GDP, employs a combination of all four models for different groups of the population (Institute of Medicine and National Research Council 2013). Another example of a healthcare system that is not easily classified is the Russian system, which is an NHS system on paper (i.e., free to all), but also requires compulsory medical insurance, and there is open and sometimes hostile competition between state-run and private healthcare services.

An overview of the impact of each system on out-of-pocket costs is given in Table 1.

From this classification, it would appear obvious that out-of-pocket costs are higher in some models than in other – with the Beveridge model at the bottom and the pure out-of-pocket system at the top. While this general hierarchy holds, even in a Beveridge model out-of-pocket costs can be a reality. Data from the World Health Organization Global Health Expenditure Database showed that in 2015, household out-of-pocket payments for healthcare were US$644 per capita in the UK. This is the average and does not reflect only those patients with a serious illness or in the last phase of life. A system which relies strongly on out-of-pocket costs runs the risk of catastrophic health expenditure in a large number of households, meaning that the financial situation in these households is one serious illness away from financial ruin (McIntyre et al. 2006). Apart from making healthcare inaccessible to a segment of the population, this causes financial insecurity among people at risk for serious illnesses and generally does not have a good impact on the economy (Xu et al. 2003).

The above classification is much-used and widely known, but it does not provide full information on the organization of a healthcare system nor on the financial burden to patients. The amount of out-of-pocket costs is not necessarily equal in countries that employ the same healthcare system. Furthermore, such general information does not necessarily tell us about the costs associated with serious illness or care in the last phase of life, which may include types of care that are less likely to be reimbursed such as specialist palliative care and care in long-term care facilities. Additionally, health insurance premiums may be higher in some countries than in others, which in itself is a type of out-of-pocket cost.

Additional information relevant to care in the case of serious illness may be found in other classifications. One such classification is the ANCIEN typology of long-term care developed as part of the ENEPRI project (Kraus et al. 2010). The ENEPRI project classified long-term care systems in European countries using two approaches, one focused on system characteristics and one focused on the use and financing of care. For the latter, they ascertained among other things how much is spent on long-term care, which portion of spending is private, and how much support is available for informal caregivers. This classification therefore takes both formal and out-of-pocket costs into account.

Table 1 Healthcare systems and out-of-pocket costs

System	Exemplary countries	Advantages	Disadvantages	Effect on out-of-pocket costs
Beveridge model	United Kingdom, Denmark, Hong Kong	Accessibility of care for all	Long waiting lists; government decides which treatments should be reimbursed	Low; all or almost all direct and supportive care is free at the point of delivery. Private alternatives that incur costs may exist
Bismarck model	Germany, Japan	Accessibility of care for all; collective negotiating power of government decreases formal costs	Economic incentives may push overtreatment and -medication	Moderate; most care is reimbursed through insurance, but additional expenses may be necessary
National Health Insurance model	Canada, South Korea	Accessibility of care for all; collective negotiating power of government decreases formal costs	Government decides which treatments should be reimbursed	Moderate; most care is reimbursed through insurance, but additional expenses may be necessary
Out-of-pocket model	Kenya, Thailand	Low formal costs	Inaccessibility of care to people of lower socio-economic strata	High; in principle all costs are paid for out-of-pocket
United States model	United States	Advanced equipment and treatment more readily available than in other systems	High insurance premiums; inaccessibility of care to uninsured people; high formal costs	Variable; heavily dependent on type of insurance and insurance provider

1. EU Cluster 1

   In countries in this cluster, many people rely on or expect to rely on formal long-term care in the last phase of life and most long-term care facilities are publicly funded. However, reliance on informal care remains important; for that reason, support for informal caregiving is high. Public spending on long-term care is low. This cluster includes Belgium, Germany, Slovakia, and the Czech Republic.
2. EU Cluster 2

   Systems in this cluster are characterized by high public spending and low private funding. As in cluster 1, many people expect to use formal long-term care at some point. While support for informal caregiving is high in cluster 2 as well, use of informal caregiving is low, possibly due to highly funded and well-developed formal long-term care options. This cluster includes Sweden, the Netherlands, and Denmark and may be termed the "Scandinavian model."
3. EU Cluster 3

   Long-term care systems in this cluster have fewer publicly funded long-term care facilities and formal long-term care is more likely to be privatized. These systems are further characterized by moderate public spending, high private funding, and a moderate use of formal care. Use of informal care is high, as is support for the use of informal care. This cluster includes Finland, France, Austria, England, and Spain.
4. EU Cluster 4

   The differences between clusters 3 and 4 are mainly in the support for informal care, which is low in cluster 4 even though usage of informal care is high. Like cluster 3, long-term care systems in this cluster are characterized by low public spending, high private funding, and low use of formal care. This cluster includes Italy and Hungary.

The impact of these systems on out-of-pocket costs is shown in Table 2. This typology of long-term care systems suggests that in clusters 3 and 4, out-of-pocket spending for long-term care will be higher as there are few publicly funded options. This may be problematic in particular for countries in cluster 4, where informal care alternatives are also badly supported. Note, however, that a use of formal over informal care is not in itself

Table 2 Long-term care typologies from the EU project ANCIEN and out-of-pocket costs

System	Exemplary countries	Advantages	Disadvantages	Effect on out-of-pocket costs
Cluster 1: High use of formal care, low spending	Belgium, Germany	Strong support for informal care	Low support for formal long-term care; strong reliance on informal care	Moderate; high out-of-pocket spending for formal long-term care, but good support for informal care
Cluster 2: High use of formal care, high spending	Sweden, the Netherlands	Strong support for both formal and informal long-term care	High formal costs	Low; public funding for formal long-term care is high and use of informal care is low
Cluster 3: Moderate use of formal care, moderate spending	Finland, Austria	Strong support for informal care; long-term care is often privatized	High out-of-pocket costs for formal long-term care; strong reliance on informal care	Moderate; high out-of-pocket spending for privatized formal care, but good support for informal care
Cluster 4: Low use of formal care, low spending	Italy, Hungary	Long-term care is often centered in the community; low formal costs	Little support for informal care, even though reliance on informal care is strong	High; out-of-pocket costs for formal long-term care are high and support for informal care low

problematic, as long as adequate support – both financial and psychological – is available for informal carers. Preferences for formal or informal care differ per country and should not be taken as absolutes (European Commission 2007).

Neither the overall healthcare system classification nor the EU ANCIEN typology of long-term care can explain all differences between countries in out-of-pocket costs for care in the context of serious illness or the last phase of life. One study that did investigate out-of-pocket costs in the last year of life in 13 European countries found substantial differences in the percentage of people who had any out-of-pocket costs for care (between 26% of decedents in Spain and 96% in Sweden), the amount these people had to pay on average (between 2% (Netherlands) and 25% (Czech Republic) of median household income), and the relative contribution of different types of healthcare to out-of-pocket costs (Penders et al. 2017). These differences did not conform to any recognizable typology of healthcare systems, but were likely a result of a combination of factors. Nevertheless, healthcare system characteristics can help us to make general predictions about the likelihood of high or low out-of-pocket costs for care.

There is currently no clear picture on how formal costs and out-of-pocket costs relate to each other in most healthcare systems. Most studies investigate either one or the other; a cursory review of the literature turned up only one study investigating both (Kotlarz et al. 2009). There are two intuitive answers regarding the relation between out-of-pocket costs and insurer costs. The first is that particular aspects of healthcare, for example, medication, that have low out-of-pocket costs must therefore have (relatively) high insurer costs and vice versa. The second is that low out-of-pocket costs are related to low insurer costs and high out-of-pocket costs are linked to high insurer costs, because some types of care are just expensive and the burden is shared. Neither view is currently supported by evidence, except for the aforementioned study which showed that for certain chronic illnesses, such as osteoarthritis, both out-of-pocket and insurer costs are high.

4 Differences in Out-of-Pocket Costs Between Diagnoses

Regardless of which proportion of costs is paid out of pocket, a person's diagnosis can influence the costs they can be expected to have at the end of life. Certain serious illnesses may require more care than others or have more treatment options available. For example, a person with dementia is

more likely to require care in a long-term care facility, whereas a person with cancer is more likely to require expensive treatments. Also, depending on the healthcare system, certain types of care required for different illnesses may be more or less expensive.

Two diagnoses with particularly high out-of-pocket costs across the board are cancer and dementia, though for different reasons. Research has found that the biggest contribution to care of cancer patients in the last 6 months of life were hospital stays (up to an average of US$20,559 in the last month of life) and hospice use, which accounted for 36% of costs in the last month of life (Chastek et al. 2012). Within people with cancer in the USA, those who use chemotherapy have a more than 50% increase in out-of-pocket costs for care, and even more if they used chemotherapy in the last 30 days of life (Bao et al. 2017). Even among insured Americans, almost half reported significant or catastrophic (subjective) financial burden and even more reduced spending on food and clothing to pay for treatment (Zafar et al. 2013). The informal caregivers of people with cancer can also expect significant costs, both in terms of money and time: a study in Ireland found that the approximate average out-of-pocket costs for informal carers of people with colorectal cancer was €4476 (including travel), on top of €25,365 of time costs, i.e., the worth of the hours spent on caregiving tasks if the carers were paid the average hourly wage in Ireland (Hanly et al. 2013). As the estimated survival time for many forms of cancer goes up, cancer is becoming more of a chronic illness in some cases, with all the additional costs this implies: more months of medication costs, longer periods of time spent on informal caregiving, and a higher chance for informal caregivers to drop out of the labor market.

For people with dementia, research in the USA showed that while their formal expenditures over the last 5 years of life were the same as for people without dementia, the average societal costs were more than $100,000 higher for those with dementia than those who died of cancer, with out-of-pocket spending for people with dementia representing 32% of wealth measured 5 years before death compared with 11% for people without dementia (Kelley et al. 2015). Meanwhile in Europe, secondary and institutional care – including care by specialist physicians, hospital care, care in a long-term care facility and hospice care – were shown to be the largest contributors to out-of-pocket costs in nine out of 13 countries studied, constituting up to 76% of out-of-pocket costs in the last year of life (Penders et al. 2017). This was primarily attributable to care in long-term care facilities, and having difficulties with activities of daily life (independently of being chronically ill), two things people with dementia in particular may be confronted with. Especially in countries in ANCIEN clusters 3 and 4, stays in long-term care facilities may be extremely burdensome.

This is not to say that other diagnoses are necessarily cheap, especially in different healthcare contexts. In China, although the government has a policy to provide free healthcare to people with tuberculosis, the average out-of-pocket cost for tuberculosis was 11% of the median annual household income (Pan et al. 2013). In India, the out-of-pocket costs for kidney transplantations start at 386% of median household income and rise to 634%, essentially making treatment for kidney failure inaccessible to the majority of the population (Ramachandran and Jha 2013). On the other hand, advanced cancer treatments may be less available in these countries, so the costs of cancer may be relatively low compared to the USA. In countries with a lower average life expectancy (e.g., 68 years in India vs. 81 in the EU-28), a dementia trajectory or chronic illness trajectory may be considerably shorter and the total out-of-pocket costs therefore lower. Which disease groups or population groups are at risk for higher out-of-pocket costs therefore depends on both the treatment options and availability of care, burden of illness, and healthcare context.

5 The Impact of Out-of-Pocket Costs on Patients, Families, and Quality of Life

A study in 13 European countries showed that out-of-pocket costs in the last year of life have been found to be up to a quarter of median

household income (Penders et al. 2017). And in countries with a pure out-of-pocket system, any serious illness carries with it the risk of financial ruin. High out-of-pocket costs, the full extent of which is often only known after death, can put patients and families for impossible choices: do we start or continue this treatment or not? Patients, but especially next-of-kin may be willing to spend "whatever it takes" on prolonging the life of their relative, to their own detriment and often without a clear view of what the benefits of certain treatments are – or indeed, if there realistically are any benefit. However, especially for chronic treatments – for instance, certain medication – the financial burden will eventually catch up. Higher out-of-pocket spending has been associated with non-adherence to treatments and higher rates of therapy discontinuation in the USA and elsewhere (Hennessy et al. 2016; Dusetzina et al. 2014). Older people in particular are vulnerable to negative effects of high out-of-pocket costs and sometimes cite high costs as a reason not to initiate or adhere to treatment or care, potentially decreasing quality of life in the final stage of life (Soumerai et al. 2006; Chao et al. 2008; Neugut et al. 2011). Older people often do not want to feel like they are a burden on their family, and high out-of-pocket costs may be one way they perceive this burden.

The financial burden of care can indeed weigh heavily on the shoulders of family carers: Hudson (2003), for example, reported that a quarter of his sample of family carers had stopped work or taken part-time work in order to care for dying family members at home. Soothill et al. (2003) in their survey of 200 carers noted that 44% retired to care for dying family members. This can reduce the capacity of households to deal with financial costs associated with long-term care. A study conducted in Italy found that a one-fourth of families of cancer patients have to use all their savings to pay for care at the end of life and around 45% have difficulties in managing their regular employment (Rossi et al. 2007).

Financial stress and a low income level are linked to a higher perceived burden and a more frequent exhibition of depressive symptoms amongst informal carers (Papastavrou et al. 2007; Andrén and Elmståhl 2007). Since most older people do not want to be a burden on their family, this may further dissuade them from engaging useful but expensive healthcare. Informal caregivers participate less in the labor market as a direct consequence of their caregiving activities, but also experience more physical problems and psychological distress. A meta-analysis of 176 studies found that caregiver depressive symptoms were associated with more physical health problems (Pinquart and Sörensen 2007). A study among female caregiving and noncaregiving twins found that caregiving was associated with lower mental health functioning, higher anxiety, higher perceived stress, and higher levels of depression and suggested that while both common genes and environment contributed to vulnerability to stress and consequently informal caregivers' functioning, caregiving lead to psychological distress even for those who were not particularly vulnerable to stress (Vitaliano et al. 2014). Another study found that up to 62% of family caregivers experience a high level of psychological distress, compared to 19% in the general population (Dumont et al. 2006).

There is also a disproportionate impact of out-of-pocket costs on people from lower socio-economic strata. Many people do not have the amount of savings recommended by financial advice bureaus, and these are mostly people from lower socio-economic strata. A bill of a few hundred dollars or euros can be disastrous for them where it would be inconvenient for most. Studies have shown that there are many differences in the use of healthcare by people from different socio-economic strata, as well as their health outcomes. For example, people from lower socio-economic strata are less likely to seek healthcare and may have less access to certain healthcare services (even with insurance) (Adamson et al. 2003; Allin et al. 2009). Additionally, there are gender disparities in the impact of out-of-pocket costs. Research has shown that most informal caregivers are women and that informal caregiving decreased women's participation in the labor market

(Viitanen 2005). As women may be relatively economically disadvantaged compared to men, their dropping out of the labor market can be particularly harmful.

In some cases, the financial burden of end-of-life care can be extremely high. The USA is a strong outlier in this respect, as a Western country where out-of-pocket costs make up a substantial proportion of healthcare costs. Studies have shown that in the USA, medical debts are the main reason for an increasing number of bankruptcies, up to 62% in 2007 (Himmelstein et al. 2009; Himmelstein et al. 2005). This does not just mean that families are left destitute: patients with cancer who filed for bankruptcy had almost twice as much risk of mortality as those who did not (Ramsey et al. 2016). The introduction of the Patient Protection and Affordable Care Act (ACA) in 2010 introduced out-of-pocket maximums, and the 2016 maximum was still a problematic 22% of the median annual personal income in the USA. This is still an improvement over the previous situation. Before the ACA, the average out-of-pocket expenditures for Medicare beneficiaries in the last 5 years of life exceeded total household assets for a quarter of decedents who were not survived by a spouse, and nonhousing assets for an additional 43% (Kelley et al. 2013). For those who were survived by a spouse, these figures were 10% and 24%, respectively, essentially leaving the widow or widower penniless. There are indications that the ACA has improved access and reduced financial burden for many patients, but it is not yet known how the situation will develop in the coming years (Dixon et al. 2017; Mahendraratnam et al. 2017).

Good support for family carers may partly alleviate the financial burden of care. Several countries, such as Belgium, France, and Germany, have policy measures in place that allow family carers to adapt their working patterns or take a leave of absence while retaining their employee rights (Maetens et al. 2017). While such regulations provide stability, financial compensation for informal caregiving occurs only in a limited number of countries.

6 The Impact of Specialist Palliative Care on Out-of-Pocket Costs

Many studies attempt to show that palliative care is cost effective, that is, not more expensive than regular (curative or life-prolonging) care. However, most evidence focusses only on formal costs and outcomes vary due to the diverse nature of palliative care initiatives. In a systematic review, it was found that specialist palliative care is most frequently found to be less costly relative to comparator groups with the difference being statistically significant in most cases when looking at formal costs (Smith et al. 2014). The same review found that, of the 46 included studies, only one focused on out-of-pocket costs – they found that there was no difference in the out-of-pocket costs of people who used hospice care in the USA and those who did not (Taylor Jr 2009). Another review on home-based palliative care services found that of 23 included studies six reported the cost-effectiveness of the tested programs, but evidence for cost-effectiveness was inconclusive (Gomes et al. 2009). Of these six, only one – a study from 1992 on home-based care for people with AIDS in northern Italy – provided a full economic evaluation using cost-utility ratios (Tramarin et al. 1992). A second study in the UK included both inpatient care and informal care in its cost-effectiveness analysis (Higginson et al. 2009). Both studies showed that home-based palliative care appeared to reduce costs, though the UK study showed no differences in costs to informal caregivers. Studies on the cost-effectiveness of hospital-based palliative care consultations show a fairly consistent impact on costs through lower (re-)hospitalization and intensive care unit admissions, but also do not take out-of-pocket costs into account (May et al. 2014, 2015). Likewise, hospice use in the USA has been shown to be cost-effective in terms of Medicare costs, but out-of-pocket costs were not studied (Kelley et al. 2013).

It is clear that although palliative care is less expensive than regular care in terms of formal costs, the impact on out-of-pocket costs is not

studied sufficiently. Often out-of-pocket costs are not measured directly in costs research, though a few studies do exist. A Canadian study looked at the various costs incurred in the last year of life of patients who received care from a multidisciplinary, home-based palliative care team. They found that while out-of-pocket expenditures in the last 12 months of life (in a single payer healthcare system) were only CA$379, the costs of formal care – the care provided by the home-care team as well as all other publicly funded medical costs – were almost 10 times as high. However, this was dwarfed by the unpaid caregiving costs – that is, the time dedicated to caregiving activities by families and friends, assigned a monetary value – which were more than CA$11,000 per month (Chai et al. 2014). With rising care needs as death approached, so did the monthly costs, with total costs in the last month of life averaging more than CA$30,000. Another study of the same palliative care service found that the societal costs were more than CA$34,000 per patient over the palliative trajectory (an average of 4 months).

What we can surmise from the available evidence is that while specialist palliative care can decrease out-of-pocket costs at the end of life, this is in no way guaranteed, and cost-effectiveness in terms of formal costs does not necessarily translate to a decrease in out-of-pocket costs. There are multiple reasons for this:

- Palliative care is often only available in the last phase of life, whereas out-of-pocket costs associated with serious illness are likely to occur earlier in the disease trajectory as well.
- Palliative care is often set up as an alternative to potentially overly aggressive hospital care or life-prolonging treatment. Its aim in these cases is not to provide support *in addition* to standard care.
- Many specialist palliative care initiatives are not community based and are thus not able to provide the type of support that is most likely to have an impact on the financial aspects of care.
- Palliative care often does not provide adequate support for family carers, both during the last phase of life and after death.
- The presence or absence of palliative care is unlikely to have an impact on certain parts of out-of-pocket costs no matter the way it is delivered, such as the missed labor market participation of both patient and family during the last phase of life.

While some of these reasons can be addressed – such as earlier initiation of specialist palliative care or better emotional support for family carers – others are almost impossible to change. It may therefore be wrong to assume that palliative care *should* have a large impact on out-of-pocket costs. However, full economic evaluations of specialist palliative care initiatives would do well to take the impact on informal and out-of-pocket costs into account.

7 Implications of Out-of-Pocket Costs for the Growing Population of Older People

Across the world, populations are aging. While many older people are able to maintain a good degree of independence, social engagement, and continued physical health, many do not – one study in the USA estimated that as few as 12% of people aged 65 and over achieve this ideal of "successful aging" (McLaughlin et al. 2010). Older people are likely to have severe or catastrophic disabilities and are at a higher risk of illnesses such as cancer and cardiovascular disease, and older people with dementia are likely to end up living and eventually dying in long-term care facilities (Reyniers et al. 2015; Gill et al. 2010). As such, an increase in the proportion of older people will have an impact on all aspects of healthcare, including chronic and long-term care, institutionalized care, and specialized end-of-life care.

First, as medical advances are made and life-prolonging treatments become more effective, certain types of care, like care for some forms of cancer, will become chronic care. Care will be provided for longer to patients with care needs that will increase, either steadily or in jolts, as time goes on. This will drive up the costs of both formal and informal care. It is unlikely in these

cases that patients will be able to reliably provide income through work, so sustained medical costs may impose a significant financial burden if not adequately compensated. Long-term caregiving may also be especially burdensome for informal carers, both physically and psychologically. Informal caregiving over a number of years may also put informal carers at higher risk of losing their job than caregiving over a shorter period of time.

Second, an aging population puts more pressure on the long-term care system, whether that is based mostly on formal or informal care. The home setting is the preferred place of care of many older people (Wiles et al. 2011; Gott et al. 2004). Governments, healthcare organizations, and next-of-kin generally want to enable people to live at home for as long as possible. Even as demand rises, the number of beds in long-term care facilities in some countries has decreased (European Commission 2007). This means that an increasing number of older people living at home will have dementia, difficulties with multiple activities of daily living, and multimorbidity and that a larger number of informal caregivers will be affected. This will affect the presumed cost-effectiveness of encouraging people to stay at home longer: while care in a care home is expensive, it does not follow that home care is "cheap." People with difficulties with more than two activities of daily living are at risk for higher out-of-pocket costs (Penders et al. 2017), and chronically ill people and those with multimorbidities use a large portion of healthcare, financially speaking, regardless of setting (Aldridge and Kelley 2015). Older people living at home are also more likely to be hospitalized than older people living in a long-term care facility, which increases care costs. A study in the Netherlands found that the average societal costs of healthcare for hospitalized older people were €30,000 per year, with almost one third of that being informal healthcare costs between hospital discharge and 12-month follow-up (Asmus-Szepesi et al. 2014). Particularly older patients with a high risk score at the time of hospital admission (i.e., those who were most frail and had most physical and mental limitations) were likely to incur high costs, with informal care costs almost twice as high as the lowest risk group and formal costs (excluding the original hospitalization) more than twice as high. Furthermore, a prospective cohort study in the Netherlands found that when a person with dementia was admitted to a long-term care facility during the course of the study, the psychological distress of informal caregivers improved (Borsje et al. 2016). By promoting informal care in the home setting as an alternative for long-term care facilities, a larger number of informal carers is at risk of physical and psychological health issues. These issues may contribute to decreased labor market participation and loss of income and may place an additional burden on the healthcare system.

Not only are care homes one of the, if not the, most expensive types of care for care receivers in European countries; they are also the type of care that it is most likely people have to pay out-of-pocket for. This is a worrying combination. As the population of Europe ages, more older people will spend their final phase of life in a care or nursing home (Houttekier et al. 2011; Gomes and Higginson 2008). Private funding of long-term care facilities is usually unaffordable for residents, with average long-term care expenditures accounting for 60% to 80% of disposable income (OECD 2005). Means-tested contributions to long-term care, where those with a higher income or more wealth pay more and those with a lower income are subsidized such as in the Netherlands and the UK, may seem to be a solution to this problem, but in practice has been shown to also have an adverse impact on the accessibility of care for people of a low socioeconomic status (Comas-Herrera et al. 2010). Keeping (or making) care in long-term care facilities affordable for people from all backgrounds and socioeconomic statuses will be necessary to ensure the growing population of older people will be able to access appropriate care.

Unfortunately, the total costs of long-term care facilities and remaining at home are very difficult to compare. A fair comparison should not only include all the costs that were already mentioned in this chapter, but also expenses such as rent and food which are included in a long-term care facility but are always out-of-pocket in the home setting. Without a detailed comparison, it is

unknown if care in a long-term care facility would still be so (relatively) expensive once food, rent, and assorted costs of living are included in the equation. On the other hand, people who move to a long-term care facility are more likely to have a severe care burden, complex multimorbidities, and dementia. If they remain at home instead, additional home care would be required which would drive up the costs of living at home. However, at least one study showed that in most countries, at least half of people who received home care did not have to pay for it out of pocket, suggesting there are systems in place to avoid the financial burden of home care falling solely on the care receivers' shoulders (Penders et al. 2017). If this is the case, policy makers should ensure these systems are robust enough to also provide for an influx of people with high care burden who would otherwise have lived in long-term care facilities.

8 Conclusion and Summary

The costs of end-of-life care are complex and sometimes hard to quantify. Out-of-pocket costs relating to care in the last phase of life affect most patients and their next-of-kin. To determine the burden of out-of-pocket costs on patients and their families in different healthcare systems, both direct and indirect costs must be taken into account. Financial stress can worsen health of both the patient and informal caregivers and in the worst case, can deter patients from seeking adequate and timely medical care. Cost-effectiveness studies of palliative care initiatives should study the total societal costs, including both formal and out-of-pocket costs.

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R. D. MacLeod, L. Van den Block (eds.), *Textbook of Palliative Care*,
https://doi.org/10.1007/978-3-319-77740-5

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