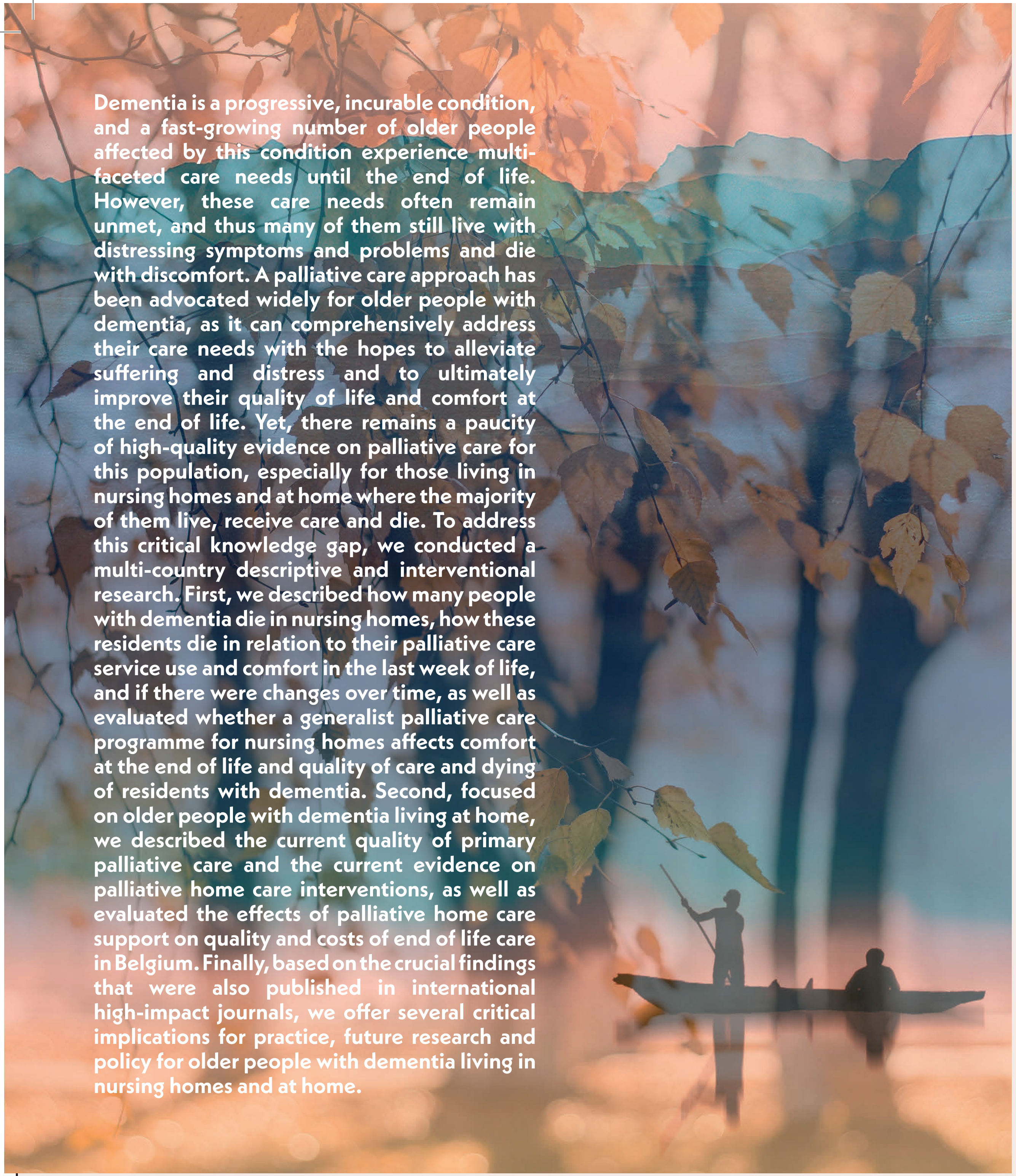

Dementia is a progressive, incurable condition, and a fast-growing number of older people affected by this condition experience multi-faceted care needs until the end of life. However, these care needs often remain unmet, and thus many of them still live with distressing symptoms and problems and die with discomfort. A palliative care approach has been advocated widely for older people with dementia, as it can comprehensively address their care needs with the hopes to alleviate suffering and distress and to ultimately improve their quality of life and comfort at the end of life. Yet, there remains a paucity of high-quality evidence on palliative care for this population, especially for those living in nursing homes and at home where the majority of them live, receive care and die. To address this critical knowledge gap, we conducted a multi-country descriptive and interventional research. First, we described how many people with dementia die in nursing homes, how these residents die in relation to their palliative care service use and comfort in the last week of life, and if there were changes over time, as well as evaluated whether a generalist palliative care programme for nursing homes affects comfort at the end of life and quality of care and dying of residents with dementia. Second, focused on older people with dementia living at home, we described the current quality of primary palliative care and the current evidence on palliative home care interventions, as well as evaluated the effects of palliative home care support on quality and costs of end of life care in Belgium. Finally, based on the crucial findings that were also published in international high-impact journals, we offer several critical implications for practice, future research and policy for older people with dementia living in nursing homes and at home.

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PALLIATIVE CARE FOR OLDER PEOPLE WITH DEMENTIA IN NURSING HOMES AND AT HOME: MULTI-COUNTRY DESCRIPTIVE AND INTERVENTIONAL RESEARCH

Rose Miranda

Dissertation submitted in the fulfilment of the requirements for the degree of
Doctor of Philosophy (PhD) in Social Health Science

1 September 2021

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Faculty of Medicine and Pharmacy, Vrije Universiteit Brussel

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Supervisor

Prof. Dr. Lieve Van den Block
Vrije Universiteit Brussel (VUB), Belgium
End of Life Care Research Group
Department of Family Medicine and Chronic Care

Co-supervisors

Prof. Dr. Tinne Smets
Vrije Universiteit Brussel (VUB), Belgium
End of Life Care Research Group
Department of Family Medicine and Chronic Care

Prof. Dr. Nele Van Den Noortgate
Ghent University Hospital, Belgium
Department of Geriatric Medicine

Examination committee

Prof. Dr. Kenneth Chambaere (Chair)
Vrije Universiteit Brussel (VUB), Belgium
End of Life Care Research Group
Department of Family Medicine and Chronic Care
University of Ghent (UGent), Belgium
Faculty of Medicine and Health Sciences
Department of Public Health and Primary Care

Prof. Dr. Sebastiaan Engelborghs
Vrije Universiteit Brussel (VUB), Belgium
Center for Neurosciences (C4N)
University Hospital Brussels, Belgium
Department of Neurology

Prof. Dr. Emily Verté
Vrije Universiteit Brussel (VUB), Belgium
Department of Family Medicine and Chronic Care

Prof. Dr. Frans Verhey
Maastricht University, Maastricht, Netherlands
Department of Psychiatry and Neuropsychology
School for Mental Health and Neuroscience
Alzheimer Center Limburg

Dr. Mudr. Iva Holmerova
Charles University, Prague, Czech Republic
Centre of Expertise in Longevity and Long-term (CELLO)
Faculty of Humanities

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Palliative care for older people with dementia in nursing homes and at home: multi-country descriptive and interventional research

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General Introduction

Introduction

Why do we need more research on palliative care for older people with dementia?

Dementia is recognised as a progressive, incurable condition, and a fast-growing number of older people affected by this condition experience multi-faceted physical, psychosocial and spiritual care needs that persist for months or years until death.(1–7) To date, there were consistent reports that the care needs of older people with dementia often remain unmet, and thus many of them still live with distressing symptoms and problems and die with discomfort.(2,8–12) Dementia is also the condition with the highest projected proportional increase in serious health-related suffering between 2016 and 2060.(13) Living and dying with dementia therefore significantly and primarily affects older people with dementia and their families, including those people close to them. Further, because providing care to older people with dementia is a highly demanding and complex work, dementia also affects family carers, healthcare professionals, communities, healthcare systems and societies worldwide.(1,2,4) Dementia also has far-reaching ramifications to economies in terms of direct medical, social and informal care costs.(1,2,14) In 2015, the global cost of dementia was estimated at about US$818 billion, and the highest economic burden was incurred in high-income countries, such as the countries in Europe, North America and Australia.(2)

While pharmacological development for dementia is ongoing, the reality is that it will take some time before treatments to prevent or alter the course of dementia are available.(15) Until such pharmacological breakthroughs are made, dementia will remain to constitute an increasing global health challenge to individuals with dementia, families, communities, healthcare systems, societies and economies now and in the foreseeable future. Due to the incurable nature of dementia combined with the associated multi-faceted care needs, a palliative care approach has been advocated widely for older people with dementia. Palliative care can comprehensively address their care needs with the hopes to alleviate suffering and distress and to ultimately improve their quality of life and comfort at the end of life.(16–18) Such a comprehensive care approach focused on quality of life and comfort is vital, because the care needs of people with dementia occur frequently, may be interrelated or expressed differently (e.g. when pain is expressed as aggression).(16,19) Yet, there remains a paucity of high-quality evidence on palliative care in dementia.(20,21) The global health challenge posed by dementia therefore underscores an urgent need to better understand and improve the current state of palliative care for older people living and dying with this condition.(18,22)

In this section of the dissertation, I will first discuss the background and context concerning the growing number of older people with dementia and their complex care needs. Second, I will explain the applicability of palliative care for this population, especially for those living in nursing homes and at home. Third, I will elucidate scientific evidences in palliative care for older people with dementia living and dying in these care settings particularly in high-income countries, while highlighting those areas where we still lack sufficient knowledge. Finally, I will describe the research aims and questions, as well as the multiple research methods used in my PhD research.

1.1. The ageing population

The world's populations continue to age.(23) This ageing population, as observed in all Western countries, is largely attributable to the demographic shift, resulting from the persistent plunge in fertility and mortality rates. Fewer births meant that the share of young people in the total population has gradually weakened, resulting in the natural growth in the share of older people. This is known as the ageing from the bottom, in reference to the shrinking of the bottom of the population pyramid. Concurrently since the 19th century, life expectancy at birth has increased, which explains the reduction in the mortality rate for all ages. This change has resulted in a phenomenon of ageing from the top, with a growing number of people surviving to old age.(24,25)

Worldwide, there were 703 million people aged 65 years and over in 2019. This number is projected to double to 1.5 billion by 2050. Between 1990 and 2019, the share of population aged 65 years and over increased from 6 to 9%. This proportion is projected to increase further to 16% by 2050, so that one in six people will be 65 years or older.(24) Similarly in the EU-27 (European Union-27) countries, the number of people aged 65 years and over will rise from 90.5 million in 2019 to 129.8 million by 2050. Projections also foresee a particularly rapid increase in the number and share of the "oldest old" (aged 80 years and over) in the population. Between 2019 and 2050, the number of the oldest old people in EU-27 is projected to more than double, from 12.5 million in 2019 to 26.8 million by 2050.(24–26)

1.2. The growing number of older people living and dying with dementia

Old age is the strongest known risk factor for dementia.(27–29) Although at least 1 in 20 people with dementia developed the condition under the age of 65, the chances of developing dementia increase significantly as a person gets older. From 65 years old onwards, a person's risk of developing dementia doubles roughly every five years. Estimates suggest that at a given time, between 5 and 8% of the general population aged 60 and over have dementia. In the United Kingdom, it was estimated that dementia affects one in 14 people over 65 years and one in six over 80 years.(30,31) In Australia, almost one in 10 people over 65 years and three in 10 people over the age of 85 have dementia.(32)

Considering the ageing population and the current lack of preventive and curative treatment for dementia, dementia has become ever more conspicuous given the growing number of older people affected by this condition, which has been estimated to grow rapidly over the next decades.(3,4,31) In 2015, it was estimated that globally, over 46 million people have dementia. By 2050, this prevalence of dementia has been projected to almost triple to about 131.5 million.(4) In Europe, the prevalence of dementia has been projected to double to about 18.8 million by 2050.(31) Dementia is also one of the most common causes of death worldwide.(33) For the first time in 2016, the global health estimates of the World Health Organisation (WHO) listed Alzheimer's disease and other dementia types in the top 10 causes of death (by number of deaths). By 2050, it has been projected that a third of people aged 65 years and over will die with dementia.(34) Across the vast majority of EU-27 countries, dementia is the most common cause of mental, behavioural and neurological disorders that were equivalent to about 3.7% of all deaths in 2016.(33) Dementia is also one of the major causes of disability and dependency among older people, primarily due to its complex disease trajectory and symptoms.(4)

1.3. The symptoms, disease trajectory and clinical course of dementia

Dementia is an overall term for a variety of diseases and injuries that primarily or secondarily affect the brain. The most common type of dementia is Alzheimer's disease, which contributes to about 60 to 70% of cases. Other types of dementia include vascular dementia, Lewy body disease, frontotemporal lobar degeneration, Parkinson's disease, hippocampal sclerosis and mixed pathologies.(35) Because dementia affects the brain, this condition is characterised by deterioration in cognitive function beyond what might be expected from normal ageing. It affects memory, thinking, orientation, comprehension, calculation, learning capacity, language, judgment and decisional capacity. Consciousness is not affected, but the cognitive impairment is often accompanied by functional impairment in terms of their ability to perform activities of daily living, and occasionally preceded by deterioration in emotional control, social behaviour, or motivation.(36,37) Dementia is also associated with physical frailty and multimorbidity (i.e. simultaneous presence of two or more chronic conditions).(38–40)

Typically, the onset of dementia is gradual, and the progression of functional decline is prolonged and accompanied by unpredictable 'dwindling' punctuated by for example exacerbations of current conditions or occurrence of acute clinical events, defined as any medical conditions that may lead to clinically significant changes in health status – e.g. pneumonia, febrile episodes or intake problems.(5,6) This disease trajectory is in stark contrast to that of people with cancer, who have relatively defined end of life care trajectories with an evident decline in function in the last months or weeks of life.(41)

Generally, the clinical course of dementia is often distinguished into three stages: early-stage or mild dementia, middle-stage or moderate dementia, and late-stage or severe dementia. Mild dementia is often overlooked due to the gradual onset of dementia. Symptoms may include confusion about orientation in time and space, deficits in a number of areas, such as memory and personal care, difficulties in making decisions, and mood swings. For moderate dementia, symptoms become more obvious and restricting. In people with severe dementia, symptoms become worse and communication problems increase. Behavioural disturbances and personality changes may also occur, such as agitation, aggression, apathy, wandering and disturbed sleep pattern.(42–44)

Nevertheless, the clinical course of dementia varies and depends on patient and environmental characteristics, as well as the specific type of dementia.(21,45–47) Hence, there can be substantial variations in the clinical course of dementia between individuals, in terms of symptoms, survival and life expectancy.(21) For instance, some patients with moderate dementia may experience communication difficulties, while others may still be able to communicate but could show severe behavioural disturbances. Survival of patients with dementia is highly variable between individuals and across studies, with a median survival from diagnosis or study entry between five and nine years.(21) From the first identification of symptoms, their life expectancy varies considerably depending on many factors, such as age or the stage of dementia during diagnosis.(48) Such variations between individual patients with dementia highlight the importance of the person-centred approach in dementia care.(16)

1.4. The different layers of complexity of the care needs of older people with dementia

In reference to the symptoms, disease trajectory and clinical course of dementia, older people with dementia often experience multi-faceted physical, psychosocial and spiritual care needs, of which the level of intensity and complexity increases over time until their death.(5–9) This level of intensity and complexity can be associated with the three stages of dementia. Due to mild symptoms of dementia, older people with mild dementia can still function independently with minimal assistance. They may still be able to perform routine tasks, such as driving, working and participating in favourite activities. Given the worsening symptoms of dementia, people with moderate dementia increasingly need assistance from others to help maintain their function at home and in the community. People with severe dementia become fully dependent on others for care and supervision.(37,47)

Because dementia has been associated with ageing, physical frailty and comorbidity, pain and other physical symptoms have been reported as prevalent in older people with dementia.(5–9) Pain is the most common symptom (52%), followed by agitation and shortness of breath.(49) A recent study suggests that the symptom burden of dementia is at comparable levels to cancer; though pain is significantly more intense among people with cancer.(11,50,51) Psychological and social needs are present in all human beings but are likely to be heightened for older people with dementia, as they become increasingly impaired functionally and cognitively. This increasing impairment make them less likely to be able to take actions to satisfy these needs, which could result in problems, such as social isolation, loneliness and depression.(52,53) Spiritual care needs could arise from the fact that dementia is life-threatening, life-changing and incurable, which could evoke people to question their illness, spirituality and existence, the purpose and meaning of life, and the inevitability of death.(54,55)

In addition to the physical, psychosocial and spiritual care needs of older people with dementia is another layer of complexity posed by the specific disease trajectory and symptoms of dementia, which might impact health service use and provision. For instance, the receipt of a timely diagnosis, which is absent about half of the time, hinders older people with dementia from accessing care and support services.(56) Diagnosing dementia is challenging owing to its prolonged and gradual onset, and symptoms resemble “normal ageing” memory loss, and a wide-range of symptoms, such as difficulty of finding words.(57) With late or no access to care and support services, their symptoms are likely to worsen, and their care needs could become more complex. Further, because of the unpredictable disease trajectory of dementia, symptoms, disability and death might occur at any stage of dementia. In fact, studies suggest that about half of the people with dementia die before they reach the advanced stage.(58) This unpredictability also relates to unexpected exacerbations of current conditions and occurrence of serious clinical events, which may or may not lead to death. Such unpredictability and uncertainty pose additional challenges for clinicians in determining prognosis and in deciding on whether or not the benefits of hospitalisations and certain medical treatments and interventions that are considered aggressive (e.g. parenteral antibiotics, tube feeding or surgery) outweigh the harm.(5,59,60) This puts older people with dementia at risk of receiving burdensome and futile treatments and interventions, potentially-avoidable hospitalisations, and dying in hospitals.(8,49,61–63)

Moreover, behavioural disturbances and personality changes, particularly agitation and aggression, could complicate care provision.(8,9) The cognitive impairment that often results in communication difficulties may leave affected people unable to verbalise their care needs,(8,9) which could also complicate the assessment and management of these needs. Such cognitive impairment may also lead to the lack of decisional capacity, which puts this population at risk of having their views and opinions ignored in care decision making and planning.(64) Because of the increasing cognitive and functional impairment, they can become fully dependent on others for care and supervision, which is an additional challenge for their family carers and health care professionals, as they often need to provide complex care for a prolonged period of time.(65)

Overall, due to the different layers of complexity of these care needs, providing care to older people with dementia is a highly demanding and complex work that requires dementia-specific knowledge and skill sets from family carers and health and social care professionals. The inability to comprehensively address these complex care needs of older people with dementia may precipitate discomfort at the end of life.

1.5. Applicability of palliative care for older people with dementia

A growing body of evidence consistently showed that palliative care could improve the symptom burden and quality of life in adults with incurable conditions.(66–70) The World Health Organisation (WHO) defined palliative care as 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, whether physical, psychosocial or spiritual*".(71) Palliative care encompasses generalist palliative care and specialist palliative care. Generalist palliative care services are provided by healthcare providers with basic palliative care knowledge, competencies and skills, while specialist palliative care is provided by a palliative care-trained multidisciplinary team, services, or clinician. Specialist palliative care is highly applicable in times when the care needs of a person become too complex that generalist palliative care providers could no longer address them alone.(72)

Recognised as a progressive incurable condition associated with multi-faceted physical, psychosocial and spiritual care needs, older people with dementia and their family can benefit from receiving palliative care, as is widely advocated by many international organisations, such as the WHO, the European Association for Palliative Care (EAPC), Alzheimer Europe and Alzheimer Association,(16,22,73–75) as well as in different countries, such as the countries in Europe, North America and Australia.(18,76–78) Although existing literature on palliative care in dementia is not large, in line with the evidence on the benefits of palliative care in general, there is a trend toward the benefits of palliative care for people with dementia across several domains, such as symptom management and emergency room visits.(79) However, there are consistent reports that the care needs of older people with dementia often remain unmet. Hence, many of them still live with distressing symptoms and problems and die with discomfort.(2,8–12) In 2019, it was also projected that between 2016 and 2060, dementia is the condition with the highest proportional increase of 264% in serious health-related suffering. In absolute term, this increase totals to an additional 6 million people who could benefit from receiving palliative care.(13) Given the fast-growing number of older people with dementia and this dire need for addressing their complex care needs, people with dementia forms a very important group, in need of high-quality and cost-effective palliative care today and in the foreseeable future.(80,81)

1.6. Nursing home and home – key settings for improving palliative care in dementia

Over the clinical course of dementia, it is common for older people with dementia to have health care encounters and receive services in a variety of care settings, including nursing home facilities, community home care, hospice facilities, inpatient hospitals, rehabilitation units, behavioural health-focused medical units, and assisted living.

From a public health perspective, nursing homes and home are the key settings where any improvement in palliative care can have the maximum population-level benefit for older people with dementia. Hence, this dissertation focuses on these two key care settings. First, due to the prolonged need for complex care, many older people with dementia are eventually transferred to nursing homes. Throughout this dissertation, 'nursing homes' are defined as collective institutional settings where on-site resident care is provided 24/7.(82) In an epidemiological study in six European countries, such as in Belgium, the Netherlands or United Kingdom (UK), between 58 and 83% of nursing home residents died with dementia.(58) International studies of the prevalence of dementia in nursing homes outside Europe show similar trends. In the United States (US) and Australia, national estimates suggest that people with dementia account for about half of all residents in nursing homes.(32,83)

Second, at any given time, many people with dementia are also cared for at home by their family. In the US, South Europe and in low-middle income countries, the majority of older people with dementia remain to live and receive care in the home setting.(1) About two-thirds of the 5.4 million Americans with dementia live at home, which is about 31% of the home care patients.(83) About 94% of people with dementia are cared for at home in low-middle income countries that have very few care and support resources.(1) In many European countries that have more resources to offer nursing home care services, the high and growing demand for dementia care, the individual's preference to stay at home for as long as possible combined with the limited supply and rising costs of institutional long-term care services put more pressure on health systems to further improve home care services to enable older people with dementia to live there for as long as possible.(14,17,84–86)

1.7. Palliative care for older people with dementia living and dying in nursing homes and at home

Despite strong calls to improve palliative care for older people with dementia, there remains a paucity of high-quality evidence on palliative care in dementia and on its effectiveness for this population.(20,21,79) Primarily, this is potentially attributable to the historical development of palliative care and to the fact that it is a relatively young discipline. Palliative care was first developed in the 1960s to address the care needs of people with advanced cancer in the last days or weeks of life.(87) However, because of the stark differences between the disease trajectories of cancer and dementia, the majority of evidence on palliative care in cancer cannot be directly translated and used for people with dementia.(59) Cancer has also been recognised consistently as an incurable or terminal condition for which palliative care is certainly applicable, whereas dementia has only been recognised as such in recent decades, and the recognition of its terminal nature remains rather inconsistent up to this day.(21,88) Further, because palliative care originally focused on addressing care needs in the last month or weeks of life, most evidence on palliative care in dementia also previously focused on end-stage/advanced dementia.(5,21) As mentioned earlier, about half of the older people with dementia die before they develop advanced dementia, and their complex care needs, disability and death can occur at any stage of the condition, which makes palliative care applicable starting early in the disease trajectory. Finally, as the majority of people with advanced dementia in resource-rich Western countries live and die in nursing homes, existing evidence on palliative care in dementia is also more concentrated in the nursing home setting.(20) These evidences emphasise the critical need to study the current state of palliative care and how it can be improved for older people with non-advanced and advanced dementia living and dying in nursing homes and at home. Doing so can ultimately improve the symptom burden, quality of life and comfort at the end of life of many older people living and dying with dementia.

Drawing on existing evidence and expert consensus, van der Steen and colleagues developed the EAPC White Paper defining optimal palliative care in dementia, which has been a milestone in the field of palliative care for older people with dementia. The experts achieved consensus on 57 salient recommendations that fall under 11 important domains of palliative care in dementia: applicability of palliative care; person-centred care, communication, and shared-decision making; setting care goals and advance planning; continuity of care; prognostication and timely recognition of dying; avoiding overly aggressive, burdensome or futile treatment; optimal treatment of symptoms and providing comfort; psychosocial and spiritual support; family care and involvement; education of the health care team; and societal and ethical issues.(16) The EAPC also highly recommends to integrate palliative care early into disease management and alongside life-prolonging treatments.(16)

Palliative care for and comfort at the end of life of nursing home residents with dementia

While comfort at the end of life is considered an important care goal and outcome of high-quality palliative care for older people with dementia, existing evidence consistently indicates that many nursing home residents with dementia remain at risk of dying with discomfort.(2,8–10,89) Even in countries with advanced level of palliative care development, such as in Belgium, the Netherlands and UK, comfort at the end of life of nursing home residents, including a large proportion with dementia, remains suboptimal.(58) Over the past decade, there have been important policy developments related to dementia and palliative care in the nursing home sector in many countries. For instance, in Flanders, Belgium and in many other Western European countries, new policies were oriented towards delaying institutionalisation of older people with dementia by enabling them to stay at home for as long as possible.(90–95) In these countries, there have also been improvements in palliative care delivery in nursing homes, such as the implementation of palliative care policy or guidelines.(96,97) Such evolution in the landscape of dementia policies and palliative care in nursing homes might have influenced which people die in nursing homes and how they die, and can impact the provision of palliative care for nursing home residents with dementia.(95,97) Yet, there is a lack of high-quality data on how the number of residents dying in nursing homes with varying stages of dementia, the extent to which they use palliative care services, and their comfort at the end of life, and how these are changing over time. Filling in these gaps in research using the context of Flanders, Belgium will offer the very first insight on areas where improvements can be made in palliative care for and comfort at the end of life of nursing home residents dying with dementia in these countries.

Discomfort at the end of life of nursing home residents with dementia has also been associated with the occurrence of clinical events, such as pneumonia.(21,98) At the end of life, acute clinical events, such as pneumonia, febrile episodes (unrelated to pneumonia) and intake problems, often occur in residents with advanced dementia, which is why it is considered a terminal condition.(6,8) However, studies suggest that such events are almost as common in moderate dementia.(10) While residents increasingly have dementia,(8) those without dementia are often very frail, highly care-dependent and have multiple comorbidities that also predispose them to developing clinical events.(8,99) It is therefore of interest to examine clinical events in residents with and without dementia, while taking dementia severity into account. Further, comfort at the end of life may differ between these groups, as the inability to verbalise a complaint due to cognitive decline risks inappropriate treatment.(59) Different clinical events have also been associated with different levels of comfort, with those dying from infections being at greater risk of discomfort than those dying with intake problems.(10,100–102) In order to better understand how different clinical events influence comfort at the end of life of nursing home residents with varying stages of dementia, it is worthwhile to investigate associations between dementia, clinical events and comfort at the end of life.

To contribute high-quality evidence to improve palliative care for nursing home residents, of whom a large proportion have dementia, we developed the 'PACE Steps to Success' programme. PACE Steps to Success is a multicomponent programme aiming to integrate generalist and non-disease-specific palliative care into nursing homes in six steps using a train-the-trainer approach. Nursing home staff are trained to deliver high-quality palliative care to all residents, from advance care planning to care up to and beyond death.(103) Between 2015 and 2017, we evaluated this programme in a seven-country cluster-randomised controlled trial (RCT). The primary trial analyses showed that 'PACE Steps to Success' did not improve the comfort in the last week of life (primary outcome) in the overall nursing home population, but it appeared to improve quality of care and dying in the last month of life for this population, although the latter was the secondary outcome. Because this programme was designed for all residents and included only three dementia-specific elements,(103) we hypothesised a priori that its effects might differ between those with and without dementia in favour of those with mild/moderate or no dementia compared with advanced dementia. It has been widely argued that for palliative care programmes to be effective for people with dementia, they should address the specific needs of this population. However, no study has yet investigated this assumption.(8,61) Hence, at the outset of the PACE cluster-RCT, we planned to investigate whether the effects of PACE Steps to Success on comfort at the end of life and quality and care dying differ between residents with advanced, non-advanced and without dementia.

Palliative care quality and interventions for older people with dementia living at home

Compared to existing evidence in the nursing home setting, the evidence on palliative care in dementia in the home setting is more limited. There were earlier reports suggesting poor quality and access to palliative care for people with dementia living at home. In particular, existing studies using death certificates show that home death is rare among people with dementia.(104,105) Patient death at home has been widely acknowledged as an important indicator for high-quality palliative care in the home setting,(106) primarily because older people with dementia often prefer to be cared for and to die at home.(84) In primary care, evidence on some circumstances of those dying with mild or severe dementia in Belgium, Italy, and Spain suggest that although transfer rates are low and treatment aims are aligned with palliative care recommendations, access to specialised palliative services and communication with general practitioners (GPs), who provide generalist palliative care, remain poor.(107,108) However, these previous studies no longer reflect the latest evidence in primary care, due partly to recent changes in palliative care legal frameworks and funding arrangements in these countries, which might have affected the quality of primary palliative care.(109,110) Additionally, they included people with dementia who died 'suddenly',(107,108) who may not have been recognised as being in the final stage of life and thus in need of palliative care.(111) Finally, they neither showed a comprehensive overview of the most important aspects of palliative care nor systematically measured its quality, something that could be achieved by using a core set of quality indicators.(112–114) Quality indicators (QIs) are explicitly defined and measurable items referring to the structure, process or outcome of care, which can be used to capture the quality of care on an aggregated e.g. national level.(112–114) Therefore, it is crucial to systematically measure the quality of primary palliative care in Belgium, Italy and Spain for older people with mild and severe dementia living at home using a core set of quality indicators that is specifically designed for this care setting.

In 2016, a Cochrane review on palliative care interventions in advanced dementia found only two low quality studies, neither of which was conducted in the home setting.(20) In a systematic review that aimed to identify populations appropriate for palliative care and effective palliative care models, they found improvements in pain and depressive symptoms in people with dementia. However, this study did not indicate whether the population with dementia were living at home.(115) Another Cochrane review evaluated palliative care services for people living at home with advanced incurable illnesses, including those with dementia. They found reliable evidence that these services could reduce symptom burden and increase the chance that people with terminal diseases will die at home. However, the evaluated services were only for people with cancer and organ failure, rather than for people with dementia.(106) These evidences underscore the very limited evidence on palliative care interventions for older people with dementia living at home, in particular the effectiveness of palliative care interventions on end of life care outcomes (e.g. patient death at home or pain) for people with dementia living at home; the facilitators and barriers to implementing these interventions; the extent to which the interventions reflected optimal palliative care in dementia as defined in the EAPC White Paper; and the gaps in evidence. Addressing these research gaps is critical to advancing our knowledge on palliative home care interventions in dementia and to identify areas where more work and research efforts regarding this topic are needed.

A 2019 matched cohort study in Belgium evaluated palliative home care support for a general palliative care population, which included a large proportion of people with dementia. This evaluation study suggests that palliative home care support improves the quality of end-of-life care and reduces resource use and costs for this general population in need of palliative care.(116) However, considering the specific disease trajectory of dementia and the associated complex care needs of people affected by this condition, it remains unknown whether this palliative home care support could have similar effects on end-of-life care for older people with dementia. To determine whether this palliative home care support in Belgium is effective for older people with dementia living at home or needs further improvement, it is therefore of paramount importance to evaluate its effects on the quality and costs of end-of-life care for this specific population.

1.8. Research aims and questions

To address the aforementioned gaps in evidence on palliative care in dementia, the aim of this dissertation was two-fold. The first research aim focused on nursing home residents with dementia, while the other focused on older people with dementia living at home. First, we aimed to describe how many people with dementia die in nursing homes, how these residents die in relation to their palliative care service use and comfort in the last week of life, and if there were changes over time, as well as to evaluate whether a generalist palliative care programme for nursing homes affects comfort at the end of life and quality of care and dying of residents with dementia differently than those without dementia. Second, focused on older people with dementia living at home, we aimed to describe the current quality of primary palliative care and the current evidence on palliative home care interventions, as well as to evaluate the effects of palliative home care support on quality and costs of end of life care in Belgium.

RESEARCH AIM 1 focused on nursing home residents with dementia. More specifically, the research questions are the following:

1. Did the prevalence of dementia in nursing homes in Flanders, Belgium and the characteristics, the palliative care service use and comfort in the last week of life of nursing home residents with dementia in change between 2010 and 2015?
2. What are the occurrence rates of clinical events in the last month of life and their associations with comfort in the last week of life of nursing home residents with advanced, non-advanced and without dementia?
3. Do the effects of the PACE Steps to Success programme on comfort in the last week of life and quality of care and dying in the last month of life differ between residents with advanced, non-advanced and without dementia?

RESEARCH AIM 2 focused on older people with dementia living and dying at home. The specific research questions are as follows:

1. What is the quality of primary palliative care in Belgium, Italy, and Spain for older people who died non-suddenly with mild or severe dementia?
2. What is the evidence on home palliative care interventions in dementia, in terms of their effectiveness on end of life care outcomes, factors influencing implementation, the extent to which they address the European Association for Palliative Care domains, and the gaps in evidence?
3. What are the effects of palliative home care support on the quality and costs of end-of-life care for older people who lived at home and died with dementia between 2010 and 2015 in Belgium?

1.10. Methods

To address the research aims of this dissertation, multiple study designs and research methods were used. **Research aim 1** was addressed using two comparable retrospective epidemiological studies and a cluster-randomised controlled trial (RCT), all conducted in nursing homes. These three studies used similar procedures in determining the presence and severity of dementia. **Research aim 2** was addressed using a mortality follow-back study using existing epidemiological surveillance system – the Sentinel Networks of General Practitioners, a systematic review and a nationwide propensity-matched decedent cohort study using routinely-collected nationwide administrative databases.

1.10.1. RESEARCH AIM 1. Palliative care for nursing home residents with dementia

Two retrospective epidemiological studies with comparable research methods

This dissertation used data from two retrospective epidemiological studies: the Dying Well with Dementia study and the PACE study (Palliative Care for Older People in care and nursing homes in Europe). The Dying Well with Dementia study was conducted in 2010 in Flanders, Belgium and aimed to describe the clinical characteristics and comfort in the last week of life of nursing home residents with dementia.(62) The PACE study was conducted in 2015 in Belgium (Flanders), Finland, Italy, the Netherlands, Poland and England, and one of its main aims was to describe and compare the six countries in terms of comfort in the last week of life of all residents, of whom the presence and severity of dementia could be determined.(117) The PACE study is a part of the EUFP7-funded PACE project. The aims, designs and results related to nursing home residents of the Dying Well with Dementia and PACE studies can be found elsewhere.(58,62,117)

To answer research question 1, we used the full data from the Dying Well with Dementia study and partial data on nursing home residents with dementia in Flanders, Belgium from the PACE study.(62,117) To answer research question 2, we used the full data from PACE study. In both studies, 'nursing homes' were defined as collective institutional settings where on-site resident care is provided 24/7.(82) Both studies also used similar research methods, unless otherwise indicated.

To obtain nationwide representative samples of nursing homes, proportional stratified random sampling method was used. From a national list, the research team randomly sampled nursing homes per country, stratified by region (five provinces), bed capacity and ownership (public, private/non-profit, private/profit). Previous studies showed that region, bed capacity and ownership are factors associated with end-of-life care quality in nursing homes.(118,119) Nursing homes were sampled from national lists in all countries except Italy, where samples were taken from a previously-created cluster of nursing homes covering three macro-regional areas and taking bed capacity and facility types into account.(62,117)

In both studies, a letter introducing the study was sent to nursing home directors or manager asking for voluntary participation and telephone or e-mail contact was made. In each participating nursing home, a contact person (a nursing home administrator, head nurse or manager) was appointed. Assisted by a researcher, the administrator/manager in each nursing home was asked to identify all residents who died in the previous three months.(62,117) Because the Dying Well with Dementia study focused on dementia, the residents who did not have dementia were excluded immediately before data collection. This was done by asking the administrators/managers to further identify residents who met the Katz scale criteria used by the Belgian health insurance system to allocate financial resources: "category Cdementia", i.e. being completely care dependent or needing help for bathing, dressing, eating, toileting, continence and transferring plus being disoriented in time and space OR "disorientation in time and space" (≥3 or "almost daily a problem with disorientation in time and space").(120) In the Dying Well with Dementia study, data were collected on residents who met at any of the Katz scale criteria, while in the PACE study, data were collected on all identified residents. In both studies, after-death questionnaires for each resident were distributed to nursing home staff most closely involved in care (preferably a nurse or, if not available, a care assistant), GP and nursing home administrator.(62,117)

Subgroup analysis of a cluster-randomised controlled trial (RCT*)*

To answer research question 3, we performed a pre-planned subgroup analysis of the PACE cluster-RCT, which is also a part of the EUFP7-funded PACE project. The PACE cluster-RCT was conducted in 78 nursing homes in Belgium, England, Finland, Italy, the Netherlands, Poland and Switzerland to compare PACE Steps to Success with usual care (2015-2017).(103) This trial was registered at http://www.isrctn.com on July 30, 2015 (ISRCTN14741671). The aims and design of the PACE cluster-RCT and the results of the primary trial analysis were published earlier.(103,121)

'PACE Steps to Success' is a multicomponent programme aiming to integrate generalist and non-disease-specific palliative care into nursing homes in six steps using a train-the-trainer approach. PACE Steps to Success was implemented over the course of one year, including two months for preparation, six months training for nursing home staff in the six steps, and four months consolidation. All countries had one or more country trainers. Each nursing home assigned one to six staff members as PACE coordinators. After being trained by two experienced trainers, the country trainers trained and supported the PACE coordinators who were in turn responsible for training and supporting fellow nursing home staff. Figure 1 illustrates the six steps included PACE Steps to Success: 1) advance care planning with residents and families; 2) assessment, care planning, and review of resident needs and problems; 3) coordination of care via monthly multidisciplinary palliative care review meetings; 4) high-quality palliative care with a focus on pain and depression; 5) care in the last days of life and 6) care after death.(103)

As the programme involved the training of nursing home staff, randomisation was performed at the nursing home level. One contact person per nursing home identified all residents who had died in the previous four months. After-death structured questionnaires for each resident were sent to the staff member most involved in care (preferably a nurse), nursing home administrator and GP at baseline (month 0) and post-intervention (months 13 and 17).(103) As sensitivity analyses showed no difference between programme effects using the two post-intervention data, these combined post-intervention data were used in the primary analyses.(121) To compare our findings with that of the primary analyses, the combined post-intervention data were also used in the subgroup analysis.

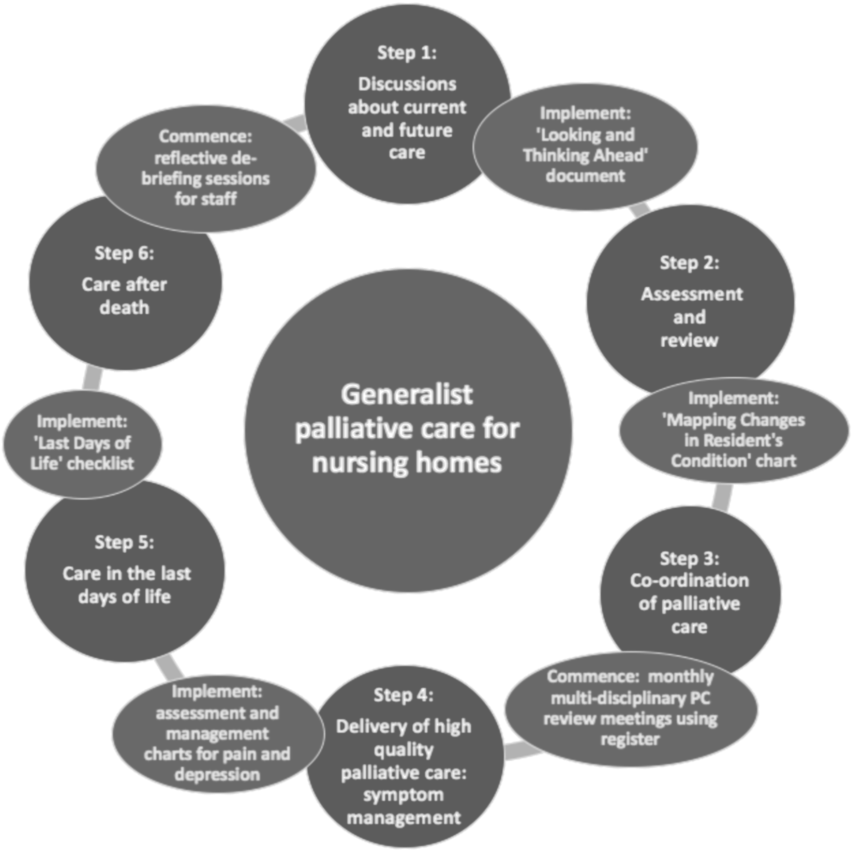

Figure 1. The PACE Steps to Success palliative care programme

Determining the presence and severity of dementia

The Dying Well with Dementia study, the PACE study and the PACE cluster-RCT used similar procedures to determine the presence and severity of dementia**.**(62,103,117) Dementia was determined by asking the GP and the nursing home staff if the resident "had dementia" or "was diagnosed with dementia". A resident was considered to have dementia if the nursing home staff and/or the GP indicated it. A resident did not have dementia when both the nursing home staff and the GP indicated it, or when one of these respondents indicated it, but the other did not return the questionnaire or did not answer the question. Dementia severity was determined using two highly-discriminatory nursing home staff-reported instruments, Cognitive Performance Scale (CPS) and Global Deterioration Scale (GDS).(122,123) CPS uses five variables from the Minimum Data Set to group residents into six hierarchical cognitive performance categories, e.g. CPS scores 5-6 indicate severe and very severe impairment.(122) GDS is divided into seven stages, of which stage 7 indicates that a resident lost all verbal abilities, was incontinent/required assistance with eating and toileting, and lost basic psychomotor skills.(123) To determine whether a resident had GDS stage 7, the nursing home staff were asked whether the resident fit all the criteria of GDS stage 7 (yes/no). Of the residents who were identified to have dementia, those with CPS scores ≥ 5 and GDS stage = 7 had advanced dementia, while the rest had non-advanced dementia.(62,103,117)

1.10.2. RESEARCH AIM 2. Palliative care for older people with dementia living and dying at home

Mortality follow-back study using an existing epidemiological surveillance network

To answer research question 4, we used data from the European Sentinel Network Monitoring End-of-Life Care (EUROSENTIMELC). EUROSENTIMELC is a mortality follow-back study monitoring palliative care in population-based samples of death in Belgium, Italy, and Spain.(124) Data were collected through existing Sentinel Networks of GPs, an epidemiological surveillance network that voluntarily monitors health problems in primary care. The Network in Belgium is representative for age, sex and the geographical distribution of GPs in the country, while the Network in Spain covers the Castile and Leon and the Valencian regions. In Italy, we used a nationally-representative GP network that only performed end-of-life care registrations.

Using a standardised registration form, GPs registered deaths weekly among patients in their practice aged 18 years or older from January 2013 to December 2014 in Belgium and Spain and from June 2013 to May 2015 in Italy. In completing the registration form, GPs may also use medical files.(124) The registration form consists of structured and closed-ended items surveying information from the GPs about QIs and patient characteristics. Based on their knowledge and expertise, the GPs estimated whether the patient had dementia ('yes, mild dementia', 'yes, severe dementia', 'no', and 'unknown' (considered as 'no')) and whether they died suddenly. The quality of primary palliative care has been systematically measured using a core set of nine quality indicators. This core set of quality indicators was based on previous work of Leemans et al (2015) and had been further developed specifically for EUROSENTIMELC using a multi-step process.(114)

Systematic review of interventions

To answer research question 5, we performed a systematic review of palliative care interventions in dementia. This systematic review adhered to the PRISMA guidelines and the protocol was registered with the PROSPERO international prospective register of systematic reviews (www.crd.york.ac.uk/prospero/-CRD42018093607). We included peer-reviewed quantitative studies evaluating palliative care interventions for people with any type of dementia living at home. To provide a comprehensive overview of existing research in this area, we included specialist palliative care services and non-specialist palliative care interventions, i.e. interventions that were not labelled as 'palliative care' but described as aiming to improve care at the end of life for people with dementia. Specialist palliative care included services with the following four elements: 1) designed primarily for people with dementia living at home; 2) aim to support people outside hospital and other institutional settings for as long as possible and to enable people to stay at home; 3) be provided by specialists in palliative care or intermediate palliative/hospice care; 4) provide comprehensive care addressing different physical and psychosocial components of palliative care. Non-specialist palliative care included interventions that focused either on people with advanced/severe/late stage dementia living at home or on people with dementia living at home with the potential impact on palliative care or death and dying or end of life care outcomes.

Nationwide propensity-matched decedent cohort study

To answer research question 6, we used a propensity-matched decedent cohort study using linked nationwide administrative databases in Belgium (2010-2015).(125) These linked data were from eight routinely-collected nationwide administrative databases in Belgium, including socio-demographic, healthcare, pharmaceutical, cancer registry, death certificate, population registry, census and fiscal databases. These databases included data of all individuals registered with a Belgian sickness fund at the time of death (98.8% of all deaths).(125) After obtaining approval from all relevant data protection agencies, data linkage was securely and ethically performed to guarantee anonymity of the individuals by a third party officially responsible for data protection and linkage in Belgium.(125,126)

Dying with dementia was based on the underlying, intermediate and associated causes of death reported on the death certificate with ICD-10 codes (F01-F03 or G30) and whether or not they received dementia-specific medications up to ten years before death, using a medication algorithm (ATC code=N06DA01 or N06DA02 or N06DA03 or N06DA04 or N06DX01 or N06DA52). Exposure was defined as receiving at least one type of palliative home care support measure for the first time between 360 and 15 days before death. Palliative home care measures include home visits by a multidisciplinary palliative home care team; home visit by a palliative care nurse or physiotherapist, or receiving financial allowance for palliative patients.(116,127,128) The unexposed group included individuals who did not receive palliative home care support in the last twoyears of life, matched to people who received it.

An included individual who received palliative home care support was matched to one who did not, based on an estimation of their propensity for receiving the support. To calculate propensity scores, predictors for receiving the exposure, identified as relevant based on clinical knowledge and previous studies, were considered as baseline covariates.(106,116,129–132) For the propensity score matching we used a greedy 1:1 exposure–control propensity scores matching algorithm.(133) For every case, the best match was made first and a next-best match next, in a hierarchical sequence until no more matches could be made. Best matches are those with the highest digit match on propensity score. The algorithm proceeds sequentially to the lowest digit match on the propensity score (eight digit to one digit). No trimming was performed.

1.11. Outline of this dissertation

The findings of my PhD research are divided into two sections, which match the two research aims. Part I of this dissertation focuses on palliative care for nursing home residents with dementia. Chapter 2 examines the difference in the prevalence of dementia in nursing homes and the characteristics, palliative care service use and comfort at the end-of-life of residents with dementia in Flanders, Belgium between 2010 and 2015. Chapter 3 investigates the occurrence rates of clinical events, such as pneumonia and intake problems, and their associations with comfort at the end of life of nursing home residents with and without dementia. Chapter 4 investigates whether the effects of PACE Steps to Success on comfort in the last week of life and quality of care and dying in the last month of life differ between residents with advanced, non-advanced, and no dementia.

Part II of this dissertation focuses on palliative care for older people living and dying at home. Chapter 5 systematically investigates the quality of primary palliative care for older people with mild and severe dementia using a core set of quality indicators. Chapter 6 examines evidence on palliative home care interventions in dementia, in terms of their effectiveness on end of life care outcomes, factors influencing implementation, the extent to which they address the EAPC palliative care domains and evidence gaps. Chapter 7 evaluates the effects of palliative home care on quality and costs of end-of-life care for older people with dementia. Finally, this dissertation contains a discussion of the findings, including methodological considerations, strengths and limitations, and implications for practice, policy and future research.

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PART I

Palliative care for nursing home residents with dementia

CHAPTER 1

Higher Prevalence of Dementia but No Change in Total Comfort While Dying among Nursing Home Residents with Dementia between 2010 and 2015: Results from Two Retrospective Epidemiological Studies

Rose Miranda, Tinne Smets, Nele Van Den Noortgate, Luc Deliens and Lieve Van den Block

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ABSTRACT

Important policy developments in dementia and palliative care in nursing homes between 2010 and 2015 in Flanders, Belgium might have influenced which people die in nursing homes and how they die. We aimed to examine differences between 2010 and 2015 in the prevalence and characteristics of residents with dementia in nursing homes in Flanders, and their palliative care service use and comfort in the last week of life. We used two retrospective epidemiological studies, including 198 residents in 2010 and 183 in 2015, who died with dementia in representative samples of nursing homes in Flanders. We found a 15%-point increase in dementia prevalence (p-value < 0.01), with a total of 11%-point decrease in severe to very severe cognitive impairment ($p = 0.04$). Controlling for residents' characteristics, in the last week of life, there was an increase in the use of pain assessment (+20%-point; $p < 0.03$) but no change in total comfort. The higher prevalence of dementia in nursing homes with no change in residents' total comfort while dying emphasizes an urgent need to better support nursing homes in improving their capacities to provide timely and high-quality palliative care services to more residents dying with dementia.

Keywords: long-term care; care homes; nursing homes; dementia; quality improvement; palliative care

INTRODUCTION

Dementia is a progressive incurable condition, for which a palliative care approach is widely recommended [1]. Palliative care can improve the quality of life of people with dementia by addressing their multi-faceted physical, psychosocial and spiritual care needs for months or years until death [1–3]. In Europe, the prevalence of dementia is projected to almost double to about 18.8 million by 2050 [4]. Because people with dementia have prolonged and complex palliative care needs [2], half or more of them eventually live and receive care in nursing homes [5,6]. Yet, the quality of dying and end-of-life care in this setting in many countries, including those with high levels of palliative care development, such as in Belgium, is apparently sub-optimal [7,8]. Especially residents with dementia remain at risk of dying with great discomfort, potentially related to sub-optimal assessment and management of their complex care needs, which highlights an urgent need to identify ways on how to improve the quality of care in nursing homes for this population [2,9–12].

Over the past decade, there have been important policy developments related to dementia and palliative care in the nursing home sector in many countries, which might have influenced which people die in nursing homes and how they die, and can impact the provision of palliative care for nursing home residents with dementia [8,13]. Yet, there is a lack of high-quality data on the number of residents dying in nursing homes with varying stages of dementia; on the extent to which palliative care services are used; and on how these number of residents dying in nursing homes and their palliative care service use are changing over time. In this study, we will examine differences between 2010 and 2015 in the prevalence and characteristics of residents with dementia in nursing homes in Flanders, the Dutch-speaking part of Belgium where about 60% of the population live [14], as well as differences in their palliative care service use and comfort in the last week of life.

Between 2010 and 2015, new dementia policies in Flanders were oriented towards delaying the institutionalization of older people with dementia by enabling them to stay at home for as long as possible [15–19]. Several initiatives for people with dementia living in communities were also implemented regionwide, e.g., information campaigns and training of primary care professionals and family caregivers [20–23]. While these developments could potentially result in fewer admissions or shorter stays in nursing homes or more admissions of those with advanced conditions unmanageable at home [24,25], representative data showing these potential changes are lacking.

Particularly three developments related to palliative care in the nursing home sector in Flanders are historically important. First, supported by the 2002 Belgian Palliative Care Law that recognizes the legal right to palliative care of ‘patients whose life-threatening illness no longer responds to curative treatments’ [26], the Flemish government passed the Decree on Residential Care in 2009 [27]. This decree officially requires Flemish nursing homes to support, sensitize, and train all regular staff regarding palliative care. Second, in 2010, the Flanders’ Federation of Palliative Care launched palliative care guidelines for professional caregivers in nursing homes in developing and implementing palliative care in their facility [28,29], including the comprehensive delivery of physical, psychosocial, and spiritual support [29]. Third, in 2013, the Flemish government introduced a strategy to evaluate the quality of care in nursing homes by having them report on 13 quality indicators [30]. Two of these quality indicators concern palliative care (‘place of death’ and ‘advance care planning’). These indicators are used to systematically monitor the aggregate quality of care in this sector and to identify areas where improvements can be made. Despite these policy developments for nursing homes, no epidemiological study has yet examined the use of palliative care services of residents with dementia and their comfort while dying before and after these developments. Examining this will inform policymakers in Belgium on how to further improve the quality of care at the end of life of nursing home residents with dementia. Results can also be used to inform policies in many countries, especially in Western Europe with similar shifts in health care policies [8,13]. Hence, focusing on Flanders, we sought to answer the following research questions:

- Are there differences in the prevalence of dementia in nursing homes between 2010 and 2015?
- Are there differences in the socio-demographic and clinical characteristics of nursing home residents with dementia between 2010 and 2015?
- Are there differences in palliative care service use and comfort in the last week of the life of nursing home residents with dementia between 2010 and 2015?

MATERIALS AND METHODS

Design

We used data from two retrospective epidemiological studies in regionwide representative samples of nursing homes in Flanders, Belgium, namely, the Dying Well with Dementia study focused on residents with dementia (2010) and the Palliative Care for Older People in care and nursing homes in Europe (PACE) study focused on all residents, of whom the presence of dementia was determined (2015) [31,32]. Both studies used similar research methods unless otherwise indicated.

Participating Nursing Homes

To obtain regionwide representative samples of nursing homes, proportional stratified random sampling methods were used. From a national list, the research team randomly sampled Flemish nursing homes, stratified by region (five provinces), bed capacity (up to or more than 90 beds, which is the median number of beds in nursing homes in Flanders), and ownership (public, private/non-profit, private/profit). Previous studies showed that region, bed capacity, and ownership are factors associated with end-of-life care quality in nursing homes [33,34]. If a nursing home refused to participate, another one was randomly selected from the same stratum until the targeted number per stratum was reached [31,32].

Data Collection and Study Population

The administrator/manager in each nursing home was asked to identify all residents who died in the previous three months. Because the 2010 study focused on dementia, the residents who did not have dementia were excluded immediately before data collection. This was done by asking the administrators/managers to further identify residents who met the Katz scale criteria used by the Belgian health insurance system to allocate financial resources: "category Cdementia", i.e., being completely care-dependent or needing help for bathing, dressing, eating, toileting, continence, and transferring plus being disoriented in time and space OR "disorientation in time and space" (≥3 or "almost daily a problem with disorientation in time and space") [31,32,35].

In 2010, data were collected on residents who met any of the Katz scale criteria, while in 2015, data were collected on all identified residents. To collect data, both studies used after-death questionnaires distributed to nursing home staff most closely involved in care, general practitioner (GP), and nursing home administrator. Dementia was determined by asking the GP and the nursing home staff if the resident “had dementia” or “was diagnosed with dementia”. We considered a resident to have dementia if the nursing home staff and/or the GP indicated it. A resident did not have dementia when both the nursing home staff and the GP indicated it, or when one of these respondents indicated it, but the other did not return the questionnaire or did not answer the question [31,32].

Response rates for staff, GPs, and administrators were, respectively, 88.4%, 52.9%, and 95.0% in 2010 and 85.1%, 68.3%, and 94.2% in 2015. We excluded residents for whom the nursing home staff did not return the questionnaire. Non-response analysis showed no difference in residents’ characteristics between cases for whom the questionnaire was returned by nursing home staff or not [7,31].

Measurements and Outcome Measures

Residents’ characteristics

Using validated instruments, the nursing home staff reported residents’ cognitive and functional impairment one month before death. Cognitive Performance Scale (CPS) uses five variables from the Minimum Data Set to group residents into six hierarchical cognitive performance categories, e.g., CPS scores 5–6 indicate severe and very severe impairment [36]. Global Deterioration Scale (GDS) is divided into seven stages, of which stage 7 indicates that a resident lost all verbal abilities, was incontinent/required assistance with eating and toileting, and lost basic psychomotor skills [37]. Hence, to determine whether a resident had GDS stage 7, the nursing home staff were asked whether the resident fit all the criteria of GDS stage 7 (yes/no). To compare with earlier studies [7,31], we determined the severity of dementia using CPS and GDS (CPS scores ≥ 5 and GDS stage = 7 had advanced dementia, while the rest had non-advanced dementia). The nursing home staff also reported the Bedford Alzheimer Nursing Severity scale (BANS-S), with total scores ranging from 7 (no impairment) to 28 (complete impairment) [38]. They also reported whether any clinical complication occurred in the last month of life, e.g., pneumonia or intake problems. The GPs reported co-existing conditions, e.g., cancer or cardiovascular disease. Nursing home administrators reported residents’ age at time of death, gender, length of stay in nursing homes, place of death, and whether the residents stayed in an open or secured unit at the time of death and in a dementia care unit or not. These residents’ characteristics could influence the palliative care service use and comfort at the of life of people with dementia [39–42].

Palliative care services used

The nursing home staff reported data on palliative care service use, including (1) whether a palliative care record was initiated for residents and the days before death when this occurred; (2) whether a resident received palliative care at any time, including whether this palliative care was provided by a GP and whether the following persons/initiatives were involved in providing this care: coordinating and advisory physician, palliative care reference nurse, palliative care task group, specialist palliative home care team, or none of them. Since 2009, nursing homes in Flanders were officially required to establish a functional relationship with general practitioners (GPs) responsible for providing medical care and developing palliative care strategies for residents and coordinating and advisory physicians responsible for coordinating with GPs to review palliative care strategies and give advice and training to staff [27,43]. Further, the nursing homes must have a palliative care reference nurse responsible for establishing a supportive palliative care culture and awareness within the nursing home, training personnel regarding palliative care, and supporting and coordinating palliative care delivery, and a palliative care task group comprising of all palliative caregivers. For complex palliative situations, palliative home care teams can either call or visit nursing homes to provide advice or support [27,43]. The nursing home staff also reported whether the residents received services related to medical or nursing treatments/procedures in the last week of life, psychosocial interventions in the last month, and spiritual and/or pastoral care before death.

Comfort in the last week of life

They also assessed comfort in the last week of life using the Comfort Assessment in Dying-End-of-Life in Dementia (CAD-EOLD) scale. CAD-EOLD is a validated 14-item scale comprising discomfort, pain, restlessness, shortness of breath, choking, gurgling, difficulty swallowing, fear, anxiety, crying, moaning, serenity, peace, and calm. Individual item scores range from 0–3, while total scores range from 14 to 42, with higher scores representing better comfort [44,45].

Data Analyses

The 2010 and 2015 databases were merged by R.M. and two palliative care researchers. The prevalence of dementia between 2010 and 2015 was compared using χ^2-test. Subsequent analyses were performed in IBM SPSS statistics version 26 (©IBM Corporation， Armonk, NY, USA) using generalized linear mixed model to account for clustering of data within nursing homes. We compared residents' characteristics and their palliative care service use and comfort scores between 2010 and 2015. We adjusted all analyses related to palliative care service use and comfort for resident characteristics while taking correlations between these resident characteristics into account. Using Benjamini-Hochberg procedure to decrease the false discovery rate, we adjusted the analyses related to comfort for multiple testing. Hypothesis testing was two-sided. Statistical significance was set at $p < 0.05$.

RESULTS

Prevalence of Dementia

The prevalence of dementia significantly increased from 43% in 2010 (205 of 477 residents) to 58% in 2015 (199 of 342 residents) (+15%-point; *p*-value < 0.01; Figure 1). Of the residents with dementia, we excluded 7 residents in 2010 and 16 in 2015, as the nursing home staff did not return the questionnaires, leaving 198 and 183 residents for further analyses. In the large majority of nursing homes in both years, the number of residents in each nursing home ranged between 1 and 8. In 2010, two nursing homes had 11 and 14 residents, while in 2015, one nursing home had 9 residents.

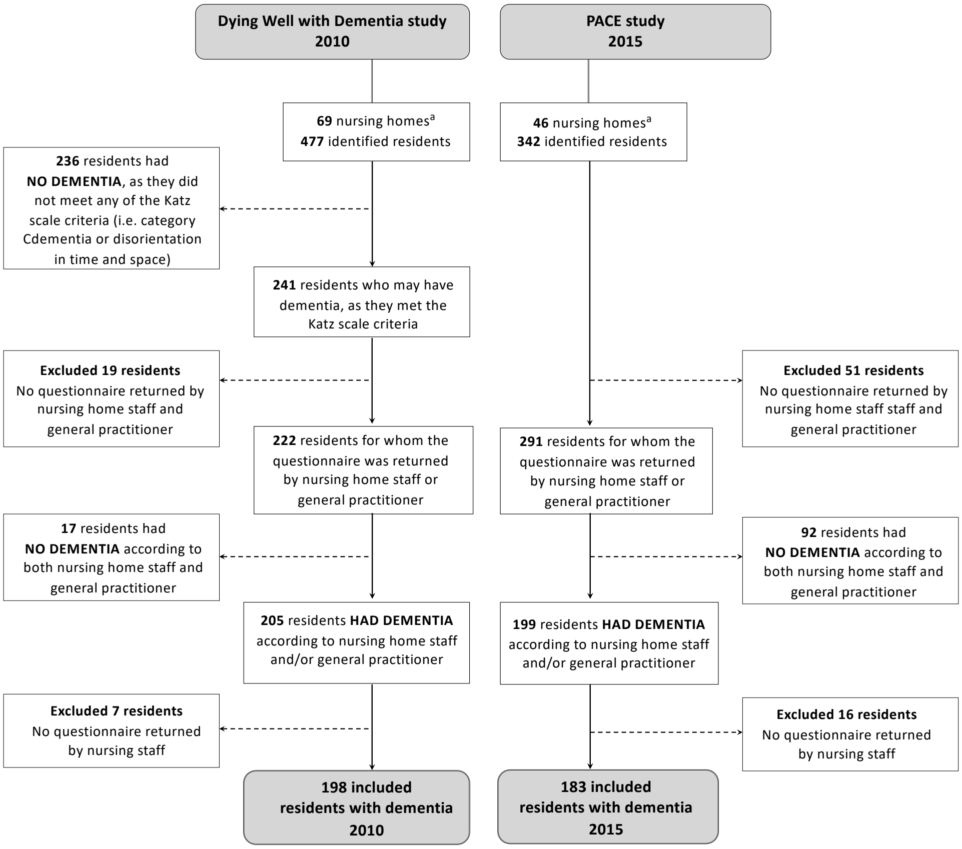

Figure 1. Overview of the identification of residents with dementia in 2010 and 2015

[a] Because we excluded a number of residents from the total sample, the final number of nursing homes were 64 in 2010 and 43 in 2015. In 2010, 205 residents had dementia (numerator) of the 477 identified residents. In 2015, 199 residents had dementia (numerator) of the 342 identified residents (denominator).

Characteristics of Residents with Dementia

Between 2010 and 2015, residents' characteristics did not change, except for scores on the Cognitive Performance Scale. One month before death, the proportion of residents with dementia with severe to very severe cognitive impairment (CPS scores 5-6) had a total of 11%-point decrease (*p* = 0.04; Table 1), while the proportion of residents with GDS stage 7 had a total of 14%-point increase (*p* = 0.04). The residents were about 86 years of age at the time of death, were predominantly women, and had BANS-S scores of 20.9 in 2010 and 20.3 in 2015. Of the residents in 2010 and 2015, respectively, 49% and 52% had advanced dementia, while 95% and 92% experienced any clinical complication a month before death. The most common co-existing conditions were cardiovascular diseases (29% in 2010 and 28% in 2015), followed by cancer and respiratory conditions. The median length of stay in nursing homes was 893 days in 2010 and 688 days in 2015. In 2010 and 2015, respectively, nursing home was the most common place of death (90% and 86%), while 9% and 14% died in hospitals.

Table 1. Comparing residents' characteristics between 2010 and 2015

Residents' Characteristics	2010 (N = 198)	2015 (N = 183)	Change	Difference between the Years *p*-values †
Socio-demographic characteristics				
Age at time of death, average in years (SD)	86.7 (7)	86.9 (7.3)	+0.2	0.73
Gender, female *n* (%)	115 (61)	114 (65)	+4	0.43
Clinical characteristics				
Cognitive performance scale (CPS), *n* (%)				0.04
- Intact, borderline intact, mild impairment (score 0-1-2)	8 (4)	21 (13)	+9	
- Moderate impairment (score 3)	27 (14)	20 (12)	−2	
- Moderately severe impairment (score 4)	9 (5)	15 (9)	+4	
- Severe impairment (score 5)	61 (33)	52 (31)	−2	
- Very severe impairment (score 6)	82 (44)	58 (35)	−9	
Global deterioration scale (GDS) stage 7, *n* (%)	105 (58)	123 (72)	+14	0.04
Bedford Alzheimer Nursing Severity scale (BANS-S) 1 month before death, mean (SD)	20.9 (3.9)	20.3 (4.3)	−0.6	0.19
Severity of dementia, *n* (%)				0.55
- Non-advanced dementia	95 (51)	75 (48)	−3	
- Advanced dementia	92 (49)	82 (52)	+3	
Occurrence of clinical complications in last month of life, *n* (%)	179 (95)	168 (92)	−3	0.31
Co-existing conditions				
- Cancer	12 (11)	19 (14)	+3	0.43
- Cardiovascular	32 (29)	37 (28)	−1	0.89
- Respiratory	15 (14)	14 (11)	−3	0.51
- Neurological (not dementia)	17 (15)	10 (8)	−7	0.08
- Urogenital	9 (8)	12 (9)	+1	0.82
- Other	18 (16)	22 (17)	+1	0.99
Length of stay in nursing home in days, median days (IQR)	893 (448–1694)	688 (283–1678)	−205	0.28
Place of death, *n* (%)				0.20
- Nursing homes	171 (90)	152 (86)	−4	
- Hospital	17 (9)	24 (14)	+5	
- Other ‡	2 (1)	0 (0)	−1	
Type of unit at time of death, *n* (%)				0.71
- Open unit	91 (48)	88 (50)	+2	
- Secured unit	98 (51)	88 (50)	−1	
Dementia care unit, yes, *n* (%)	99 (53)	93 (53)	0	0.95

SD = standard deviations; IQR = Interquartile range; GLMM = generalized linear mixed model analyses.

† Calculated using GLMM to account for correlation of data within nursing homes; 'other' categories not included in calculation of *p*-values. Analyses showed correlation of CPS with GDS, BANS-S and severity of dementia, and this might be because they similarly cover residents' cognitive and functional status. The type of unit at the time of death was correlated with dementia care unit, and this might be because one nursing home can have both types of unit. Further analyses will be adjusted for CPS, dementia care unit, and the rest of the residents' characteristics.

‡ Examples of places of death other than nursing homes or hospitals include facility hospice/palliative care unit. Missing values, *n*: age, 2010 = 12; 2015 = 8 | gender, 2010 = 11; 2015 = 9 | severity of dementia, 2010 = 11; 2015 = 26 | CPS, 2010 = 11 ; 2015 = 17 | GDS, 2010 = 16; 2015 = 12 | BANS-S, 2010 = 4; 2015 = 2 | clinical complications, 2010 = 10; 2015 = 15 | all co-existing conditions except other, 2010 = 87; 2015 = 51 | other co-existing conditions, 2010 = 88; 2015 = 51 | length of stay in nursing homes, 2010 = 13; 2015 = 10 | place of death, 2010 = 10; 2015 = 7 | type of unit, 2010 = 9; 2015 = 7 | dementia care unit, 2010 = 10; 2015 = 8.

Palliative Care Service Use among Residents with Dementia

In the multivariable analyses controlled for residents' characteristics, in 2010 and 2015, respectively, a palliative care record was initiated for 62% and 72% of residents ($p = 0.17$), of which 51% and 60% occurred within 14 days before death ($p = 0.63$; Table 2). According to nursing home staff, 83% in 2010 and 82% in 2015 of residents received palliative care. For 17% (2010) and 20% (2015) of these people who received palliative care, no coordinating and advisory physician, palliative care reference nurse, palliative care task group, and palliative home care teams were involved (*p* = 0.83).

In the last week of life, there was a significant increase in the percentages of residents for whom pain assessment was conducted (from 63% in 2010 to 83% in 2015; *p* = 0.03). In the last month of life, 37% (2010) and 47% (2015) of residents did not receive any psychosocial intervention (*p* = 0.78). In 2010 and 2015, respectively, shortly before death, 48% and 57% of residents received spiritual care, meaning that 52% and 43% did not receive it (*p* = 0.11).

Table 2. Comparing palliative care service use between 2010 and 2015

Palliative Care Service Use	2010 (N = 198)	2015 (N = 183)	%-Point	Difference between Years (*p*-values ‡)	
	n (%)	*n* (%)	Change †	Crude	Adjusted
Residents who had a palliative care record	121 (62)	97 (72)	+10	0.10	0.17
Time before death when the palliative care record initiated					
- < 14 days	51 (51)	38 (60)	+9	0.10	0.63
- 15 to 90 days	32 (32)	22 (35)	+3		
- > 90 days	18 (18)	3 (5)	−13		
Residents who received palliative care at any time according to nursing home staff	162 (83)	145 (82)	−1	0.69	0.21
Palliative care was provided by GP	136 (84)	123 (86)	+2	0.84	0.89
Other person/initiatives involved in providing the palliative care					
- Coordinating and advisory physician	44 (27)	35 (23)	−4	0.44	0.11
- Palliative care reference nurse	110 (66)	94 (62)	−4	0.64	0.35
- Palliative care task group within the nursing home	81 (49)	64 (42)	−7	0.35	0.34
- Palliative home care teams (external)	16 (10)	8 (5)	−5	0.24	0.30
- No one from this list was involved	28 (17)	30 (20)	+3	0.55	0.83
Residents who received medical or nursing treatments/procedures during the last week of life					
- Mouthcare	159 (80)	152 (88)	+8	0.055	0.54
- Pain assessment	124 (63)	143 (83)	+20	0.001	0.03
- Prevention of pressure ulcers	162 (82)	151 (87)	+5	0.15	0.72
- Wound care	45 (23)	48 (28)	+5	0.27	0.97
- Assistance with eating/drinking	142 (72)	141 (82)	+10	0.04	0.37
Residents who received psychosocial interventions in the last month of life					
- Adjustments of environmental factors ¶	19 (10)	28 (16)	+6	0.10	0.18
- Activity programmes	25 (13)	16 (9)	−4	0.33	0.85
- Music therapy	48 (24)	28 (16)	−8	0.17	0.24
- Behavioural therapy	0 (0)	1 (1)	+1	0.87	0.78
- Experiential approaches #	52 (26)	47 (28)	+2	0.90	0.32
- No psychosocial interventions received	74 (37)	81 (47)	+10	0.15	0.78
Residents who received spiritual and/or pastoral care shortly before death					
- Spiritual care provider/Pastoral worker	98 (48)	72 (57)	+9	0.10	0.11

GLMM = generalized linear mixed model; GP = general practitioners; pp = percentage point. Crude model is the unadjusted model. Adjusted model is adjusted for all residents' characteristics, except for GDS, BANS-S, severity of dementia, and type of unit at the time of death to avoid multi-collinearity.

† %-point = percentage point. %-point difference was calculated between 2010 and 2015.

‡ Calculated using GLMM analyses to account for correlation of data within nursing homes while accounting for differences in resident characteristics; 'other' categories not included in the calculation of *p*-values.

¶ Example of adjustments of environmental factors includes a modified environment for walking around safely. # Examples of experiential approaches include multisensory environment, validation therapy.

Missing values, *n*: palliative care record, 2010 = 2; 2015 = 49 | receipt of palliative care, 2010 = 4; 2015 = 6 | palliative care provided by GP, 2010 = 5; 2015 = 9 | time before death when palliative care record was started, 2010 = 22; 2015 = 34 | all physical care, 2015 = 10 | all psychosocial care, 2015 = 12 | spiritual care, 2010 = 10; 2015 = 15.

Comfort in the Last Week of Life

In multivariable analyses controlled for residents' characteristics, a week before death, there was a 0.2-point increase in the comfort scores related to moaning (*p* = 0.03) (Table 3). However, this statistically significant increase in comfort scores disappeared after adjusting for multiple testing (*p* = 0.45). The estimated marginal means for the total comfort scores did not change between 2010 (30.0; 95% CI = 29.2–30.8) and 2015 (30.8; 29.2–30.9; *p* = 0.87).

Table 3. Comparing comfort in the last week of life between 2010 and 2015

COMFORT IN THE LAST WEEK OF LIFE	2010 (N = 198)	2015 (N = 183)	Score-Point	Difference between Years (*p*-values ‡)	
CAD-EOLD individual items	CAD-EOLD scores 0 (worst) to 3 (best)	CAD-EOLD scores 0 (worst) to 3 (best)	Change †	Crude	Adjusted
- Discomfort	2.1 (2.0–2.2)	2.1 (2.0–2.2)	–	0.46	0.88
- Pain	2.0 (1.9–2.1)	2.2 (2.1–2.3)	+0.2	0.03	0.62
- Restlessness	2.1 (2.0–2.2)	2.1 (2.0–2.2)	–	0.72	0.39
- Shortness of breath	2.2 (2.1–2.3)	2.4 (2.3–2.5)	+0.2	0.03	0.14
- Choking	2.1 (2.0–2.2)	2.1 (2.0–2.2)	–	0.77	0.75
- Gurgling	2.3 (2.2–2.4)	2.5 (2.3–2.6)	+0.2	0.13	0.83
- Difficulty swallowing	1.9 (1.8–2.0)	1.9 (1.8–2.0)	–	0.61	0.84
- Fear	2.0 (1.9–2.2)	2.2 (2.1–2.3)	+0.2	0.04	0.45
- Anxiety	2.1 (2.1–2.3)	2.2 (2.1–2.3)	+0.1	0.32	0.88
- Crying	2.7 (2.6–2.8)	2.7 (2.6–2.8)	–	0.49	0.89
- Moaning	2.3 (2.3–2.4)	2.5 (2.4–2.6)	+0.2	0.02	0.03
- Serenity	2.0 (1.9–2.2)	2.1 (2.0–2.2)	+0.1	0.69	0.07
- Peace	2.0 (1.9–2.1)	2.0 (1.9–2.2)	–	0.63	0.24
- Calm	2.0 (1.9–2.1)	2.0 (1.9–2.1)	–	0.33	0.31
Total score ¶, estimated marginal means (95% CI)	**30.0 (29.2–30.8)**	**30.8 (29.2–30.9)**	**+0.8**	**0.22**	**0.87**

CAD-EOLD = Comfort Assessment in Dying—End of Life in Dementia; CI = confidence intervals.
Crude model is the unadjusted model. Adjusted model is adjusted for all residents' characteristics, except for GDS, BANS-S, severity of dementia and type of unit at the time of death to avoid multi-collinearity.
† Score point change was calculated between 2010 and 2015.
‡ Calculated using GLMM analyses to account for correlation of data within NHs while accounting for differences in resident characteristics.
¶ Total scores are averages per whole scale multiplied by total number of items (i.e., 14).Cases with missing values on more than 25% of items per scale were excluded from total score calculation; scores range from 14 to 42; higher scores indicate better comfort when dying.
Missing values, *n*: discomfort, 2010 = 19; 2015 = 12 | pain, 2010 = 9; 2015 = 10 | restlessness, 2010 = 15; 2015 = 10 | shortness of breath, 2010 = 12; 2015 = 10 | choking, 2010 = 16; 2015 = 9 | gurgling, 2010 = 18; 2015 = 11 | difficulty swallowing, 2010 = 11; 2015 = 11 | fear, 2010 = 13; 2015 = 10 | anxiety, 2010 = 14; 2015 = 10 | crying, 2010 = 17; 2015 = 10 | moaning, 2010 = 16; 2015 = 9 | serenity, 2010 = 16; 2015 = 12 | peace, 2010 = 18; 2015 = 12 | calm, 2010 = 19; 2015 = 12 | total score, 2010 = 16; 2015 = 10.

DISCUSSION

Our study showed that between 2010 and 2015 in nursing homes in Flanders, Belgium, there was a 15%-point increase in the prevalence of dementia. Almost all residents' characteristics did not change, except for the level of cognitive impairment in the last month of life, with a total of 11%-point decrease in residents with severe and very severe cognitive impairment, and the level of cognitive and functional impairment, with a total of the 14%-point increase in residents who lost all verbal abilities, was incontinent/required assistance with eating and toileting and lost basic psychomotor skills. The percentages of residents with advanced dementia were 49% in 2010 and 52% in 2015. Pain assessment in the last week of life was performed proportionally more often for residents in 2015 than in 2010. However, in both years, between 37% and 52% of residents neither received psychosocial intervention in the last month of life nor spiritual care shortly before death. In the last week of life, we found no change in residents' total comfort in the last week of life.

This is the first time that two retrospective epidemiological studies are used to investigate changes over time for residents with dementia in the context of important developments in the landscape of dementia and palliative care policies and initiatives in nursing homes. Retrospective data collection is a feasible method for population-based epidemiological end-of-life studies, as it limits potential bias in prospective sampling, e.g., underrepresentation of people who live longer than the follow-up period [7]. Although these are separate studies, both utilized similar study designs, aiming to reach representative samples, and all variables of interest were measured in the same way. Finally, while the measurement of palliative care services is limited to services measured in both studies, these services comprise important components of palliative care in dementia, e.g., comprehensive delivery of physical, psychosocial, or spiritual support [1]. However, this study also has limitations. As these are two separate studies, and the study in 2010 primarily focused on dying nursing home residents with dementia, the variables that could be explored and compared between the years were limited, especially on nursing home characteristics, that might influence palliative care service use or comfort. While accounting for the clustering of data within nursing homes in the analyses could partly limit this limitation of our data, our inability to control for unmeasured variables that could influence palliative care service use or comfort remains a clear limitation of our study. Because data were collected after death, there might be some recall bias [7]. Further, only 2010 Dying Well with Dementia study used the Katz-scale criteria to exclude residents without dementia before data collection [35]. Nevertheless, such residents without dementia would have also been identified by the nursing home staff and/or the GPs in the PACE study, as they were involved closely in resident care [46,47]. For 19 residents in 2010 and 51 residents in 2015, we could not determine the presence or absence of dementia, which may influence the prevalence of dementia. In certain variables, such as the CAD-EOLD, we have a relatively large proportion of missing values (>5%), which we have reported in detail in the footnotes of Tables 1 to 3. Finally, given the cross-sectional nature of the study, it is not possible to identify explanations for the findings within our study. For instance, we could explore whether the extent of residents' palliative care service use relates to the identified lack of change in their total comfort in the last week of life (i.e., temporal relationship).

Our study clearly showed that between 2010 and 2015, there is a substantially higher prevalence of nursing home residents with dementia with very minimal change in their clinical and socio-demographic characteristics. Over this relatively short period, almost an additional 15% of the residents die with dementia. Perhaps, this is because such increase in the prevalence of dementia also occurred in the home setting, as the 2016 estimates in Flanders suggest that there were 15,855 more people with dementia in 2015 than in 2010 [48], which is congruent with the current trends in dementia prevalence in other countries in Europe [4]. At the end of life, people with dementia also have complex care needs that could complicate primary care delivery and could thus become unmanageable at home [11,12]. Hence, more people with dementia living at home may have been transferred eventually to nursing homes [24,25]. Further, over the years, nursing home residents with dementia apparently remain to have almost similar clinical and demographic characteristics, which suggests that their complex and prolonged care needs at the end of life persist over the years [11,12]. We found that among residents in 2010 and 2015, about half had advanced dementia, more than 90% developed any clinical complication in the last month of life, and the majority stayed in nursing homes for about two years. While we found a somewhat lower percentage of residents who died with severe cognitive impairment (i.e., CPS scores 5-6) in 2015 than in 2010, the percentage of residents who lost all verbal abilities, was incontinent/required assistance with eating and toileting, and lost basic psychomotor skills (i.e., GDS stage 7) increased over the years. These findings might explain the slightly higher but non-statistically significant difference in the proportion of residents with advanced dementia in 2015 than in 2010. The identified lower proportion of residents with severe cognitive impairment based on CPS scores suggests that these residents died from other diseases that do not result in cognitive impairment. Comorbidities, which often occur alongside old age and dementia, present additional challenges for nursing home staff and healthcare service delivery to residents living and dying with dementia [49].

In addition, our study showed that in the last week of the life of residents with dementia between 2010 and 2015, there was an increase in their use of medical/nursing procedures, in particular pain assessment. This is encouraging, as pain is highly prevalent among older people with dementia [50]. However, the use of other medical/nursing procedures, psychosocial interventions, and spiritual care at the end-of-life seemed to lag behind. For instance, the residents' use of assistance with eating and drinking did not change over time, which needs urgent attention, as intake problems are common in advanced dementia [11,12]. Further, there was still a substantial proportion of residents with dementia, who neither received psychosocial interventions nor spiritual care at the end of life. These findings underscore the persistent lack of attention given to the comprehensive care encompassing physical, psychosocial, and spiritual support, which are paramount to improving residents' overall comfort at the end-of-life [1].

Promoting comfort for nursing home residents with dementia is a key policy goal of care in many countries and a palliative care approach has been widely advocated to improve comfort in this population [1,51–55]. However, providing high-quality and comprehensive palliative care to and improving comfort in nursing home residents with dementia is a highly demanding and complex work for care professionals [40,41]. Our identified increase in the prevalence of nursing home residents with dementia and the minimal change in the complexity of their care needs at the end-of-life highlight the increasing complexity of the challenges faced by the nursing home sector. This evolution is likely to continue in the future, as the prevalence of dementia in Flanders has been projected to almost double by 2060 [48]. Such evolution might also be comparable with evolution in other countries that implemented similar dementia and palliative care policies and initiatives and have similarly increasing dementia prevalence [4,8,13]. Further, we found that despite an encouraging improvement in the use of pain assessment of residents with dementia, there remains a lack of change in their total comfort in the last week of life. In order to better support nursing home staff to maintain the high quality of care in nursing homes and to improve comfort at the end-of-life of a growing number of residents with dementia [9,48], there is an urgent need for continued and stronger public health investments and a more comprehensive palliative care approach in this sector [1]. The timely and consistent implementation of comprehensive palliative care in dementia approach requires a strong national and regional policy commitment and the incorporation of this approach in the attitudes and skills of nursing home staff [56,57]. Because there is still no known effective palliative care program for nursing home residents with dementia [58], future research should continue developing and evaluating palliative care programs that could improve comfort at the end-of-life in this population. Strategies on how to develop, implement, and evaluate complex palliative care interventions in nursing homes and the factors that need to be addressed in doing so have been published [59–61].

Conclusions

Our study suggests that between 2010 and 2015, there was a higher prevalence of residents with dementia in nursing homes in Flanders, Belgium who persistently have complex care needs at the end-of-life. Further, despite an encouraging improvement in the use of pain assessment of residents with dementia, there remains a lack of change in their total comfort in the last week of life. These findings highlight the increasing complexity of challenges faced by the nursing home sector, which underscores an urgent need to better support nursing homes in improving their capacities to provide timely, high-quality, and comprehensive palliative care to a growing number of nursing home residents living and dying with dementia.

Author Contributions

R.M., T.S., and L.V.d.B. made an equal substantial contribution to conceptualizing the design of the work; T.S. and N.V.D.N. collected the data; R.M. analyzed the data and drafted and revised the manuscript critically for important intellectual content. All authors made a substantial contribution to interpreting the data and revising the manuscript critically, have given the final approval of the manuscript to be submitted for publication, and have participated sufficiently in the work to take responsibility for appropriate portions of the content. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

Ethical approvals were obtained from the Medical Ethical Committee of UZ Brussel (University Hospital of Brussels; Dying Well with Dementia=B.U.N. 14320108163; PACE=B.U.N. 143201422845). All respondents (nursing home staff, general practitioners, and nursing home managers) participated voluntarily in the study and remained anonymous. Returning a questionnaire was taken as consent to participate.

Informed Consent Statement

The respondents participated voluntarily, returning a questionnaire was taken as consent to participation, and their anonymity was guaranteed by using a unique anonymous identifier.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Conflicts of Interest

The authors declare no conflict of interest.

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CHAPTER 2

Comfort and clinical events at the end of life of nursing home residents with and without dementia: The six-country epidemiological PACE study

Rose Miranda, Jenny T. van der Steen, Tinne Smets, Nele Van den Noortgate, Luc Deliens, Sheila Payne, Marika Kylänen, Katarzyna Szczerbińska, Giovanni Gambassi, Lieve Van den Block, on behalf of PACE

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ABSTRACT

Objectives. We aimed to investigate the occurrence rates of clinical events and their associations with comfort in dying nursing home residents with and without dementia.

Methods. Epidemiological after-death survey was performed in nationwide representative samples of 322 nursing homes in Belgium, Finland, Italy, Netherlands, Poland and England. Nursing staff reported clinical events and assessed comfort. The nursing staff or physician assessed the presence of dementia; severity was determined using two highly-discriminatory staff-reported instruments.

Results. The sample comprised 401 residents with advanced dementia, 377 with other stages of dementia and 419 without dementia (N=1197). Across the three groups, pneumonia occurred in 24-27% of residents. Febrile episodes (unrelated to pneumonia) occurred in 39% of residents with advanced dementia, 34% in residents with other stages of dementia and 28% in residents without dementia (P=0.03). Intake problems occurred in 74% of residents with advanced dementia, 55% in residents with other stages of dementia and 48% in residents without dementia (P<0.001). Overall, these three clinical events were inversely associated with comfort. Less comfort was observed in all resident groups who had pneumonia (advanced dementia, P=0.04; other stages of dementia, P=0.04; without dementia, P<0.001). Among residents with intake problems, less comfort was observed only in those with other stages of dementia (P<0.001) and without dementia (P=0.003), while the presence and severity of dementia moderated this association (P=0.03). Developing 'other clinical events' was not associated with comfort.

Conclusions. Discomfort was observed in dying residents who developed major clinical events, especially pneumonia which was not specific to advanced dementia. It is crucial to identify and address the clinical events potentially associated with discomfort in dying residents with and without dementia.

KEY WORDS

Dementia, palliative care, terminal care, hospice care, nursing homes

KEY POINTS

- It is crucial to better understand associations between the presence and severity of dementia, clinical events and comfort at the end of life of nursing home residents.
- Our six-country epidemiological after-death survey showed that pneumonia is associated with lower comfort in all dying nursing home residents, while intake problems are associated with lower comfort only in those without advanced dementia.
- Partially in contrast to earlier studies, our findings suggest that pneumonia is not a hallmark of advanced dementia, while intake problems are.
- Our study stresses an urgent need to address symptoms of pneumonia in a mixed nursing home population with and without dementia and supports current recommendations to forego tube feeding in residents with advanced dementia.

INTRODUCTION

As populations continue to age, the number of people with dementia in Europe is projected to almost double to about 18.8 million by 2050.[1] Dementia is incurable and characterized by a trajectory of severe disabilities persisting for months or years until death.[2,3] Because of the prolonged need for high levels of complex care,[2] half or more of people with dementia in many resource-rich countries eventually live and die in nursing homes (NH).[4] Recent estimates indicate that between 58% and 83% of NH residents have dementia, about half may be at an advanced stage.[5] While comfort may be an appropriate goal of care, residents with advanced dementia remain at risk of dying with great discomfort, potentially linked to suboptimal symptom management, overly burdensome treatments and unnecessary hospitalizations, and dying in hospitals.[2,6-10]

At the end of life, 'clinical events', i.e. any medical conditions that may lead to clinically significant changes in health status e.g. pneumonia, febrile episodes (unrelated to pneumonia) and intake problems, often occur in residents with advanced dementia, which is why it is considered a terminal condition.[2,7] However, studies suggest that such events are almost as common in moderate dementia.[10,11] While residents increasingly have dementia,[6,10] those without dementia are often very frail, highly care-dependent and have multiple comorbidities that also predispose them to developing clinical events.[6,12] It is therefore of interest to examine clinical events in residents with and without dementia, while taking dementia severity into account. Further, comfort while dying may differ between these groups, because the inability to verbalize a complaint due to cognitive decline risks inappropriate treatment.[13] Different clinical events have also been associated with different levels of comfort, with those dying from infections being at greater risk of discomfort than those dying with intake problems.[11,14-16] Therefore, a better understanding of associations between dementia, clinical events and comfort when dying will be helpful. The PACE study provides this opportunity, with relevant epidemiological data about many NH residents for whom the presence and severity of dementia was determined.[17]

We sought to determine the rates of occurrence of clinical events in the last month of life and their associations with comfort in the last week of life of NH residents with advanced dementia, other stages of dementia and without dementia.

METHODS

Design

We used data collected in the context of the PACE study, which is an epidemiological study using after-death questionnaires to collect data about residents in nationwide representative samples of NHs in Belgium, Finland, Italy, the Netherlands, Poland and England (2015).[17] The PACE study protocol and the results regarding the quality of dying and quality of end-of-life care of residents have been published.[5,17] The six countries represent different stages of development of palliative care policies and practice; Belgium, the Netherlands and England are at a more advanced stage of palliative care development.[18] In each country, NHs were selected using proportional stratified random sampling, taking region, NH type and bed capacity into account.[17] They were sampled from national lists in all countries except Italy, where samples were taken from a previously-created cluster of NHs covering three macro-regional areas and taking bed capacity and facility types into account.[19] To improve the participation rate in England, additional NHs were recruited through ENRICH, a specialist research network for NHs.[17]

Setting and participants

'Nursing homes' were collective institutional settings where on-site resident care is provided 24/7.[20] In 322 participating NHs, data were collected on 1,384 deceased residents with an overall response rate of 82%. Non-response analysis revealed no significant difference in age, sex, length of stay and place of death whether staff returned questionnaires or not.[6] Residents for whom the presence and severity of dementia could be determined were divided into three groups: advanced, other stages and no dementia.

Data collection

All PACE researchers were trained extensively to ensure standardized data collection across the countries.[17] A letter introducing the study was sent to NH directors/owner/manager asking for voluntary participation and telephone or e-mail contact was made. In each participating NH, a contact person (a NH administrator, head nurse or manager) was appointed. Assisted by a researcher, the contact person retrospectively identified all residents who died in and outside the facilities over the previous three-month period. Using administrative files, the contact person filled in a structured checklist which consisted of two parts. Part A contained identifiable names of residents and respondents, which was kept in the NH and never accessible to the researchers for the privacy of both residents and respondents. Part B contained pseudonymized codes. The contact person used the structured checklist to assign codes to paper after-death questionnaires, which he/she mailed to respondents. For each resident identified, questionnaires were distributed to nursing staff who were most involved in their care (preferably a nurse or, if not available, a care assistant), NH administrator/manager/head nurse and treating physician (general practitioner or elderly care physician). The contact person sent up to two reminders (ethics committees allowed only one in Poland and England). Respondents mailed the questionnaires directly to the research team.[17]

Measurements

The presence and severity of dementia

Dementia was considered present if the nursing staff and/or the treating physician indicated it, and no dementia where both indicated it or one where the other did not return the questionnaire or did not answer the question. To compare with earlier studies,[2,11,21,22] we defined the stages of dementia using two highly-discriminatory staff-reported instruments, Cognitive Performance Scale (CPS) and Global Deterioration Scale (GDS).[23,24] CPS uses five variables from the Minimum Data Set to group residents into six hierarchical cognitive performance categories, with higher scores indicating worse cognitive impairment.[23] GDS classifies dementia into seven stages, of which stage 7 indicates very severe cognitive decline with minimal to no verbal communication; incontinence/require assistance to eating and toileting; and loss of basic psychomotor skills.[24] Among residents with dementia, those with CPS scores of 5 to 6 and GDS stage 7 were considered to have advanced dementia, while the rest had other stages of dementia.

Clinical events in the last month of life

Clinical events in the last month of life were determined by asking the nursing staff if the resident suffered from one or more of the following events: pneumonia, febrile episodes (unrelated to pneumonia), eating or drinking problem, hip fracture, stroke, gastrointestinal bleeding, cancer or other important events. Whether these 'other important events' can be considered clinical events was discussed by RM, JVDS, TS and NVDN, who have research, nursing and medical backgrounds. Pneumonia, febrile episodes and intake problems were considered as major categories of clinical events.[2] Another category was created for the occurrence of hip fracture, stroke, gastrointestinal or other clinical events (e.g. muscular atrophy or subdural hematoma). We excluded cancer (n=146), because we could not determine whether cancer had only developed in the last month of life.

Comfort in the last week of life

Comfort in the last week of life was assessed by the nursing staff using a validated 14-item scale: Comfort Assessment in Dying-End-of-Life in Dementia (CAD-EOLD).[25,26] CAD-EOLD comprises four subscales: physical distress, dying symptoms, emotional distress and well-being. Total scores range from 14-42, with higher scores representing more comfort. CAD-EOLD has better psychometric properties and user-friendliness than other comfort measures including a mixed NH population with and without dementia.[27-29]

Potential confounders

Potential confounding factors considered were age when dying, sex, length of stay in NHs and place of death, all of which were reported by NH administrators. Place of death may differ between people with and without dementia and this has been shown to affect comfort of people with advanced dementia.[30] We also determined whether the respondent was a nurse or other staff.

Data analyses

Analyses were conducted in IBM SPSS statistics version 25 (© IBM Corporation). We reported resident characteristics, occurrence rates of the clinical events and comfort by group (dementia). We presented the frequencies for the CAD-EOLD total scores along with estimated marginal means and 95% confidence intervals (CI). To account for the multilevel nature of the data (e.g. residents nested within country, nursing homes or nursing staff most involved in care), generalized linear mixed models (GLMM) analyses were performed. Firstly, we compared resident characteristics, occurrence rates of the clinical events and comfort between the groups. Secondly, in the total sample, we estimated the association between each clinical event and comfort. Thirdly, separately for each of the groups, we estimated the association between each clinical event and comfort. Finally, to investigate whether this association differed between the three defined groups, we conducted association analyses in the total sample while adding the interaction term 'dementia*clinical events' as a covariate in the models. All association analyses were adjusted for age, sex, length of stay and place of death. All variables that were fitted in the GLMMs can be found in Supplementary table 1. Sensitivity analyses explored comfort of residents who had combined pneumonia and intake problems or febrile episodes and intake problems. Testing was two-sided. Statistical significance was set at $P<0.05$.

Ethics

In each country, we obtained ethical approval from respective ethics committees or waivers to collect data of deceased residents (Netherlands and Italy). The respondents participated voluntarily and returning a questionnaire was taken as consent to participation.

RESULTS

Resident characteristics

The sample comprised 1,197 residents, of whom 401 had advanced dementia, 377 had another stage of dementia and 419 had no dementia. At the time of death, residents with other stages of dementia were the oldest (mean age 86.6 years), followed by those with advanced dementia (mean age 85.5 years) and those without dementia (82.4 years; *P*<0.001, Table 1). All groups were predominantly female, in particular 60% (without dementia), 63% (with other stages of dementia) and 68% (with advanced dementia) (*P*=0.04). Those with advanced dementia had the longest length of stay (63% one year or more, 26% six months or less), followed by those with other stages of dementia (58% one year or more, 31% six months or less) and those without dementia (50% one year or more, 42% six months or less; *P*<0.001). The majority died in the NH, in particular 69% without dementia, 72% with other stages of dementia, and 78% with advanced dementia (*P*=0.001).

Table 1. Resident characteristics by resident groups (N=1197)

	advanced dementia (N=401)		**other stages of dementia (N=377)**		**no dementia (N=419)**		**Between-group difference** *P*-values[†]
Age at time of death, mean [SD]	85.5	[7.9]	86.6	[7.8]	82.4	[11.6]	**<0.001**
Sex, female n (%)	274	(68)	239	(63)	250	(60)	**0.04**
Place of death[‡]**,** nursing home n (%)	311	(78)	270	(72)	287	(69)	**0.001**
Length of stay in nursing home, n (%)							
up to 6 months	101	(26)	110	(31)	164	(42)	**<0.001**
6-12 months	41	(11)	40	(11)	33	(8)	
1 year or more	239	(63)	206	(58)	198	(50)	
Respondent for resident, n (%)							0.83
Nurse most involved in care[§]	306	(76)	287	(76)	302	(72)	
Other staff most involved in care[¶]	91	(23)	87	(23)	113	(27)	

Abbreviations: SD=standard deviation.

[†] Calculated using generalized linear mixed model analyses to account for correlation of data within country and nursing homes; 'other' categories not included in calculation of *P*-values.

[‡] Examples of places of death other than nursing homes include facility hospice/palliative care unit or general ward and ICU in hospital.

[§] Nurse most involved in care included registered nurse, head nurse/matron and reference nurse; and licensed practical nurse in Finland.

[¶] Other staff most involved in care included nursing assistants, care assistants and other nursing role.

Missing data: advanced dementia: age=12 (3%); sex=15 (4%); place of death=12 (3%); length of stay=20 (5%); respondent for resident=4 (1%) | other stages of dementia: age=14 (4%); sex=10 (3%); place of death=19 (5%); length of stay=21 (6%); respondent for resident=3 (1%) | no dementia: age=25 (6%); sex=19; place of death=19 (5%); length of stay=24 (6%); respondent for resident=4 (1%).

Clinical events and comfort

In the last month of life, 24-27% of residents in all groups had pneumonia (no group difference; *P*=0.91; Table 2). Febrile episodes occurred at different rates in residents with advanced dementia (39%), other stages of dementia (34%) and without dementia (28%; *P*=0.03). Similarly, intake problems occurred in advanced dementia (74%), other stages of dementia (55%) and without dementia (48%; *P*<0.001). Across the groups, the occurrence rates of ‘other clinical events’ ranged from 18% (advanced dementia) to 24% (without dementia; *P*=0.16). The estimated marginal means of comfort total scores did not differ (*P*=0.25), while it ranged from 30.7 in advanced dementia to 31.3 in other stages. For combined occurrence of major clinical events, sensitivity analyses showed no substantial difference in the association with comfort in the three groups (Supplementary table 2).

Table 2. Clinical events and comfort by resident groups (N=1197)

	advanced dementia (N=401)		other stages of dementia (N=377)		no dementia (N=419)		Between-group difference *P*-values[†]
Clinical events, n(%)							
Pneumonia	102	(25)	100	(27)	101	(24)	0.91
Febrile episode	155	(39)	128	(34)	118	(28)	**0.03**
Intake problem	297	(74)	206	(55)	200	(48)	**<0.001**
Other clinical events[‡]	76	(19)	68	(18)	99	(24)	0.24
CAD-EOLD total scores,[§] n%	384	(96)	358	(95)	385	(92)	
Estimated marginal means, (95% CI)	30.7	(29.3-32.1)	31.3	(29.9-32.7)	31.2	(29.7-32.6)	0.25

Abbreviations: CAD-EOLD=Comfort Assessment in Dying – End of Life Dementia Scale; CI= confidence interval.

[†] Calculated using generalized linear mixed model analyses to account for correlation of data within country, nursing homes and nursing staff most involved in care.

[‡] ‘Other clinical events’ was considered present if any of the following clinical events was reported: hip fracture, stroke, gastrointestinal bleeding and other events reported.

[§] Total scores are averages per whole scale multiplied by total number of items (i.e. 14). Cases with missing values on more than 25% of items per scale were excluded from total score calculation; scores range from 14 to 42; higher scores indicate better comfort at death. Missing data: CAD-EOLD: advanced dementia=17 (4%); other stages of dementia=19 (5%); no dementia=34 (8%).

Associations between clinical events and comfort

We found that comfort was inversely associated with pneumonia (P<0.001), febrile episodes (*P*=0.001) and intake problems (P<0.001). No significant association was found between ‘other clinical events’ and comfort (*P*=0.83). Results persisted after adjustment for confounding factors.

Associations between clinical events and comfort in the three resident groups

Pneumonia

In all groups, the estimated mean comfort scores were lower among residents who had pneumonia than those who did not (Table 3, crude models 1). Among those with pneumonia, comfort scores amounted to approximately 30 (between 29.2 for those without dementia and 30.3 for those with other stages of dementia). Among those who did not have pneumonia, comfort scores were 31.1 (advanced dementia) and 31.6 in the other two groups. The presence and severity of dementia did not moderate the association between pneumonia and comfort (*P*=0.30). After adjustment for confounding factors, the association between lower comfort and pneumonia remained significant in all groups with no moderation by dementia (Table 3, adjusted models 1).

Table 3. Associations between clinical events and comfort by resident groups (N=1197)

Association analyses		advanced dementia (N=401)		other stages of dementia (N=377)		no dementia (N=419)		**Between-group difference in the association** *P* -values§
		CAD-EOLD total scores†						
Models	**Clinical events**	Estimated marginal means (95% CI)	*P*-values‡	Estimated marginal means (95% CI)	*P* -values‡	Estimated marginal means (95% CI)	*P* -values‡	
1. Pneumonia								
Crude models 1	Yes	29.8 (28.1-31.5)	**0.03**	30.3 (29.0-31.6)	**0.03**	29.2 (27.5-30.8)	**<0.001**	0.30
	No	31.1 (29.6-32.6)		31.6 (30.5-32.7)		31.6 (30.2-32.9)		
Adjusted models 1	Yes	29.5 (27.7-31.3)	**0.04**	30.2 (29.0-31.4)	**0.04**	28.9 (27.4-30.3)	**<0.001**	0.33
	No	30.8 (29.2-32.4)		31.6 (30.6-32.6)		31.3 (30.0-32.5)		
2. Febrile episodes (unrelated to pneumonia)								
Crude models 2	Yes	30.1 (28.6-31.7)	0.11	30.1 (29.0-31.3)	**0.003**	30.4 (29.0-31.9)	0.18	0.78
	No	31.0 (29.6-32.5)		31.8 (30.8-32.8)		31.3 (30.0-32.5)		
Adjusted models 2	Yes	29.7 (28.1-31.4)	0.10	29.9 (28.7-31.1)	**0.004**	29.9 (28.6-31.2)	0.09	0.77
	No	30.7 (29.2-32.2)		31.7 (30.8-32.7)		31.0 (30.0-32.0)		
3. Intake problems								
Crude models 3	Yes	30.7 (29.2-32.2)	0.65	30.3 (29.2-31.4)	**<0.001**	30.2 (28.8-31.5)	**0.004**	0.052
	No	30.9 (29.2-32.6)		32.5 (31.3-33.6)		31.8 (30.5-33.1)		
Adjusted models 3	Yes	30.4 (28.7-32.4)	0.78	30.0 (29.0-31.0)	**<0.001**	29.7 (28.6-30.9)	**0.003**	**0.03**
	No	30.6 (28.7-32.4)		32.4 (31.4-33.4)		31.4 (28.6-30.9)		
4. Other clinical events								
Crude models 4	Yes	30.3 (28.5-32.1)	0.40	30.6 (29.0-32.1)	0.24	31.7 (30.0-33.4)	0.21	0.14
	No	30.8 (29.4-32.3)		31.4 (30.4-32.4)		30.9 (29.5-32.2)		
Adjusted models 4	Yes	30.2 (28.2-32.1)	0.63	30.1 (28.6-31.7)	0.13	31.4 (29.9-32.8)	0.23	0.12
	No	30.5 (28.9-32.1)		31.3 (30.4-32.2)		30.5 (29.5-31.6)		

Abbreviations: CAD-EOLD=Comfort Assessment in Dying – End of Life Dementia Scale; CI=confidence interval.

† Total scores are averages per whole scale multiplied by total number of items (i.e. 14). Cases with missing values on more than 25% of items per scale were excluded from total score calculation; scores range from 14 to 42; higher scores indicate better comfort when dying.

‡ Calculated using generalized linear mixed model (GLMM) analyses to account for correlation of data within country, nursing homes and nursing staff most involved in care.

§ In addition to the previous GLMM analyses, the interaction term 'dementia*clinical events' was added as a covariate.

Crude models=crude associations between each of the clinical events and comfort; Adjusted models=adjusted for residents' age at time of death, sex, length of stay in nursing homes and place of death.

Febrile episodes (unrelated to pneumonia)

Only those with other stages of dementia who had febrile episodes had lower comfort scores than those who did not have febrile episodes (30.1 *vs.* 31.8, *P*=0.003, Table 3, crude models 2). Although not statistically significant, a similar pattern of association between febrile episodes and comfort was found in those with advanced dementia and without dementia; the association did not differ between groups (*P*=0.78). The results were similar after adjusting the analyses for confounding factors (Table 3, adjusted models 2).

Intake problems

Among residents with other stages of dementia and without dementia, those with intake problems had lower comfort scores than those without (Table 3, crude models 3). However, intake problems were not associated with comfort in advanced dementia (*P*=0.65). These results persisted after adjustment for confounding factors (Table 3, adjusted models 3). The presence and severity of dementia did not moderate the associations between intake problems and comfort in the crude models (*P*=0.052), but it did after adjustment for confounding factors (*P*=0.03).

To better understand the differential associations between intake problems and comfort, we performed two secondary analyses. Firstly, we examined whether potential differences in administration rates of enteral or parenteral nutrition and fluid may have confounded this association. We found group differences in the administration rates of enteral nutrition (*P*=0.005), for which we adjusted the analyses. However, this did not change the results (Supplementary table 3). Secondly, we investigated the associations between intake problems and the four CAD-EOLD subscales. We found similar patterns of associations between intake problems and the subscale ‘dying symptoms’, but none between intake problems and ‘well-being’. Only in residents with other stages of dementia were intake problems associated with the subscales physical and emotional distress. After further adjustment for enteral administration of nutrition, only the association between intake problems and ‘physical distress’ differed between the groups (*P*=0.049; Supplementary table 4).

Other clinical events

In all groups, ‘other clinical events’ was not associated with comfort. The presence and severity of dementia did not moderate the association between ‘other clinical events’ and comfort (Table 3, crude models 4). These results persisted after adjusting for confounding factors (Table 3, adjusted models 4).

DISCUSSION

Our study demonstrates that in the last month of life about a quarter of NH residents developed pneumonia across the three groups of residents with advanced, other stages and no dementia. Febrile episodes and intake problems were more common, but occurrence rates differed between groups; those with advanced dementia more frequently developed febrile episodes and intake problems. Overall, developing these three major clinical events was associated with less comfort, but this varied according to the presence and severity of dementia. While the presence and severity of dementia did not moderate a consistently negative association between pneumonia and comfort across the three groups, it did moderate the association between intake problems and comfort. Among residents who developed intake problems, less comfort was observed only in residents with other stages of dementia and without dementia. Developing 'other clinical events' was not associated with comfort in any of the groups.

Overall, our findings suggest that the major clinical events are associated with discomfort when dying, particularly pneumonia which affects about a quarter of the NH population regardless of the presence and severity of dementia. While earlier studies regard pneumonia and intake problems as hallmarks of advanced dementia,[2,7,11] our study provides evidence that partially suggests otherwise. The finding that the occurrence rates of pneumonia and its association with comfort did not differ between the three groups suggests that pneumonia is not a hallmark of advanced dementia but can possibly be related to frailty more generally.[31,32] The distressing respiratory symptoms of pneumonia, e.g. dyspnea, laboured/rapid breathing or dry/hacking cough, may be perceived as profoundly uncomfortable for affected residents.[33-36] Further, even among cognitively-impaired residents who could not communicate, breathing difficulties remain easily observable.[36-38]

Our findings concur with earlier studies suggesting that intake problems are a hallmark of advanced dementia.[2,11,39] In line with earlier studies,[2,11,40] our findings suggest that intake problems are common in residents with advanced dementia. Further, we found that compared with residents without dementia and with other stages of dementia, intake problems were more likely to occur but remarkably less likely to be negatively associated with comfort in residents with advanced dementia. These results persisted even after accounting for potential differences in administration rates of enteral or parenteral nutrition and fluid. Perhaps nursing staff perceive intake problems as 'natural' or inherent in advanced dementia and may not link them with discomfort.[7,40] However, a genuine difference is more likely, as we used a validated scale to assess (dis)comfort, inviting staff to consider each of 14 items separately.[27-29] Further, causes may differ; residents with advanced dementia often develop intake problems gradually, whereas in frail residents without dementia, intake problems may develop more suddenly secondary to acute infections or other conditions.[41-42] Our study suggests that the cause and origin of intake problems, which can be multifactorial, may differ between those with advanced dementia and without dementia. Nonetheless, this finding supports current recommendations to forego tube feeding in residents with advanced dementia, as it may be burdensome and lack clinical benefit in ameliorating malnutrition, maintaining skin integrity or preventing aspiration pneumonia.[7,43] Tube feeding-related complications were also found to account for about half of all emergency department visits in advanced dementia.[44]

Further, we found that 'other clinical events' was associated with neither comfort nor dementia status, maybe because this category is too heterogeneous, e.g. muscular atrophy may not cause substantial discomfort.

Implications for clinical care and research

Our study provides more insight into the associations between different clinical events and comfort at the end of life in NH residents with advanced, other stages and no dementia. It highlights an urgent need for physicians, and especially nurses, to be aware that developing pneumonia likely involves substantial discomfort in all, regardless of the presence and severity of dementia.[45] While this finding may not be surprising,[16] it is remarkable that despite numerous efforts to improve end-of-life care in NHs, pneumonia still seems to cause considerable suffering. Providing those who are dying with symptom-relieving treatments such as antipyretics, opioids or oxygen may promote comfort and relieve suffering.[36] Nonetheless, it should be considered that there is a myriad of potential causes of pneumonia and there may be no single approach to address related discomfort.[46] In the future, more research is needed to develop and evaluate interventions that can improve comfort in a mixed NH population with pneumonia.

Finally, although intake problems may not be associated with comfort in residents with advanced dementia, if such problems are present it remains essential to consider rigorous clinical assessment to exclude acute conditions (e.g. stroke) and to address easily-reversible causes (e.g. dental problems).[7,40] High-calorie supplements and other oral feeding options can also be offered to this population as an alternative to tube feeding.[47] Further, while we found that intake problems may be associated with discomfort in residents without dementia and with other stages of dementia, the evidence base to guide clinicians about artificial nutrition and hydration is still small.[40,48] Clinicians can address intake problems after careful assessment and consideration of different options as guided by the goals of care that should be discussed where possible with the resident who is dying and those close to them.[40,48] Nevertheless, future research should explore differences in the cause and origin of intake problems and pneumonia and investigate how they relate to comfort in those with and without dementia.

Strengths and limitations

This is the first study to examine associations between dementia, clinical events and comfort in dying NH residents. Retrospective data collection through the nursing staff most closely involved in care is a feasible method for large-scale population-based epidemiological studies on the end of life. This limits potential bias in prospective sampling related to the underrepresentation of people who live longer than the study follow-up period or who have dementia for whom the terminal phase is difficult to predict. The CAD-EOLD scale which was used to measure comfort in the last week of life of residents has been shown to be valid in advanced dementia, less advanced dementia and mixed NH population.[27-29] However, because data were collected after death, there might be some recall bias. Finally, given the cross-sectional nature of data, we could not explore whether the timing of the occurrence of intake problems relate to the observed discomfort in residents with advanced dementia (i.e. temporal relationship). Further, we could not make causal inferences between clinical events and comfort.

Conclusions

Overall, developing clinical events such as pneumonia, febrile episodes and intake problems was associated with discomfort in dying NH residents. However, this negative association varied according to the presence and severity of dementia only for particular events. Regardless of the presence and severity of dementia, discomfort was observed in residents who had pneumonia, while among residents who had intake problems, discomfort was observed only in those without dementia and with other stages of dementia. To promote comfort in dying NH residents, it is crucial to identify and manage symptoms of the clinical events potentially associated with substantial discomfort, especially pneumonia in a mixed NH population with or without dementia.

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DATA STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

AUTHORSHIP

All authors meet criteria for authorship as stated in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals. All authors gave final approval of the submitted manuscript and agreed to be accountable for all aspects of the work. All authors' specific contributions are listed below.

- Study concept and design: RM, JTVDS, TS, LD, MK, KS, GG and LVDB
- Acquisition of data: TS, NVDN, SP, MK, KS, GG
- Analysis and interpretation of data: RM, JTVDS, TS, NVDN, LD, MK, SP, KS, GG and LVDB
- Preparation of manuscript: RM, JTVDS, TS, NVDN, LD, MK, SP, KS, GG and LVDB

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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SUPPLEMENTARY FILES – CHAPTER 2

Supplementary table 1. Variables fitted in the generalized linear mixed models

Data analyses	Random factors	Fixed effect	Covariates
Sample characteristics	Country and nursing homes[†]	**Dementia**	**Age at time of death; sex; place of death; length of stay in nursing home; respondent for resident**
Occurrence rates of clinical events	Country, nursing homes and nursing staff most involved in care[‡]	**Dementia**	Each of the clinical events[§]
Comfort	Country, nursing homes and nursing staff most involved in care[‡]	**Dementia**	**CAD-EOLD total scores**
Association analyses			
Crude association of clinical events with comfort **in the total sample**	Country, nursing homes and nursing staff most involved in care[‡]	**CAD-EOLD total scores**	**Each of the clinical events[§]**
Adjusted association of clinical events with comfort **in the total sample**	Country, nursing homes and nursing staff most involved in care[‡]	**CAD-EOLD total scores**	Each of the clinical events[§] ; **age at time of death; sex; place of death; length of stay in nursing home**
Crude association of clinical events with comfort for each group[¶]	Country, nursing homes and nursing staff most involved in care[‡]	**CAD-EOLD total scores**	Each of the clinical events[§]
Adjusted association of clinical events with comfort for each group[¶]	Country, nursing homes and nursing staff most involved in care[‡]	**CAD-EOLD total scores**	Each of the clinical events[§] **; age at time of death; sex; place of death; length of stay in nursing home**
Crude association of clinical events with comfort between the groups[#]	Country, nursing homes and nursing staff most involved in care[‡]	**CAD-EOLD total scores**	Each of the clinical events[§] ; dementia*each of the s clinical events
Adjusted association of clinical events with comfort between the groups[#]	Country, nursing homes and nursing staff most involved in care[‡]	**CAD-EOLD total scores**	Each of the clinical events[§] ; dementia*each of the clinical events **; age at time of death; sex; place of death; length of stay in nursing home**

[†] Accounted the analyses for clustering at the level of country and nursing homes, because data on sample characteristics were nested in these levels.

[‡] In addition to the analyses being adjusted for clustering at the level of country and nursing homes, the nursing staff level was accounted for because the nursing staff most involved in care provided these data for multiple residents.

[§] Each of the clinical events = pneumonia OR febrile episodes OR intake problems OR any other clinical events.

[¶] These association analyses were conducted separately for each of the three groups.

[#] These association analyses were conducted in the total sample while adding the interaction term 'dementia*each of the clinical events' as a covariate in the model.

Supplementary table 2. Sensitivity analyses to investigate the association between combined occurrence of clinical events and their association with comfort

Residents who had pneumonia and/or intake problems (N=561)								
		advanced dementia (N=154)		**other stages of dementia (N=181)**		**no dementia (N=226)**		**Between-group difference** P-values[§]
1. Residents who had both pneumonia and intake problems		n (%) 76 (49.4)		n (%) 55 (30.4)		n (%) 54 (23.9)		**<0.001**
2. Association of (both) pneumonia and intake problems with CAD-EOLD total scores		**CAD-EOLD total scores[†]**						**Between-group difference in association** P-values[§]
		Estimated marginal means and 95% CI	p-values[‡]	Estimated marginal means and 95% CI	p-values[‡]	Estimated marginal means and 95% CI	p-values[‡]	
Crude models	Both	29.5 (27.7-31.4)	0.10	29.3 (27.9-30.7)	**<0.001**	28.3 (26.6-30.0)	**<0.001**	0.054
	Either	30.9 (29.1-32.8)		32.7 (31.7-33.8)		32.1 (30.9-33.3)		
Adjusted models	Both	29.6 (27.5-31.7)	0.09	29.1 (27.5-30.7)	**<0.001**	27.2 (25.4-29.0)	**<0.001**	0.08
	Either	31.1 (29.0-33.2)		32.7 (31.5-34.0)		31.3 (30.1-32.5)		

Residents who had febrile episodes (unrelated to pneumonia) and/or intake problems (N=633)								
		advanced dementia (N=185)		**other stages of dementia (N=205)**		**no dementia (N=243)**		**Between-group difference** P-values[§]
1. Residents who had both febrile episodes and intake problems		n (%) 118 (63.8)		n (%) 81 (39.5)		n (%) 71 (29.2)		**<0.001**
2. Association of (both) febrile episodes and intake problems with CAD-EOLD total scores		**CAD-EOLD total scores[†]**						**Between-group difference in association** P-values[§]
		Estimated marginal means and 95% CI	p-values[‡]	Estimated marginal means and 95% CI	p-values[‡]	Estimated marginal means and 95% CI	p-values[‡]	
Crude models	Both	30.1 (28.4-31.7)	0.19	29.1 (27.8-30.5)	**<0.001**	29.3 (27.6-30.9)	**0.002**	0.14
	Either	31.1 (29.4-32.9)		32.8 (31.6-34.0)		31.7 (30.5-33.0)		
Adjusted models	Both	29.9 (28.1-31.7)	0.07	29.0 (27.3-30.7)	**<0.001**	28.6 (26.9-30.3)	**0.001**	0.17
	Either	31.4 (29.4-33.3)		33.1 (31.6-34.5)		31.3 (30.1-32.5)		

Abbreviations: CAD-EOLD=Comfort Assessment in Dying – End of Life Dementia Scale; CI=confidence interval; GLMM= generalized linear mixed model.

[†] Total scores are averages per whole scale multiplied by total number of items (i.e. 14). Cases with missing values on more than 25% of items per scale were excluded from total score calculation; scores range from 14 to 42; higher scores indicate better comfort.

[‡] Calculated using GLMM analyses to account for correlation of data within country, nursing homes and nursing staff most involved in care.

[§] In addition to the previous GLMM analysis, the Interaction term dementia*clinical events was added as a covariate.

Crude models depicted the crude associations between the combined clinical events and comfort.; Adjusted models were adjusted for residents' age at time of death, sex, length of stay in nursing homes and place of death.

Supplementary table 3. Secondary analyses to understand the differential associations between intake problems and comfort

1) Administration rates of enteral nutrition, parenteral nutrition and artificial fluid in the last month of life by dementia							
	advanced dementia (N=401)		other stages of dementia (N=377)		no dementia (N=419)		Between-group Difference *P*-values†
	n	(%)	n	(%)	n	(%)	
Enteral nutrition‡	40	(12)	16	(4)	48	(13)	**0.005**
Parenteral nutrition‡	55	(17)	23	(6)	32	(9)	0.23
Artificial fluids‡	119	(35)	89	(27)	11	(30)	0.51

2) Further adjusted the association between intake problems and CAD-EOLD scores for enteral administration of nutrition								
		advanced dementia (N=401)		other stages of dementia (N=377)		no dementia (N=419)		Between-group difference in association *P*-values#
		CAD-EOLD total scores§						
		Estimated marginal means and 95% CI	*P*-values¶	Estimated marginal means and 95% CI	*P*-values¶	Estimated marginal means and 95% CI	*P*-values¶	
Adjusted model A	Yes	30.7 (29.1-32.3)	0.75	28.1 (26.3-29.8)	**<0.001**	29.3 (27.9-30.6)	**0.02**	**0.01**
	No	30.5 (28.6-32.4)		30.4 (28.4-32.3)		30.7 (29.3-32.1)		

Abbreviation: ref=reference; CAD-EOLD=Comfort Assessment in Dying – End of Life Dementia Scale; CI=confidence interval; GLMM= generalized linear mixed model.

[†] Calculated using GLMM analyses to account for correlation of data within country, nursing homes and nursing staff.

[‡] Dichotomous variables indicating whether the treatments for intake problems were administered or not in the last month of life. These dichotomous variables were created by combining three separate variables: YES, if (i) treatment was administered in the last month of life (excluding last week) or (ii) last week of life | and NO, if the (iii) the treatment was not administered in the last month of life.

[§] Total scores are averages per whole scale multiplied by total number of items (i.e. 14). Cases with missing values on more than 25% of items per scale were excluded from total score calculation; scores range from 14 to 42; higher scores indicate better comfort.

[¶] Calculated using generalized linear mixed model analyses to account for correlation of data within country, nursing homes and nursing staff most involved in care.

[#] In addition to the previous GLMM analyses, the Interaction term dementia*clinical events was added as a covariate.

Adjusted model A was adjusted for confounding factors (residents' age at time of death, sex, length of stay in nursing homes and place of death) and enteral administration of nutrition in the last month of life.

Missing data: enteral administration of nutrition: advanced dementia=71 (18%); other stages of dementia=42 (11%); no dementia=48 (12%) | parenteral administration of nutrition: advanced dementia=77 (19%); other stages of dementia=54 (14%); no dementia=58 (14%) | artificial administration of fluid: advanced dementia=60 (15%); other stages of dementia=42 (11%); no dementia=45 (11%).

Supplementary table 4. Secondary analyses to investigate the association between intake problems and the four CAD-EOLD subscales

Models	Clinical events	advanced dementia (N=401)		other stages of dementia (N=377)		no dementia (N=419)		Between-group difference in association
		CAD-EOLD subscale scores[†]						
		Estimated marginal means and 95% CI	*P*-values[‡]	Estimated marginal means and 95% CI	*P*-values[‡]	Estimated marginal means and 95% CI	*P*-values[‡]	*P*-values[§]
3.1 Intake problems and CAD-EOLD subscale – Physical distress[¶]								
Crude model 3.1	Yes	30.4 (28.8-31.9)	0.93	29.5 (27.9-31.2)	**0.01**	28.9 (27.3-30.5)	0.15	0.15
	No	30.3 (28.5-32.1)		31.3 (29.6-33.1)		30.0 (28.4-31.5)		
Adjusted model 3.1	Yes	30.0 (28.2-31.8)	0.94	29.0 (27.2-30.8)	**0.002**	28.1 (26.4-29.8)	0.15	0.09
	No	30.0 (27.8-32.1)		31.2 (29.4-33.1)		29.2 (27.7-30.8)		
Adjusted model 3.1a	Yes	30.2 (28.3-32.1)	0.53	27.0 (24.4-29.6)	**0.01**	28.3 (26.2-30.3)	0.10	**0.049**
	No	29.7 (27.4-32.0)		28.9 (26.2-31.7)		29.6 (27.5-31.7)		
3.2 Intake problems and CAD-EOLD subscale – Dying symptoms[¶]								
Crude model 3.2	Yes	30.6 (28.7-32.5)	**0.03**	31.2 (29.6-32.7)	**<0.001**	31.1 (29.5-32.7)	**<0.001**	0.32
	No	32.4 (30.2-34.6)		34.2 (32.5-35.8)		34.6 (33.0-36.2)		
Adjusted model 3.2	Yes	30.6 (28.4-32.8)	0.07	30.9 (29.1-32.6)	**<0.001**	30.4 (28.6-32.3)	**<0.001**	0.18
	No	32.2 (29.7-34.7)		34.5 (32.7-36.2)		34.0 (32.3-35.8)		
Adjusted model 3.2a	Yes	29.6 (27.4-31.8)	0.08	27.3 (24.7-30.0)	**<0.001**	29.3 (26.9-31.7)	**0.004**	0.25
	No	31.3 (28.6-33.9)		30.6 (27.8-33.4)		31.8 (29.4-34.3)		
3.3 Intake problems and CAD-EOLD subscale – Emotional distress[¶]								
Crude model 3.3	Yes	33.0 (31.3-34.5)	0.49	32.7 (31.5-33.9)	**<0.001**	33.1 (31.8-34.4)	0.19	0.18
	No	33.5 (31.5-35.4)		35.3 (34.0-36.5)		34.0 (32.8-35.3)		
Adjusted model 3.3	Yes	32.9 (31.3-34.5)	0.49	32.7 (31.3-34.1)	**0.001**	33.1 (31.8-34.5)	0.13	0.18
	No	33.5 (31.5-35.4)		35.2 (33.8-36.6)		34.2 (33.0-35.4)		
Adjusted model 3.3a	Yes	34.4 (32.7-36.2)	0.92	31.5 (29.1-33.9)	**0.001**	33.2 (31.5-35.0)	0.21	0.06
	No	34.4 (32.1-36.6)		34.1 (31.5-36.7)		34.2 (32.4-36.0)		
3.4 Intake problems and CAD-EOLD subscale – Well-being[¶]								
Crude model 3.4	Yes	27.3 (24.3-30.3)	0.36	27.1 (24.5-29.7)	0.27	26.7 (23.0-30.5)	0.58	0.50
	No	26.4 (23.2-29.7)		28.0 (25.4-30.7)		27.2 (23.4-30.9)		
Adjusted model 3.4	Yes	27.5(24.4-30.5)	0.45	26.9 (24.2-29.6)	0.31	26.4 (22.6-30.2)	0.35	0.56
	No	26.8 (23.5-30.1)		27.8 (25.1-30.5)		27.1 (23.4-30.9)		
Adjusted model 3.4a	Yes	27.6 (24.0-31.1)	0.24	25.5 (22.0-28.9)	0.43	25.8 (21.8-29.8)	0.53	0.27
	No	26.3 (22.5-30.2)		26.2 (22.6-29.9)		26.4 (22.3-30.4)		

Abbreviations: CAD-EOLD=Comfort Assessment in Dying – End of Life Dementia Scale; CI=confidence interval; GLMM= generalized linear mixed model.

[†] Scores are averages per subscale multiplied by total number of items per subscale. Cases with missing values on more than 25% of items per subscale were excluded; higher scores indicate better comfort.

[‡] Calculated using GLMM analyses to account for correlation of data within country, nursing homes and nursing staff most involved in care.

[§] In addition to the previous GLMM analyses, the Interaction term dementia*clinical events was added as a covariate.

[¶] Physical distress subscale - discomfort, pain, restlessness and shortness of breath | Dying symptoms subscale – shortness of breath, choking, gurgling and difficulty swallowing | Emotional distress subscale – fear, anxiety, crying and moaning | Well-being subscale (reverse coded) – serenity, peace and calm.

Crude models 3.1 to 3.4 depicted the crude associations between each of the clinical events and comfort; Adjusted models 3.1 to 3.4 were adjusted for confounding factors (residents' age at time of death, sex, length of stay in nursing homes and place of death); Adjusted models A were further adjusted for enteral administration of nutrition in the last month of life.

CHAPTER 3

No difference in effects of ‘PACE Steps to Success’ palliative care program for nursing home residents with and without dementia: A pre-planned subgroup analysis of the seven-country PACE trial

Rose Miranda, Tinne Smets, Nele Van Den Noortgate, Jenny T. van der Steen, Luc Deliens, Sheila Payne, Katarzyna Szczerbińska, Sophie Pautex, Liesbeth Van Humbeeck, Giovanni Gambassi, Marika Kylänen, and Lieve Van den Block, on behalf of PACE.

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ABSTRACT

Background. 'PACE Steps to Success' is a multicomponent training program aiming to integrate generalist and non-disease-specific palliative care in nursing homes. This program did not improve residents' comfort in the last week of life, but it appeared to improve quality of care and dying in their last month of life. Because this program included only three dementia-specific elements, its effects might differ depending on the presence or stage of dementia. We aimed to investigate whether the program effects differ between residents with advanced, non-advanced, and no dementia.

Methods. Pre-planned subgroup analysis of the PACE cluster-randomized controlled trial in 78 nursing homes in seven European countries. Participants included residents who died in the previous four months. The nursing home staff or general practitioner assessed the presence of dementia; severity was determined using two highly-discriminatory staff-reported instruments. Using after-death questionnaires, staff assessed comfort in the last week of life (Comfort Assessment in Dying–End-of-Life in Dementia-scale; primary outcome) and quality of care and dying in the last month of life (Quality of Dying in Long-Term Care scale; secondary outcome).

Results. At baseline, we included 177 residents with advanced dementia, 126 with non-advanced dementia and 156 without dementia. Post-intervention, respectively in the control and the intervention group, we included 136 and 104 residents with advanced dementia, 167 and 110 with non-advanced dementia and 157 and 137 without dementia. We found no subgroup differences on comfort in the last week of life, comparing advanced versus without dementia (baseline-adjusted mean sub-group difference 2.1; p-value=0.177), non-advanced versus without dementia (2.7; p=0.092), and advanced versus non-advanced dementia (-0.6; p=0.698); or on quality of care and dying in the last month of life, comparing advanced and without dementia (-0.6; p=0.741), non-advanced and without dementia (-1.5; p=0.428), and advanced and non-advanced dementia (0.9; p=0.632).

Conclusions The lack of subgroup difference suggests that while the program did not improve comfort in dying residents with or without dementia, it appeared to equally improve quality of care and dying in the last month of life for residents with dementia (regardless of the stage) and those without dementia. A generalist and non-disease-specific palliative care program, such as PACE Steps to Success, is a useful starting point for future palliative care improvement in nursing homes, but to effectively improve residents' comfort, this program needs further development.

Trial registration. ISRCTN, ISRCTN14741671. Registered 8 July 2015 – Retrospectively registered.
http://www.isrctn.com/ISRCTN14741671

Key words

Nursing home care, end of life care, bereavement, pain, communication, neurological conditions

BACKGROUND

Between 14% and 29% of people aged 65 years and over in many developed countries die in nursing homes.[1] However, the quality of dying and end-of-life care in this setting, even in countries with high levels of palliative care development, is sub-optimal.[2,3] To contribute high-quality evidence to address this problem, we developed 'PACE Steps to Success', which is a multicomponent program aiming to integrate generalist and non-disease-specific palliative care into nursing homes in six steps using a train-the-trainer approach. Nursing home staff are trained to deliver high-quality palliative care to all residents, from advance care planning to care up to and beyond death.[4] Between 2015 and 2017, we evaluated this program in a seven-country cluster-randomized controlled trial. The primary trial analyses showed that 'PACE Steps to Success' did not improve the comfort in the last week of life (primary outcome) in the overall nursing home population, but it appeared to improve quality of care and dying in the last month of life for this population, although the latter was the secondary outcome.[5]

Because this program was designed for all residents and included only three dementia-specific elements,[4] we hypothesized that its effects might differ between those with and without dementia in favor of those with mild/moderate or no dementia compared with advanced dementia. People with dementia, especially those with advanced dementia, have wide-ranging physical, cognitive and behavioral impairments, which make their palliative care needs distinct from those without dementia.[6,7] It is often assumed that for palliative care programs to be effective for people with dementia, they should specifically address the needs of this population.[7-9] Therefore, at the outset of the trial, we planned a subgroup analysis using the same outcome measures as in the primary trial analyses to test this hypothesis.[10] Understanding whether the program effects differ between people with and without dementia while taking dementia severity into account could inform future development of palliative care programs for nursing home residents, of whom between 60% and 83% die with dementia.[11] The present study aims to answer the research question: "Do the effects of the PACE Steps to Success program on comfort in the last week of life and quality of care and dying in the last month of life differ between residents with advanced, non-advanced and without dementia?".

METHODS

This is a pre-planned subgroup analysis of the PACE cluster randomized controlled trial (see data analyses plan submitted as an official deliverable to the European Commission in Supplementary file 1).[4,5,10] This cluster-RCT was conducted in 78 nursing homes in Belgium, England, Finland, Italy, the Netherlands, Poland and Switzerland to compare PACE Steps to Success with usual care (2015-2017). This trial was registered at http://www.isrctn.com on July 30, 2015 (ISRCTN14741671). Randomization was performed at the nursing home level as the program involved the training of nursing home staff. After baseline measurement, randomization was stratified by country and median number of beds in a 1:1 ratio. Randomization was blinded and performed by independent statisticians. Because of the nature of the study, blinding of treatment was not possible for researchers or participants. More details about the PACE cluster-RCT have been published elsewhere.[4,5] We reported this study following the CONSORT guidelines for randomized trials.

Program description

PACE Steps to Success was implemented over the course of one year, including two months for preparation, six months training for nursing home staff in the six steps, and four months consolidation. All countries had one or more country trainers. Each nursing home assigned one to six staff members as PACE coordinators. After being trained by two experienced trainers, the country trainers trained and supported the PACE coordinators who were in turn responsible for training and supporting fellow staff. The six PACE Steps included: 1) advance care planning with residents and families; 2) assessment, care planning, and review of resident needs and problems; 3) coordination of care via monthly multidisciplinary palliative care review meetings; 4) high-quality palliative care with a focus on pain and depression; 5) care in the last days of life and 6) care after death.[4] The program included three dementia-specific elements: communication training in advanced dementia for the PACE coordinators, and two elements integrated into the training for all nursing home staff which emphasized dementia as a terminal illness (as part of Step 2) and offered symptom control strategies for residents with and without dementia (in Step 4).[4,5]

Participating nursing homes

From a list of nursing homes, those located in a predefined country-specific geographical location were approached randomly by telephone or e-mail to invite them to participate in the study and to evaluate eligibility criteria using a standardized checklist. Inclusion criteria were the provision of on-site nursing care and personal assistance with activities of daily living and off-site medical care by general practitioners (GPs), having at least 30 beds, 15 or more residents having died in or outside the nursing home in the previous year to obtain sufficient power, consent to participation from management in writing before randomization, and agreement to allocate approximately 0.5 days per week for staff to act as PACE coordinators. We excluded nursing homes that had pilot-tested the program materials or used detailed palliative care guidelines/planning tools, the Gold Standards Framework and InterRAI-PC.[4,5]

Data collection and respondents

One contact person per nursing home identified all residents who had died in the previous four months. After-death structured questionnaires for each resident were sent to the staff member most involved in care (preferably a nurse), nursing home administrator and GP at baseline (month 0) and post-intervention (months 13 and 17). As sensitivity analyses showed no difference between program effects using the two post-intervention data, these combined post-intervention data were used in the primary analyses.[5] In this subgroup analysis, we included residents for whom the presence and severity of dementia was determined, classified into three subgroups: advanced, non-advanced and without dementia. We deviated from our pre-planned subgroups (residents with and without dementia), so that we could better investigate the difference between residents with advanced and without dementia.

Measurements and outcomes

Nursing home staff and GP reported whether a resident “had dementia” or “was diagnosed with dementia”. Dementia was considered present if at least one indicated it was and not present when both indicated it was not or when one indicated this but the other neither returned the questionnaire nor answered the question. Dementia severity was determined using two highly-discriminatory staff-reported instruments, Cognitive Performance Scale (CPS) and Global Deterioration Scale (GDS); those with CPS scores of 5-6 and GDS stage 7 were classified as having advanced dementia, the others as non-advanced dementia. CPS classifies residents into six hierarchical cognitive performance categories, with higher scores indicating worse cognitive impairment.[12] GDS stage 7 indicates very severe cognitive and functional deterioration.[13]

Nursing home administrators reported a resident’s sex and age at time of death. Staff assessed functional status one month before death in terms of dependency level with eating, dressing and mobility using the Bedford Alzheimer Nursing Severity-Scale: categorized into ‘independent’, ‘needs assistance’, or ‘fully dependent’.[14]

Primary outcome was staff-reported comfort in the last week of life using the validated Comfort Assessment in Dying–End-of-Life in Dementia (CAD-EOLD) scale; see comprehensive description of outcomes in Supplementary files 2.[15,16] CAD-EOLD comprises four subscales: physical distress, dying symptoms, emotional distress and well-being. The CAD-EOLD total scores range between 14 and 42, with higher scores indicating better comfort. CAD-EOLD was found to have better psychometric properties and user-friendliness than other comfort measures in a mixed nursing home population, including residents with and without dementia.[17-19] Secondary outcome was staff-reported quality of care and dying in the last month of life measured using the validated Quality of Dying in Long Term Care (QOD-LTC) scale, comprising ‘personhood’, ‘preparatory tasks’ and ‘closure’ subscales.[20] The QOD-LTC total score range between 11 and 55, with higher scores indicating better quality of care and dying.

Statistical analyses

Linear mixed models were used to analyze continuous outcomes and account for the clustered nature of data, with staff, nursing home and country as random factors (only random intercepts) and group (intervention versus usual care), time (post-intervention combining data collected at months 13 and 17 versus baseline) and their interaction as fixed factors. We analyzed differential effects by calculating differences in mean change (post-intervention combining data collected at months 13 and 17 minus baseline) between the subgroups, both for the intervention and control groups (interaction group*time*dementia). For the differential effects, we present estimated differences (and 95% Confidence Intervals) in mean change between the subgroups. All hypothesis testing was two-sided. P-values and 95% Confidence Intervals were not adjusted for multiple testing. To address multiplicity concerns with Bonferroni correction, p-values should be compared against a 1% significance level to address multiplicity concerns examining dementia subgroups.[21] In individual subgroups, we presented estimated mean scores and mean differences between groups post-intervention. All analyses were on an intention-to-treat and a complete-case basis, assuming data were missing at random. All statistical analyses were conducted using SAS 9.4 software (©SAS Institute Inc., USA).

RESULTS

Of the 160 nursing homes assessed for eligibility, 82 were excluded (43 were excluded as the required number of nursing homes were reached in the country and 39 did not meet the inclusion criteria) (Figure 1). Of the 78 nursing homes randomized, 1 nursing home in the control group and 2 nursing homes in the intervention group dropped out. Between the program implementation and the post-intervention measurements, 2 nursing homes in the control group dropped out. At baseline, we included 177 residents with advanced dementia, 126 with non-advanced dementia and 156 without dementia (Figure 1). In the control group post-intervention, we included 136 residents with advanced dementia, 167 with non-advanced dementia and 157 without dementia. In the intervention group post-intervention, we included 104 residents with advanced dementia, 110 with non-advanced dementia and 137 without dementia. We excluded 92 residents at baseline and 98 (control group) and 75 (intervention group) residents post-intervention, as the presence and severity of dementia could not be determined.

Table 1 provides a detailed description of the characteristics of the residents in the three subgroups for the baseline and the post-intervention measurements. At time of death, average age was between 82.5 and 87.5 years at baseline and between 84.0 and 86.9 years post-intervention. (They were predominantly female, with percentages ranging from 53.7% to 70.7% at baseline and from 56.1% to 67.7% post-intervention. Between 73.3% and 97.8% of residents with advanced dementia were ADL-(activities of daily living) dependent for eating, dressing and mobility. Among those with non-advanced and no dementia, between 42.4% and 71.4% were ADL-dependent for dressing and mobility, while between 19.1% and 32.8% were fully dependent for eating.

The program effects on comfort in the last week of life did not differ statistically between residents with advanced and without dementia (subgroup differences in baseline-adjusted mean differences 2.1; 95% CI -0.9–5.1; p=.177), those with non-advanced and without dementia (2.7; -0.4–5.9; p=.092), or those with advanced and non-advanced dementia (-0.6; -3.8–2.5; p=.698) (Table 2). The baseline-adjusted mean differences in comfort scores were -1.9 without dementia to 0.8 with non-advanced dementia (Table 3).

The program effects on quality of care and dying in the last month of life also did not differ statistically between advanced and no dementia (-0.6; -4.1–2.9; p=.741), non-advanced and no dementia (-1.5; -5.2–2.2; p=0.428), or advanced and non-advanced dementia (0.9; -2.8–4.6; p=.632) (Table 2). The baseline-adjusted mean differences in quality of care and dying scores were 2.7 in non-advanced dementia to 4.2 in no dementia (Table 3).

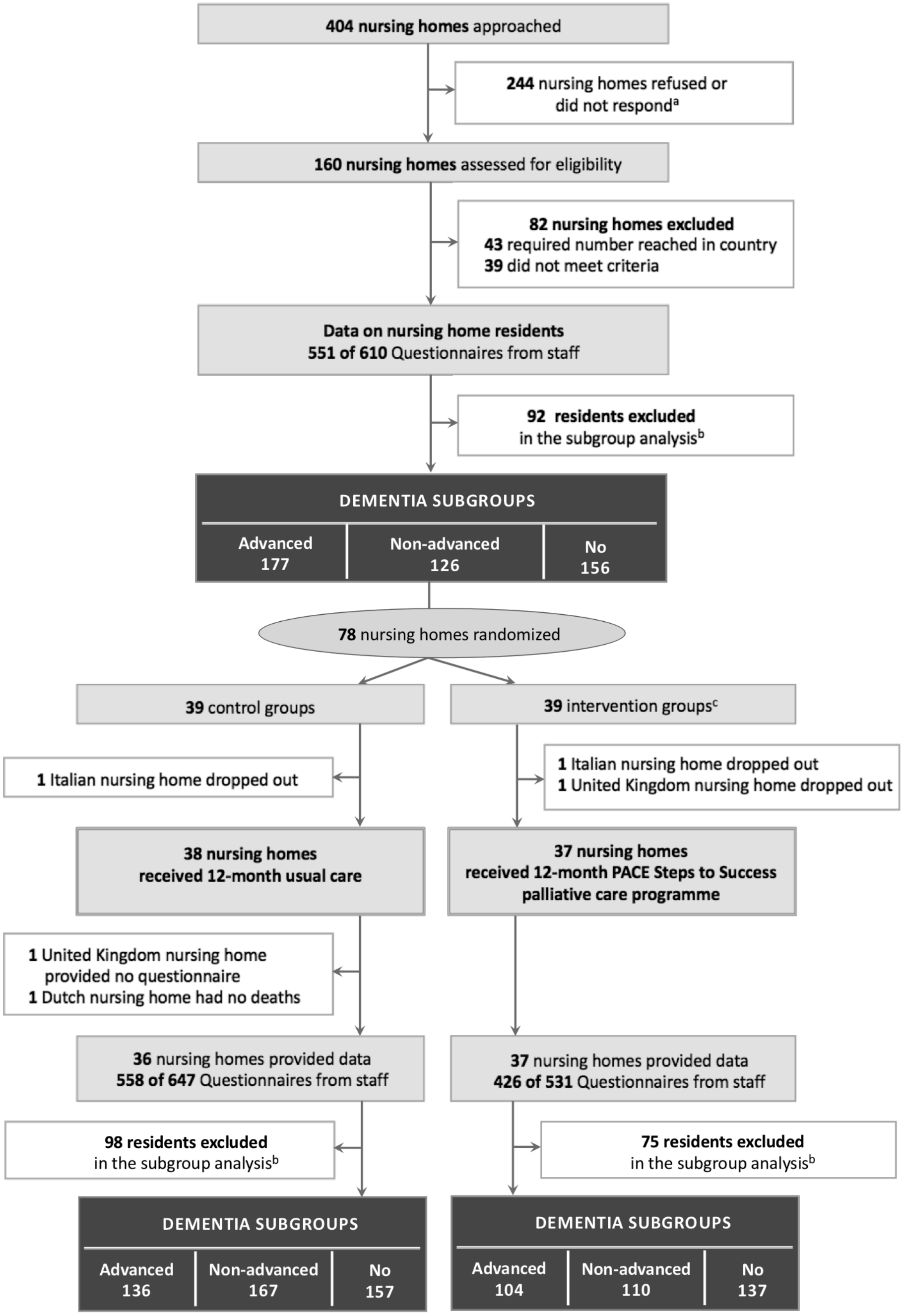

Figure 1. Flowchart of the identification of subgroups at baseline and post-intervention

[a] Reasons for refusal included insufficient time, no interest, understaffing, already involved in other studies, change in management.

[b] Excluded in the subgroup analysis, because the presence and severity of dementia could not be determined.

[c] Pre-implementation phase (months 1-2), implementation phase (months 3-8), and consolidation phase (months 9-12).

Table 1. Characteristics of residents by subgroups

TOTAL SAMPLE FOR THE SUBGROUP ANALYSIS	Baseline scores (T0)		Post-intervention (T1+T2)	
	Control	Intervention	Control	Intervention
	N=238	N=221	N=460	N=351
Advanced dementia	**(n=99)**	**(n=78)**	**(n=136)**	**(n=104)**
Age at time of death, unadjusted mean (SD)	85.5 (7.3)	86.3 (8.6)	86.1 (8.0)	86.5 (8.3)
Gender, female, unadjusted frequency, n (%)	70 (70.7)	47 (60.3)	88 (64.7)	64 (61.5)
Eating dependency[a], n (%)				
- Independent	0 (0)	1 (1.3)	0 (0)	3 (2.9)
- Needs assistance	17 (17.3)	18 (23.4)	26 (19.1)	21 (20.4)
- Fully dependent	81 (82.7)	58 (73.3)	110 (80.9)	79 (76.7)
Dressing dependency[a], n (%)				
- Independent	0 (0)	0 (0)	0 (0)	0 (0)
- Needs assistance	6 (6.1)	4 (5.2)	3 (2.2)	7 (6.7)
- Fully dependent	92 (93.4)	73 (94.8)	133 (97.8)	97 (93.3)
Mobility dependency[a], n (%)				
- Independent	1 (1.0)	2 (2.6)	2 (1.5)	2 (1.9)
- Needs assistance	12 (12.4)	9 (11.7)	11 (8.3)	16 (15.5)
- Fully dependent	84 (86.6)	66 (85.7)	120 (90.2)	85 (82.5)
Non-advanced dementia	**(n=65)**	**(n=61)**	**(n=167)**	**(n=110)**
Age at time of death, unadjusted mean (SD)	87.1 (7.9)	87.5 (7.5)	85.7 (7.8)	86.9 (6.1)
Gender, female, unadjusted frequency, n (%)	47 (57.7)	36 (59.0)	113 (67.7)	73 (66.4)
Eating dependency[a], n (%)				
- Independent	6 (9.4)	13 (21.7)	33 (20.1)	28 (25.5)
- Needs assistance	37 (57.8)	30 (50.0)	97 (59.1)	61 (55.5)
- Fully dependent	21 (32.8)	17 (28.3)	34 (20.7)	21 (19.1)
Dressing dependency[a], n (%)				
- Independent	1 (1.6)	3 (5.2)	8 (4.8)	6 (5.6)
- Needs assistance	17 (27.0)	19 (32.8)	58 (34.9)	41 (38.0)
- Fully dependent	45 (71.4)	36 (62.1)	100 (60.2)	61 (56.5)
Mobility dependency[a], n (%)				
- Independent	13 (20.3)	6 (10.2)	29 (17.5)	14 (13.0)
- Needs assistance	18 (28.1)	28 (47.5)	57 (34.3)	39 (36.1)
- Fully dependent	33 (51.6)	25 (42.4)	80 (48.2)	55 (50.9)
Without dementia	**(n=74)**	**(n=82)**	**(n=157)**	**(n=137)**
Age at time of death, unadjusted mean (SD)	82.5 (12.2)	83.2 (9.6)	84.0 (10.9)	84.2 (10.2)
Gender, female, unadjusted frequency, n (%)	50 (67.6)	44 (53.7)	88 (56.1)	79 (57.7)
Eating dependency[a], n (%)				
- Independent	18 (25.0)	25 (31.6)	55 (35.5)	47 (35.6)
- Needs assistance	34 (47.2)	33 (41.8)	68 (43.9)	51 (38.6)
- Fully dependent	20 (27.8)	21 (26.6)	32 (20.6)	34 (25.8)
Dressing dependency[a], n (%)				
- Independent	3 (4.2)	11 (13.8)	14 (9.0)	21 (6.1)
- Needs assistance	25 (34.7)	25 (31.3)	63 (40.6)	103 (29.9)
- Fully dependent	44 (61.1)	44 (55.0)	78 (50.3)	220 (64.0)
Mobility dependency[a], n (%)				
- Independent	4 (5.5)	14 (18.2)	22 (14.2)	25 (18.9)
- Needs assistance	29 (39.7)	24 (31.2)	55 (35.5)	42 (31.8)
- Fully dependent	40 (54.8)	39 (50.6)	78 (50.3)	65 (49.2)

Abbreviations: SD=standard deviation; BANS-S=Bedford Alzheimer Nursing Severity-Scale.

[a] Measured using BANS-S one month before death (range 7-28). Higher scores indicate greater severity. Unadjusted frequencies.

Missing cases – Advanced dementia, baseline: age=3; gender=4; BANS-S=3 | post-intervention measurements: age=6; gender=3; BANS-S=3). Non-advanced dementia, baseline: age=6; gender=5; BANS-S=3 | post-intervention measurements: age=6; gender=6; BANS-S=2). Without dementia, baseline: age=3; gender=4; BANS-S =7 | post-intervention measurements: age=12; gender=8; BANS-S=7.

Table 2. Effects on comfort and quality of care and dying by subgroups

Comparison between the subgroups	Subgroup differences in baseline-adjusted mean difference (95% CI)	p-values[c]
COMFORT IN THE LAST WEEK OF LIFE[a]		
- Advanced dementia *vs* Without dementia	2.1 (-0.9-5.1)	0.177
- Non-advanced dementia *vs* Without dementia	2.7 (-0.4-5.9)	0.092
- Advanced dementia *vs* Non-advanced dementia	-0.6 (-3.8-2.5)	0.698
QUALITY OF CARE AND DYING IN THE LAST MONTH OF LIFE[b]		
- Advanced dementia *vs* Without dementia	-0.6 (-4.1-2.9)	0.741
- Non-advanced dementia *vs* Without dementia	-1.5 (-5.2-2.2)	0.428
- Advanced dementia *vs* Non-advanced dementia	0.9 (-2.8-4.6)	0.632

Abbreviations: CAD-EOLD=Comfort Assessment in Dying–End of Life in Dementia; QOD-LTC=Quality of Dying in Long Term Care; CI=confidence intervals.

All mean total scores and p-values are cluster-adjusted.

[a] Comfort in the last week of life was measured using CAD-EOLD scale (total scores range 14-42). Higher scores indicate better comfort.

[b] Quality of care and dying in the last month of life was measured using QOD-LTC scale (total scores range 11-55). Higher scores indicate better quality of care and dying.

[c] Subgroup differences in the estimated baseline-adjusted mean differences between intervention and control groups post-intervention (group x time x dementia interaction).

Table 3. Cluster-adjusted mean scores and differences by subgroups

Individual subgroups	Baseline scores (T0)				Post-intervention scores (T1 + T2) ^{d}				Baseline-adjusted mean difference intervention versus control group post-intervention
	Control		Intervention		Control		Intervention		
	Cases No.	Mean^{b}	Cases No.	Mean^{b}	Cases No.	Mean^{b}	Cases No.	Mean^{b}	
COMFORT IN THE LAST WEEK OF LIFE^{a}									
- Advanced dementia	n=99		n=78		n=136		n=104		0.2
	91	30.6	74	30.8	131	30.3	97	30.7	
- Non-advanced dementia	n=65		n=61		n=167		n=110		0.8
	60	30.0	57	30.0	157	31.0	102	31.8	
- Without dementia	n=74		n=82		n=157		n=137		-1.9
	70	29.7	75	30.6	146	31.3	128	30.2	
QUALITY OF CARE AND DYING IN THE LAST MONTH OF LIFE^{b}									
- Advanced dementia	n=99		n=78		n=136		n=104		3.6
	97	38.1	75	37.1	135	38.0	103	40.6	
- Non-advanced dementia	n=65		n=61		n=167		n=110		2.7
	65	38.4	59	38.3	163	39.5	104	42.2	
- Without dementia	n=74		n=82		n=157		n=137		4.2
	74	41.2	78	39.3	152	39.8	133	42.2	

Abbreviations: CAD-EOLD=Comfort Assessment in Dying – End of Life in Dementia; QOD-LTC=Quality of Dying in Long Term Care.

All mean differences between groups post-intervention are cluster and baseline adjusted.

[a] Comfort in the last week of life was measured using CAD-EOLD scale (total scores range 14-42). Higher scores indicate better quality of dying.

[b] Quality of care and dying in the last month of life was measured using QOD-LTC scale (total scores range 11-55). Higher scores indicate better quality of end-of-life care.

[c] Total scores are averages per subscale multiplied by total number of items. Cases with missing data on more than 50% of items per subscale were excluded from the calculation of the total scale scores.

[d] Post intervention measurements collected for residents at T1 (=month 13) and T2 (=month 17).

DISCUSSION

This subgroup analysis showed that the effects of PACE Steps to Success on comfort in the last week of life and on quality of care and dying in the last month of life did not differ between residents with advanced, non-advanced and no dementia.

Using a subgroup analysis of a large pragmatic cluster-RCT, this study offers insight on the effects of a generalist, non-disease-specific palliative care training program designed to train nursing home staff to deliver high-quality palliative care to nursing home residents with dementia (advanced and non-advanced) and without dementia.[22] We also included a large number of residents for whom the severity of dementia was determined using validated instruments. Further, following the formal rules for planning and analysis of subgroup analysis, this subgroup analysis was pre-planned and used statistical tests of interactions, which enhance the validity of study results.[21] Nonetheless, because power calculation was not conducted for this subgroup analysis, our study might not have detected potentially important but small subgroup difference in program effects. For instance, although we found a 2.7 CAD-EOLD score point difference between residents with non-advanced and no dementia, which is close to what we considered as a clinically-important effect (i.e. CAD-EOLD score of 3 points),[4,5] the limited power might not have allowed us to detect statistically significant differences. In addition, as the presence of dementia relied on the estimation of the staff or the GP, there might be some misclassifications, particularly among residents with difficult-to-observe mild dementia symptoms. Finally, since data were collected after death, there might also be some recall bias.[4,5]

Contrary to our hypothesis, this study showed that the effects of the program did not differ between residents with advanced, non-advanced and no dementia. For the primary outcome – comfort in the last week of life – it did not achieve better outcomes for residents without dementia or with non-advanced dementia than for those with advanced dementia. Hence, as was clear from the primary trial analyses,[5] the stepwise training of nursing home staff over a one-year period was not sufficient to improve comfort in the final days of life, which might be related to the intervention itself, the quality of its implementation in several nursing homes, a possible mismatch between the intervention and the primary outcome, or a combination of these factors.[5,23] For instance, PACE Steps to Success was fully implemented as intended only in 28 of the 37 intervention nursing homes in terms of the number, order and timing of training sessions; and all 6 steps were taught in the right order and within 8 months. In seven other nursing homes, the six steps were taught but not in the right order and/or not within 8 months. In two nursing homes, they only completed five steps. Further, the adoption rates for the program materials (e.g. advance care planning material for residents) varied between countries but also fluctuated within countries.[23] While PACE Steps to Success might have addressed essential domains of palliative care that have been widely recommended for residents with and without dementia (i.e. person-centered care, advance care planning, optimal symptom assessment and management until the end of life, education of and support for healthcare providers, and support for family),[24-26] the sub-optimal implementation of the program in several nursing homes might have attenuated its effects on residents' comfort at the end-of-life.[23]

Regarding the secondary outcome, the PACE program appeared to improve quality of care and dying in the last month of life equally for those with dementia (regardless of the stage) and those without dementia. Although these findings need to be interpreted cautiously as this is a secondary outcome, they are remarkable, as this palliative care program only had a limited number of dementia-specific elements as part of the training.[4] (In particular, it is remarkable that the Quality of Dying in Long Term Care (QOD-LTC) subscale 'preparatory tasks' differed between the intervention and control groups, including items such as 'residents had treatment preferences in writing', 'residents' funeral was planned' and 'residents had named a decision-maker'.[5] These items are related to the process of advance care planning, which appears to be equally improved by the PACE program. As the process evaluation showed, 'advance care planning with patients and family' was also the first and best implemented step in the PACE program.[23])[1].

Overall, our study implies that such a generalist and non-disease-specific palliative care program for nursing homes has the potential to improve quality of care and dying in the last month of life for both residents with and without dementia, though this finding requires further investigation and effects were only medium-sized.[5] Nevertheless, our study provides crucial insight for future developers of palliative care programs aiming to improve quality of life and dying of nursing home residents with and without dementia. A broad palliative care training program, such as PACE Steps to Success, can be a useful starting point for further improvement in palliative care in nursing homes. However, as in the primary trial analyses,[5] this subgroup analysis emphasizes that this program needs to be developed further for both residents with and without dementia, e.g. to effectively promote comfort in the last days of life, either in terms of its components or the implementation processes in practice.[26,28] Especially for dementia, as end-of-life symptoms might be very specific compared with other diseases, a strong collaboration among experts in research and practice in palliative care and dementia seems important.[11,26] Future research evaluating palliative care programs should take into account dementia as an important subgroup, as prevalence is high in all countries, and nursing home residents die at varying stages of dementia.[3]

Conclusion

This subgroup analysis showed that the effects of PACE Steps to Success did not differ between residents with advanced, non-advanced and no dementia. These findings suggest that this program did not improve comfort in the last week of life for residents with or without dementia, but it appeared to improve quality of care and dying in the last month of life equally for residents with dementia (regardless of the stage) and without dementia. A generalist and non-disease-specific palliative care training program, such as PACE Steps to Success, can be a useful starting point for future development of palliative care programs in nursing homes. However, PACE Steps to Success needs to be developed further, so that it can effectively improve the quality of life and dying of both residents with and without dementia, e.g. by integrating components to improve residents' comfort at the end of life.

LIST OF ABBREVIATIONS

ADL	Activities of Daily Living

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[1] Erratum: The texts inside the parenthesis '(…)' deviate from the article published in BMC Palliative Care. Due to a minor error in the reported QOD-LTC scale individual items in the Supplementary Online Appendix of the primary trial analyses article (JAMA Internal Medicine), we also need to perform an analogous correction in this subgroup analysis.

BANS-S	Bedford Alzheimer Nursing Severity-Scale
CAD-EOLD	Comfort Assessment in Dying–End-of-Life in Dementia
CI	Confidence interval
CPS	Cognitive Performance Scale
QOD-LTC	Quality of Dying in Long Term Care
GDS	Global Deterioration Scale
GP	General practitioners
RCT	Randomized controlled trial

DECLARATIONS

Ethics approval and consent to participate

Ethics approval were obtained from the relevant ethics committees in all countries. Belgium: Commissie Medische Ethiek UZBrussel, 27/05/2015; England: NHS – NRES Committee North West-Haydock, 10/09/2015; Finland: Terveyden jahyvinvoinnin laitos, Institutet för hälsa och välfärd, 30/6/2015; Italy: Comitato Etico, Universita Cattolica del Sacro Cuore, 6/11/2017; Netherlands: Medisch Ethische Toetsingscommissie VUMedisch Centrum, 2/7/2015; Poland: Komisja Bioetycza, Uniwersytetu Jagiellonskiego, 25/6/2015; Switzerland: Commission cantonaled'éthique de la recherché scientifique de Genève (CCER), 6/8/2015. In accordance with national laws and guidelines, each partner involved in data collection developed a protocol for researchers in case adverse events occur in a participating nursing home. No adverse events were reported by researchers during the trial. All respondents gave prior informed consent in writing. In Poland and the Netherlands, informed consent was not required by the ethics committees based on the conditions for consent in both countries, as the questionnaires were filled in anonymously by the respondents.

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available upon request by e-mail to the project coordinator of PACE. The data can be accessed by researchers whose proposed use of the data for research purposes has been approved by the PACE consortium.

Competing interests

The authors declare that there is no conflict of interest.

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Authors' contributions

RM, TS and LVDB made equal substantial contribution to conceptualising the design of the work. TS, NVDN, SP, KS, SP, LVH, GG and MK acquired the data. RM and TS conducted the data analyses. RM, TS, and LVDB drafted and revised the manuscript critically for important intellectual content. All authors made substantial contribution to interpreting the data and revising the manuscript critically; have given the final approval of the manuscript to be submitted for publication; and have participated sufficiently in the work to take responsibility for appropriate portions of the content.

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*Other PACE collaborators not in the list: Yuliana Gatsolaeva, Lara Pivodic, Elisabeth Honinx, Marc Tanghe, Hein van Hout, Katherine Froggatt, Bregje Onwuteaka-Philipsen, H. Roeline W. Pasman, Ruth Piers, Ilona Baranska, Mariska Oosterveld-Vlug, Anne B. Wichmann, Yvonne Engels, Myrra Vernooij-Dassen, Jo Hockley, Suvi Leppäaho, Catherine Bassal, Federica Mammarella, Martina Mercuri, Paola Rossi, Ivan Segat, Agata Stodolska, Eddy Adang, Suvi Leppäaho, Paula Andreasen, Outi Kuitunen-Kaija, Teija Hammar, Rauha Heikkilä, Danni Collingridge Moore, Violetta Kijowska, Maud ten Koppel, Emilie Morgan de Paula, and the European Association for Palliative Care, European Forum For Primary Care, Age Platform Europe, and Alzheimer Europe.

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SUPPLEMENTARY FILES – CHAPTER 3

Supplementary file 1.

Outcome, process, and cost-effectiveness evaluation of 'PACE Steps to Success' palliative care programme in long-term care facilities in Europe: Cluster-randomised controlled trial (PACE Study II)
31 January 2017

Important note: The plan for the subgroup analysis can be found hereunder. For the full outcome, process and cost-effectiveness evaluation plans for the PACE cluster-RCT, please visit the BMC Palliative Care journal website at https://static-content.springer.com/esm/art%3A10.1186%2Fs12904-021-00734-1/MediaObjects/12904_2021_734_MOESM1_ESM.pdf

I. Outcome evaluation plan – prepared by the VUB

SUB-ANALYSES

The primary aim of the sub-analyses is to evaluate the effectiveness of the 'PACE Steps to Success' palliative care programme on different subgroups. For instance, the sub-analysis may aim to elucidate whether the effects of the 'PACE Steps to Success' palliative care programme on quality of dying of residents vary by characteristics of the deceased resident (i.e. age and gender, socio-economic status, clinical characteristics – e.g. cognitive status – dementia diagnosis –, and functional status). Each partner organization will create their own sub-analysis plan relevant to their research questions and hypotheses.

An example of a sub-group analysis

To demonstrate how a sub-analysis can be performed, a concrete example is provided.

Research aim: In this example, the sub-analysis aims to assess whether the outcomes of the 'PACE Steps to Success' palliative care programme on quality of dying differ between residents with and without dementia.

SUB-GROUP DATA ANALYSIS

For information regarding the **OUTCOME MEAUSURES**, **SAMPLE**, **EXPLORATION OF DATA AND DATA ASSUMPTIONS**, **PROCEDURES TO HANDLE MISSING VALUES**, and **DATA ANALYSIS APPROACH** (ITT and per protocol analysis), please refer to the main STATISTICAL ANALYSIS PLAN. Below the specifics for the sub-analyses are described.

Descriptive statistics

The characteristics of the deceased residents with and without dementia in facilities using the 'PACE Steps to Success' palliative care programme and in facilities which provide care as usual will be provided in terms of age, gender, socio-economic status, cause of death or disease underlying death, and functional and cognitive status.

Baseline and post-intervention measurement characteristics will be summarized separately for residents with and without dementia, both for facilities using the 'PACE Steps to Success' palliative care programme and facilities which provide care as usual. The mean and standard deviation or proportion will be given for the descriptive variables. Anova (normal distribution) or Mann-Whitney U-test (non-normal distribution) for continuous, and χ^2 tests for categorical variables will be used to assess differences between residents with and without dementia in the baseline and post-intervention measurements and for non-response analysis, both for the intervention group and the control group.

A visual representation of differences in the characteristics of the samples between residents with and without dementia, both for the control group and the intervention group, and between baseline and post-intervention measurements may also be provided by using graphs or plots.

Regression analyses

For this sub-analysis, several regression analyses will be conducted based on the exploration of data and data assumptions, as well as on the data analysis approach to be used (ITT and per protocol). Generally, the EOLD-CAD or QOD-LTC variables are by nature continuous variables, which would require multivariate linear regression analysis techniques. However, if the assumptions of normal distribution and/or linearity is/are violated, multivariate logistic regression analyses may be applicable. The specific procedure on how to further analyse skewed or non-linear data will rely upon the decision of the consortium. Basically, multivariate linear or logistic regression analyses may be performed to assess and compare the baseline and post-intervention measurement differences in the quality of dying between residents with and without dementia, both for the intervention group and the control group, while adjusting for sample characteristics that may differ between groups.

Additionally, multi-level mixed model regression analyses will be performed to account for the baseline measurement and the multilevel nature of the data – e.g. residents and staff nested within LTCFs or country. The kind of multilevel mixed model regression analyses will depend on the nature of the outcome variables and the statistical package to be used for the main analyses.

With the multi-level mixed model analyses, the outcomes will be analysed with LTCFs and country as random factor, and group, time point, and their interaction as fixed factors. Differences in mean change (post-intervention measurements minus baseline) between deceased residents with and without dementia, both for the intervention group and the control group (interaction group*time*dementia) will be calculated. Estimated means with corresponding 95% CI will be reported at baseline and follow-up, both for the intervention and control group. Moreover, estimated differences (and 95%CI) in change between intervention and control will be reported. The effect sizes (Cohen’s *d*) using the baseline-adjusted mean differences and the variance between residents or care staffs, between LTCFs, and between country will be estimated to assess the magnitude of the effects for the different outcome measures.

All analyses will be two-tailed and considered significant if $\alpha = 0.05$. In addition, data will be analysed by using statistical software program suitable for the necessary statistical analyses, such as multilevel mixed model analysis and multiple imputation – e.g. STATA, SAS, or IBM SPSS.

Supplementary files 2. Comprehensive description of the primary and secondary outcomes

Primary outcome: Comfort Assessment in Dying–End-of-Life in Dementia-scale (CAD-EOLD)

Comfort Assessment in Dying–End-of-Life in Dementia-scale (CAD-EOLD) scale was used to measure comfort in the last week of life. The EOLD-CAD scale comprises 14 individual items (discomfort, pain, restlessness, shortness of breath, choking, gurgling, difficulty swallowing, emotional support, fear, anxiety, crying, moaning, serenity, peace and calm) grouped into four subscales (physical distress, dying symptoms, emotional symptoms and well-being). The individual items were scored on a scale of 1 (not at all) to 3 (a lot). Items are summed to calculate an overall score between 14 and 42. The items serenity, peace and calm were reverse coded, so higher scores indicate better comfort in the last week of life.

CAD-EOLD: When you think about the resident's physical and emotional state, can you please indicate to what extent he or she experienced the following during the last week of life?
(*for each line, please tick a single box in the column that applies*)

	a lot	somewhat	not at all
a. discomfort	☐	☐	☐
b. pain	☐	☐	☐
c. restlessness	☐	☐	☐
d. shortness of breath	☐	☐	☐
e. choking	☐	☐	☐
f. gurgling	☐	☐	☐
g. difficulty swallowing	☐	☐	☐
h. fear	☐	☐	☐
i. anxiety	☐	☐	☐
j. crying	☐	☐	☐
k. moaning	☐	☐	☐
l. serenity	☐	☐	☐
m. peace	☐	☐	☐
n. calm	☐	☐	☐
o. resistiveness to care	☐	☐	☐

Secondary outcome: Quality of Dying in Long Term Care (QOD-LTC) scale

Quality of Dying in Long Term Care (QOD-LTC) scale was used to measure quality of care and dying. The QOD-LTC scale assesses perspectives on quality of personhood, closure and preparatory tasks, including 11 individual items. Higher mean score indicates better quality of care and dying.

Please think back over the last month of life of the resident. Here are some statements that have been considered important during the last phase of life. How true is each statement for (the situation of) the resident? *(for each line, please tick a single box in the column that applies)*

		not at all	a little	a moderate amount	quite a bit	**completely**
A	There was a nurse or aide with whom the resident felt comfortable	☐	☐	☐	☐	☐
B	The resident received affectionate touch daily	☐	☐	☐	☐	☐
C	The resident appeared to be at peace	☐	☐	☐	☐	☐
D	The resident's physician knew him or her as a whole person including life and personality	☐	☐	☐	☐	☐
E	The resident had treatment preferences in writing	☐	☐	☐	☐	☐
F	The resident indicated he or she was prepared to die	☐	☐	☐	☐	☐
G	The resident's funeral was planned	☐	☐	☐	☐	☐
H	The resident had named a decision-maker in the event that he or she was no longer able to make decisions	☐	☐	☐	☐	☐
I	The resident maintained his or her sense of humour	☐	☐	☐	☐	☐
J	The resident's dignity was maintained	☐	☐	☐	☐	☐
K	The resident's clothes and body were clean	☐	☐	☐	☐	☐

PART II

Palliative care for older people with dementia living at home

CHAPTER 4

Quality of primary palliative care for older people with mild and severe dementia: an international mortality follow-back study using quality indicators

Rose Miranda, Yolanda W.H. Penders, Tinne Smets, Luc Deliens, Guido Miccinesi, Tomás Vega Alonso, Sarah Moreels, and Lieve Van den Block

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ABSTRACT

Background. Measuring the quality of primary palliative care for older people with dementia in different countries is important to identify areas where improvements can be made.

Objective. Using quality indicators, we systematically investigated the overall quality of primary palliative care for older people with dementia in three different countries.

Design/setting. A mortality follow-back survey through nation- and region-wide representative Sentinel Networks of General Practitioners (GPs) in Belgium, Italy, and Spain. GPs registered all patient deaths in their practice. We applied a set of nine quality indicators developed through literature review and expert consensus.

Subjects. Patients aged 65 years or older, who died non-suddenly with mild or severe dementia as judged by GPs (n=874).

Results. Findings showed significantly different quality indicator scores between Belgium and Italy for regular pain measurement (mild dementia: BE=44%, IT=12%, SP=50% | severe dementia: BE=41%, IT=9%, SP=47%), acceptance of approaching death (mild: BE=59%, IT=48%, SP=33% | severe: BE=41%, IT=21%, SP=20%), patient-GP communication about illness (mild: BE=42%, IT=6%, SP=20%), and involvement of specialised palliative services (mild: BE=60%, IT=20%, SP=77%). The scores in Belgium differed from Italy and Spain for patient-GP communication about medical treatments (mild: BE=34%, IT=12%, SP=4%) and repeated multidisciplinary consultations (mild: BE=39%, IT=5%, SP=8% | severe: BE=36%, IT=10%, SP=8%). The scores for relative-GP communication, patient death outside hospitals, and bereavement counselling did not differ between countries.

Conclusion. While the countries studied differed considerably in the overall quality of primary palliative care, they have similarities in room for improvement, in particular pain measurement and prevention of avoidable hospitalisations.

Key points

- Many older people with dementia particularly in primary care receive poor quality and access to palliative care.
- To identify room for improvement, we assessed the qual- ity of primary palliative care in dementia in Belgium, Italy and Spain.
- Quality was systematically assessed using a set of QIs developed through literature review and expert consensus.
- The countries differed in quality, but they have similar opportunities for improvement, e.g. pain measurement and hospitalisation.
- Our findings are useful to reflect on how primary palliative care can be improved for older people with dementia.

INTRODUCTION

Dementia affects about 47 million people worldwide and is projected to almost triple by 2050 as populations age.[1] It is characterised by widespread physical, cognitive, and behavioural impairment which may lead to severe disabilities that persist until death.[2,3] To improve the quality of life of older people with dementia and their families, a recent white paper from the European Association for Palliative Care recommends palliative care.[4] However, concerns have been raised about the poor quality and access to palliative care for older people with dementia,[1] particularly in primary care where the majority will be cared for.[5]

Existing studies using death certificates show that home death is rare among people with dementia and the majority die in nursing homes.[6,7] Those dying in nursing homes are more likely to receive burdensome interventions, be hospitalised unnecessarily, and die with great suffering.[8-10] In primary care, evidence on some circumstances of those dying with mild or severe dementia in Belgium, Italy, and Spain suggest that although transfer rates are low and treatment aims are aligned with palliative care recommendations, access to specialised palliative services and communication with general practitioners (GPs) remain poor.[11,12] However, previous studies no longer reflect the latest evidence in primary care, due partly to recent changes in palliative care legal frameworks and funding arrangements in these countries.[13,14] Additionally, they included people with dementia who died 'suddenly',[11,12] who may not have been recognised as being in the final stage of life and thus in need of palliative care.[15] Finally, they neither showed a comprehensive overview of the most important aspects of palliative care nor systematically measured its quality, something that could be achieved by using a core set of quality indicators.[16-18]

Quality indicators (QIs) are explicitly defined and measurable items referring to the structure, process or outcome of care, which can be used to capture the quality of care on an aggregated e.g. national level.[16-18] Because there is still no norm to determine when a certain QI score indicates 'high-quality' primary palliative care, comparing QI scores between countries is useful. Such cross-country comparisons can shed light on the average level of quality across different countries,[19] giving insight into where improvements can be made.[20]

In this study, we aimed to answer the research question: "What is the quality of primary palliative care in Belgium, Italy, and Spain for older people who died non-suddenly with mild or severe dementia?". We applied a core set of nine validated QIs, which cover eight important domains of palliative care and are highly-applicable and easily-implementable in primary care in an international context according to experts. We used international population-based data (2013-2015) from existing representative GP Sentinel Networks in Belgium, Italy, and Spain. Comparing these countries is interesting, as they have all integrated palliative care in their health systems, but their health systems are different and the outcomes may still vary.[13,14,21]

METHODS

Design

The current study is part of the European Sentinel Network Monitoring End-of-Life Care (EUROSENTIMELC), a mortality follow-back study monitoring palliative care in population-based samples of death in Belgium, Italy, and Spain. Data were collected through existing Sentinel Networks of GPs, an epidemiological surveillance system that voluntarily monitors health problems in primary care. The network in Belgium is representative for age, sex and the geographical distribution of GPs in the country, while the network in Spain covers the Castile and Leon and the Valencian regions. In Italy, we used a nationally-representative GP network that only performed end-of-life care registrations. Using a standardised registration form, GPs registered deaths weekly among patients in their practice aged 18 years or older from January 2013-December 2014 in Belgium and Spain and from June 2013-May 2015 in Italy. In completing the registration form, GPs may also use medical files. The design and aims of EURO SENTIMELC have been explained in detail elsewhere.[22]

Sample

Data was collected on 2,435 patients in Belgium, 983 in Italy, and 591 in Spain. All those aged 65 years or older who died non-suddenly with either mild or severe dementia as judged by the GP were included, making a total sample of 874 (531 in Belgium, 242 in Italy, 101 in Spain).

Measurements

The registration form consists of structured and closed-ended items surveying information from the GPs about QIs and patient characteristics. Based on their knowledge and expertise, the GPs estimated whether the patient had dementia ('yes, mild dementia', 'yes, severe dementia', 'no', and 'unknown' (considered as 'no')) and whether they died suddenly.

Dependent variables - selecting quality indicators

Table 1 summarises the selection of the EUROSENTIMELC QIs and the calculation of QI scores. The core set of EUROSENTIMELC QIs was based on previous work of Leemans et al (2015), who identified nine important domains of palliative care (i.e. physical, psychosocial, communication with patients and relatives, multidisciplinary consultation, type of end-of-life care, continuity of care, support for relatives, and structure of care) and evaluated a set of QIs designed to measure the quality of palliative care services in Belgium.[18] Of those QIs found to have good face validity, feasibility, discriminative power and usefulness, we identified 43 QIs that can be measured retrospectively using GPs as respondents. These QIs were reformulated as questions, so that sentinel GPs could respond to them. Based on usefulness and relevance to primary palliative care in an international context, 22 primary palliative care experts from Belgium, Italy, Spain, the Netherlands, and France evaluated the 43 QIs on a scale of 1-10. Those with a minimum average score of 7.5 remained. Where possible, we reduced the QIs to 1-2 per domain by selecting the best scored QIs. We only selected the QIs measuring the process and outcomes of care, resulting in 17 QIs covering eight palliative care domains, which were included in the registration form.

Through a multi-step process of assessing the psychometric qualities of the QIs explained hereunder, we finally selected nine and discarded eight QIs (e.g. 'Percentage of patients with more than one visit to an emergency department in the last 30 days before their death' due to 26% missing cases).[23] For the detailed selection of QIs, see Supplementary table 1.

- All questions were analysed for data quality. Any QIs with missing values of 10% or more were excluded, assuming that GPs may have had difficulty answering.

- All questions were also analysed based on usability by examining potential ceiling or floor effects and variability between disease groups and countries. Questions with positive answers of more than 90% or less than 10% over all countries were excluded.
- The question and answer categories were used to calculate the following core set of QIs, of which two cover the third palliative care domain:

(1) Percentage of patients whose pain was known by the GP to be monitored regularly during the last three months of life

(2) Percentage of patients known by the GP to have accepted that they were nearing the end of their life

(3.1) and (4) Extent to which patients and relatives receive information from the GP about diagnosis, prognosis, disease progression, advantages and disadvantages of treatments, and palliative care options

(3.2) Percentage of patients who expressed a specific wish about a medical treatment

(5) Repeated (on several occasions) formal multidisciplinary consultation with and between care providers (between settings, including GP) about care goals and palliative care option

(6) Percentage who received palliative care services [24] involved in last three months of life

(7) Percentage of patients who did not die in a regular hospital unit

(8) Percentage of patients for whom the GP has contacted or has plans to contact the relatives regarding bereavement counselling

Independent variables

Besides age at death and gender, GPs indicated the cause of death: 'malignancy', 'cardiovascular disease (excluding stroke)', 'disease of the nervous system', 'respiratory diseases', and 'other (specified)'. The place of longest residence in the last year of life was also requested: 'at home or living with family', 'care home', and 'elsewhere'.

Data analyses

Generalised linear mixed model (GLMM) analysis was carried out to calculate cross-country differences in characteristics of those with mild and severe dementia, while accounting for their clustering within GP practices. GLMM analysis was also conducted to analyse differences in QI scores between countries, while adjusting for sample characteristics that varied between countries and accounting for the clustering. Statistical analyses were conducted with IBM SPSS Statistics 24: Release 24 (IBM Corporation).

Ethics approval

Ethics approval was obtained from the Ethical Review Board of Brussels University Hospital of the Vrije Universiteit Brussel and from the Local Ethical Committee Comitato Etico della Azienda Sanitaria Firenze in Tuscany (April 2013). No formal ethical approval is required to collect posthumous anonymous patient data in Spain.

Table 1. The selection of the EURO SENTIMELC quality indicators and the calculation of quality indicator scores

Phase 1	**From previous work [18], we identified 43 validated palliative care QIs covering nine domains of palliative care, which can be measured retrospectively using GPs and respondents**
Phase 2	**Expert consultation and steering group to evaluate the 43 QIs and reduce the QI set to 1-2 per domain – Result:** 17 QIs included in the registration form.
Multi-step process	**Further evaluation of the psychometric qualities of the QIs based on data quality and usability–** We only selected the QIs covering the process and outcomes of care domains and excluded the 'structure of care domain'. **Result:** Nine QIs covering eight domains of palliative care were selected and operationalised (see the list below). Eight QIs were discarded (1. Number of contacts between the GP and the patient in the last 3 months of life, 2. Percentage of patients whose GP is aware of their wishes regarding resuscitation, 3. Percentage of patients whose nominated proxy decision-maker was involved when the patient became mentally incompetent, 4. Percentage of patients with more than one visit to an emergency department in the last 30 days before their death, 5. Percentage of patients who are admitted to an intensive care department in the last 30 days before their death. 6. Percentage of patients with more than one hospital admissions in last 30 days, 7. Percentage of patients who *remained* in their preferred location in the last month before their death, 8. Percentage of patients who *died* in their preferred location).

Palliative care domains	Numerator and denominator†	Calculation of quality indicator scores (Questions, Answers, and Scoring)
1: Physical aspects of care	**(QI 1) Numerator:** Number of patients whose pain was measured often or very often in the last 3 months of life	**Question:** How often did you or another caregiver measure the patient's pain (with or without using a pain scale) in the last 3 months of life? **| Answer:** never; rarely; occasionally; often; very often - **Positive score:** If the GP knew pain to be measured 'often' or 'very often'
2: Psychosocial and spiritual aspects of care	**(QI 2) Numerator:** Number of patients who accepted death completely or for the most part **Denominator:** Number of patients for whom the GP answered anything but 'I don't know'	**Question:** According to you, did the patient accept his/her approaching end? **| Answer:** Yes, completely; yes, for the most part; no, not entirely; no, not all; I don't know (reported separately in Table 1). - **Positive score:** If the GP thought the patient had accepted their nearing end. All 'don't know' answers were not included in this indicator (*n* was reported)
3: Information, communication, planning and decision-making with the patient	**(QI 3.1) Numerator:** Number of patients with whom the GP discussed at least three of the listed topics	**Question:** Put a cross against topics you have discussed with the patient **Answer:** Diagnosis; Course of the disease/prognosis; The approaching end of life; Advantages and disadvantages of the treatments; Options in terms of end-of-life care - **Positive score:** If the GP communicated about at least 3 of the 5 illness-related topics
	(QI 3.2) Numerator: Number of patients who expressed a specific wish about a medical treatment (i.e. "Yes")	**Question:** Did the patient ever express specific wishes about a medical treatment that he/she would or would not want in the final phase of life? **| Answer:** Yes; No; Don't know - **Positive score:** Yes | The answers 'don't know' were considered as 'no', as this QI focuses on GP-patient discussion
4: Information, communication, planning and decision-making with family and friends	**(QI 4) Numerator:** Number of patients for whom the GP discussed at least three of the listed topics with a relative	**Question:** Put a cross against topics you have discussed with the relative **Answer:** Diagnosis; Course of the disease/prognosis; The approaching end of life; Advantages and disadvantages of the treatments; Options in terms of end-of-life care - **Positive score:** If the GP communicated about at least 3 of the 5 illness-related topics.
5: Information, communication, planning and decision-making with other care providers	**(QI 5) Numerator:** Number of patients for whom a multidisciplinary consultation took place approximately once a week or approximately every day	**Question:** How often in the last month of life did a pre-planned multidisciplinary consultation take place (face-to-face or via phone) between the care providers to discuss the care objectives and/or options in terms of palliative care? **Answer:** No such consultation/Once in the last month of life/Approximately once a week/Approximately every day - **Positive score:** If the multidisciplinary consultation occurred 'once a week' or 'once a day or more'.
6: Type of palliative care	**(QI 6) Numerator:** Number of patients for whom at least one specialized palliative care services [19] was initiated in the last 3 months of life	**Question:** Which specialized palliative care initiatives were involved in the last 3 months of this patient's life? **Answer:** Country-specific specialized palliative care initiatives; other, namely…; none - **Positive score:** If specialized palliative care services were involved in the in the last 3 months of life.
7: Coordination & continuity of care	**(QI 7) Numerator:** Number of patients who did not die in hospital (exclusive palliative care unit)	**Question:** Place of death? **| Answer:** At home or living with family (incl. service flat); care home: home for elderly persons/nursing home; hospital (excl. palliative care unit); palliative care unit (hospital); elsewhere, please specify - **Positive score:** If death occurred outside the hospital. The original indicator was 'percentage of people who died at home'. We adapted it to allow for deaths in palliative care units, which are indicative of high quality palliative care.
8: Support for family/friends and informal carers	**(QI 8) Numerator:** Number of patients for whom the GP has contacted or plans to contact the relatives with regard to bereavement counselling	**Question:** After the death, did you have contact with any of the relatives with regard to bereavement counselling? **Answer:** Yes, once; Yes, more than once; No, but has been planned; No and not planning to - **Positive score:** If GP has contacted or plans to contact the relatives with regard to bereavement counselling.

† **Denominator:** All patients for whom this question was answered (unless otherwise indicated)

RESULTS

Patient characteristics

Among the mild dementia group, those in Belgium were the youngest (mean age 86.4 years), and in Spain the oldest (88.9; *P* = 0.026, Table 2); the average age for those with severe dementia was 85.8 in Belgium to 88.5 in Spain (*P* = 0.001). All groups were predominantly female (from 53.1% in Spain to 74.6% in Italy (*P* = 0.031). In the last year of life of those with mild dementia, 55.7% resided in care homes in Belgium, whereas 85.1% in Italy and 78.8% in Spain resided at home (*P* < 0.001) as with severe dementia, though the difference was not significant. The most common cause of death in mild dementia in Belgium and Italy was cardiovascular disease (24.2% and 39.6% respectively), while in Spain, a third died of stroke (*P* = 0.009). In all countries, almost a third of those with severe dementia died from nervous system disease.

Table 2. Patient characteristics between Belgium, Italy, and Spain (n = 874)

	Mild dementia (*n* = 385)				**Severe dementia** (*n* = 489)			
	Belgium (*n* = 219)	**Italy** (*n* = 114)	**Spain** (*n* = 52)	*P*-value†	**Belgium** (*n* = 312)	**Italy** (*n* = 128)	**Spain** (*n* = 49)	*P*-value†
	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	
Mean age at death [SD]	86.4 [7.3]	87.6 [5.7]	88.9 [6.2]	0.026*	85.8 [6.7]	87.9 [6.7]	88.5 [4.7]	0.001*
Gender, female	137 (63.1)	66 (59.5)	36 (69.2)	0.502	216 (69.7)	94 (74.6)	26 (53.1)	0.031*
Longest place of residence in the last year of life‡				<0.001*				<0.001*
At home	95 (43.4)	97 (85.1)	41 (78.8)		87 (28.0)	104 (81.3)	32 (66.7)	
Care home§	122 (55.7)	16 (14.0)	11 (21.2)		223 (71.7)	24 (18.8)	16 (33.3)	
Main cause of death				0.009*				0.080
Malignancy	51 (23.3)	9 (8.1)	9 (17.3)		32 (10.3)	5 (4.0)	8 (16.3)	
Cardiovascular disease	53 (24.2)	44 (39.6)	13 (25.0)		59 (19.0)	34 (27.0)	6 (12.2)	
Disease of nervous system	25 (11.4)	8 (7.2)	5 (9.6)		100 (32.2)	39 (31.0)	19 (38.8)	
Respiratory disease	32 (14.6)	18 (16.2)	3 (5.8)		19 (6.1)	15 (11.9)	4 (8.2)	
Stroke (CVA)	23 (16.0)	17 (13.5)	6 (30.8)		43 (13.8)	11 (8.7)	3 (6.1)	
Other	35 (16.0)	15 (13.5)	16 (30.8)		58 (18.6)	22 (17.5)	9 (18.4)	

Missing cases for mild dementia, gender, *n*=5 (BE=2 | IT=3); cause of death, *n*=3 (IT=3)

Missing cases for severe dementia, gender, *n*=4 (BE=2 | IT=2); longest place of residence prior to death, *n*=3 (BE=2 | SP=1); cause of death, *n*=3 (BE=1 | IT=2)

SD, standard deviation; CVA, cerebrovascular accident.

* Significant at the 0.05 probability level.

† *P*-value was determined by conducting multi-level mixed model analysis to account for the clustering at the level of GPs

‡ Longest place of residence in the last year of life: 'Elsewhere' reported as missing cases (mild dementia, *n*: Belgium, 2; Italy, 1; Spain, 0 | severe dementia, *n*: Belgium, 1; Italy, 0; Spain, 0)

§ Includes care/nursing homes in Belgium and Italy and residential homes in Spain.

Quality of primary palliative care in Belgium, Italy, and Spain

In the last three months of life, GPs indicated that regular pain measurement was conducted in 44% of those with mild dementia in Belgium, 12% in Italy (OR=0.15, 95%CI=0.06-0.40) and 50% in Spain (n.s., Table 3). This pattern was also found in the severe dementia group (Belgium (41%), Italy (9%; OR=0.10, 95%CI=0.04-0.29), Spain (47%, n.s.)). In Belgium, 59% of those who died with mild dementia accepted their death according to the GP, compared with 48% in Italy (OR=0.26, 95%CI=0.10-0.65) and 33% in Spain (n.s.) with a similar pattern for severe dementia (Belgium (41%), Italy (21%; OR 0.25, 95%CI 0.08-0.76), and Spain (20%, n.s.)).

GPs indicated that at least three of the five illness-related topics were discussed with patients with mild dementia more often in Belgium (42%) than in Italy (6%; OR=0.09, 95%CI=0.03-0.22), though no significant difference was found between Belgium and Spain (20%, n.s.). Additionally, the preferences of patients with mild dementia about end-of-life treatment were discussed more frequently in Belgium (34%) than in Italy (12%; OR=0.21, 95%CI=0.09-0.47) and Spain (4%; OR=0.07, 95%CI=0.01-0.30); in severe dementia, figures were lower (0%-14%) but no significant difference was found between countries, nor with communication between GPs and relatives (81-85% mild dementia; 84%-88% severe dementia).

In the last month of life, repeated multidisciplinary consultations about end-of-life care for those with mild dementia were more likely in Belgium (39%) than in Italy (5%; OR=0.08, 95%CI=0.03-0.24) and Spain (8%; OR 0.11, 95%CI 0.04-0.37); (severe dementia: Belgium (36%), Italy (10%; OR=0.30, 95%CI=0.15-0.61), and Spain (8%; OR=0.21, 95%CI=0.08-0.55)). During the last three months of life, specialised palliative services were involved more frequently in mild dementia in Belgium (60%) than in Italy (20%; OR=0.17, 95%CI=0.08-0.38), while no difference was found in Spain (77%); (severe dementia Belgium (62%), Italy (11%; OR 0.08, 95%CI=0.03), and Spain (73%, n.s)).

The percentages of those who did not die in a hospital varied from 64% to 74% (mild dementia) and 72% to 85% (severe dementia), though there was no cross-country difference. The percentages of relatives the GP had contacted or had plans to contact about bereavement counselling was similar across countries (62-69% for mild dementia and 56-67% for severe dementia). A visual overview of the QIs in Belgium, Italy, and Spain is shown in three radar charts in Supplementary figure 1.

DISCUSSION

Our findings show considerable cross-country differences on regular pain measurement, acceptance of approaching death, patient-GP communication about illness and medical treatments, involvement of specialised palliative services, and repeated multidisciplinary consultations about end-of-life care. QI scores in Belgium were higher than Italy, but not appreciably higher than Spain. Scores for relative-GP communication, death outside hospital, and bereavement counselling for relatives did not differ between countries, and ranged from 56% to 88%.

Our study was the first to measure the quality of primary palliative care for older people with mild or severe dementia using a core set of validated QIs, which cover eight important palliative care domains and are highly-applicable and easily-implementable for this study according to experts from five different countries. We also provided a good understanding of the final phase of life from a population-based perspective. Through the GP Sentinel Networks, we had representative samples of patient deaths in primary care [22] and included people who had and had not received specialised palliative services. The inclusion of all non-sudden deaths in our study also enabled us to assess the quality of care delivered in the context of dying.

Table 3. Scores of the nine quality indicators for patients with mild and severe dementia between Belgium, Italy, and Spain (n = 874)

	Mild dementia (*n* = 385)					Severe dementia (*n* = 489)				
	Belgium (*n* = 219)	**Italy** (*n* = 114)		**Spain** (*n* = 52)		**Belgium** (*n* = 312)	**Italy** (*n* = 128)		**Spain** (*n* = 49)	
	n (%)	*n* (%)	OR (95% CI)	*n* (%)	OR (95% CI)	*n* (%)	*n* (%)	OR (95% CI)	*n* (%)	OR (95% CI)
QI 1. Pain measured often or very often in last 3 months of life	95 (44)	14 (12)	0.15 (0.06-0.40)*	25 (50)	1.67 (0.63-4.46)	124 (41)	11 (9)	0.10 (0.04-0.29)*	22 (47)	2.28 (0.76-6.88)
QI 2. GP thinks that patient was able to accept their approaching end completely or for the most part†	127 (59)	54 (48)	0.26 (0.10-0.65)*	17 (33)	0.32 (0.10-1.00)	123 (41)	26 (21)	0.25 (0.08-0.76)*	9 (20)	0.26 (0.07-1.01)
QI 3.1. GP discussed at least 3 illness-related topics‡ with patient	76 (42)	7 (6)	0.09 (0.03-0.22)*	3 (20)	0.33 (0.08-1.30)	28 (14)	0 (0)	NA	1 (11)	0.93 (0.10-8.62)
QI 3.2. GP was aware of patient preferences about medical treatments	74 (34)	13 (12)	0.21 (0.09-0.47)*	2 (4)	0.07 (0.01-0.30)*	31 (10)	4 (3)	0.40 (0.15-1.12)	2 (4)	0.52 (0.14-2.03)
QI 4. GP discussed at least 3 illness-related topics‡ with relatives	162 (81)	93 (82)	0.61 (0.27-1.38)	39 (85)	0.99 (0.35-2.81)	244 (84)	107 (84)	0.95 (0.42-2.13)	42 (88)	1.03 (0.34-3.14)
Qi 5. Multidisciplinary consultation at least once a week during the last month of life	84 (39)	5 (5)	0.08 (0.03-0.24)*	4 (8)	0.11 (0.04-0.37)*	111 (36)	13 (10)	0.30 (0.15-0.61)*	4 (8)	0.21 (0.08-0.55)*
QI 6. Palliative care services involved in last 3 months of life	125 (60)	20 (20)	0.17 (0.08-0.38)*	30 (77)	2.94 (1.14-7.61)	185 (62)	12 (11)	0.08 (0.03-0.18)*	29 (73)	1.83 (0.72-4.67)
QI 7. Patient did not die in hospital§	162 (74)	83 (73)	1.59 (0.86-2.93)	32 (64)	0.82 (0.39-1.69)	264 (85)	105 (82)	1.68 (0.86-3.28)	34 (72)	0.61 (0.27-1.39)
QI 8. GP contacted or plans to contact relatives about bereavement counselling	150 (69)	72 (65)	0.64 (0.28-1.44)	32 (62)	0.55 (0.23-1.33)	189 (62)	84 (67)	0.88 (0.44-1.73)	27 (56)	0.49 (0.22-1.09)

Missing cases for patients with mild dementia, QI 1, *n*=4 (BE=1 | IT=1 | SP=2); QI 2, *n*=4 (BE=2 | IT=1 | SP=1); QI 3.1, *n*=76 (BE=39 | SP=37); QI 3.2, *n*=1 (IT=1); QI 4, *n*=25 (BE=19 | SP=6); QI 5, *n*=7 (BE=2 | IT=2 | SP=3); QI 6, *n*=36 (BE=11 | IT=13 | SP=12); QI 7, *n*=2 (SP=2); QI 8, *n*=5 (BE=2 | IT=3).
Missing cases for patients with severe dementia, QI 1, *n*=14 (BE=10 | IT=2 | SP=2); QI 2, *n*=13 (BE=8 | IT=2 | SP=3); QI 3.1, *n*=155 (BE=115 | SP=40); QI 3.2, *n*=4 (BE=2 | IT=2); QI 4, *n*=23 (BE=22 | SP=1); QI 5, *n*=11 (BE=7 | IT=3 | SP=1); QI 6, *n*=34 (BE=12 | IT=14 | SP=8); QI 7, *n*=4 (BE=2 | SP=2); QI 8, *n*=9 (BE=6 | IT=2 | SP=1).
Reference group = Belgium. Accounted for the clustering at the level of GPs and adjusted for age, gender, cause of death, and longest place of residence in the last year of life.
QI, quality indicators; CI, confidence interval; OR, odds ratio; Ref., reference category; NA, not applicable.
* Significant at the 0.05 probability level.
† Excluded “don’t know” (mild dementia, 132; severe dementia, 282).
‡ The topics are diagnosis, course of the disease/prognosis, the approaching end of life, advantages and disadvantages of the treatments, options in terms of end-of-life care.
§ Regular hospital wards excluding palliative care units.

Nevertheless, our findings should be interpreted in light of the study's limitations. Firstly, we relied on the GP's estimation of the presence and severity of dementia. GP's specificity in diagnosing dementia is good, making false positive less likely to occur.[25] However, there might be limited misclassifications, which could explain the difference in proportions of dementia severity. Secondly, to limit recall bias, we instructed GPs to use medical files and register deaths within a week.

Although Belgium, Italy, and Spain have national palliative care legal frameworks and have integrated it into their health systems,[13,14] our findings suggest that the overall quality in Belgium is higher than Italy, but not appreciably higher than in Spain. This may be because Belgium has the highest ratio of palliative care resources per million inhabitants [13,14] and provides detailed guidelines for palliative home care teams and networks, promoting collaborative practice and reciprocal sharing of knowledge and expertise with GPs.[26,27] This collaborative practice may also explain our findings regarding the significantly higher scores for repeated multidisciplinary end-of-life care consultations in Belgium. The comparable QI scores for Spain and Belgium may result from their efforts to expand palliative care from cancer to non-cancer patients, including older people and those with dementia.[13,28] Whereas in Italy, palliative care remains focused on the needs of cancer patients,[13] which may explain why Italy had the lowest scores in five of the six QIs wherein the countries studied differed significantly.

While the countries studied differ in the overall quality of primary palliative care, they have similarities in room for improvement. First, the pain of more than half of patients across countries was not regularly measured, which is comparable to what was found in long-term and acute care settings [29]. Pain is highly prevalent among older people with dementia, and if not treated adequately may lead to depression, agitation, and aggression.[30,31] Even where self-reporting is not possible due to cognitive decline, other strategies can be used, such as direct observation of behavioural cues and the use of validated tools such as Pain Assessment in Advanced Dementia (PAINAD) scale.[32,33] In line with an earlier study,[12] more than two thirds of patients, particularly in Italy and Spain, appeared to have poor communication with GPs. The relatively higher score for patient-GP communication in Belgium may be due to their continued efforts in advance care planning [23] and the culture of wanting to be informed about health-related issues.[34] While this poor communication with patient may be understandable due to cognitive decline, our study suggests that this is a problem even for people with mild dementia. Similar with an earlier study,[12] we found high levels of relative-GP communication across the three countries, implying that GPs communicate more often with relatives than with patients, which seems to be an alternative to the poor communication with patients. Finally, although most older people prefer to die at home or in a care home,[35] about a third of people studied died in hospital. Reducing avoidable hospitalisations at the end-of-life may prevent unnecessarily burdensome medical treatments and lower risk for functional decline and mortality.[36]

Conclusion

Our study suggests considerable cross-country differences and similarities in the overall quality of primary palliative care for older people with dementia, potentially as a result of different national health systems (e.g. palliative care resources and focus on dementia) and culture. It also highlights similar opportunities for improvement, in particular pain measurement and prevention of avoidable hospitalisations. Our findings are useful to guide efforts to improve primary palliative care for older people with dementia, while the core set of QIs are useful for monitoring the overall quality of care over time.

Authorship

LVDB, LD, GM, and TVA designed the study. YWHP and LVdB contributed to the construction of quality indicators. SM, GM, and TVA collected the data. RARM and YWHP analysed the data. All authors contributed equally to data interpretation. RARM, YWHP, TS, and LVDB drafted the article. All authors critically revised the article and granted approval for publication.

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Declaration of conflicts of interest

The authors declare that there is no conflict of interest.

Data management and sharing

The data that support the findings of this study are available from the Belgian Scientific Institute of Public Health, the Dutch NIVEL Primary Care Database, the Italian Cancer Prevention and Research Institute and the Spanish Regional Ministry of Health of Valencia and Castile and Leon, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the appropriate institute.

Research ethics and patients consent

After being fully informed about the study objectives and method, the participating general practitioners (GPs) provided written informed consent at the start of each registration year. During data collection and entry, we followed strict procedures about patient anonymity. The GPs provided an anonymous reference for each registered death. Any data that may potentially reveal the identity of the GP or patient were replaced by aggregate categories or anonymous codes. Patients of the GPs who were part of the Sentinel Network in Belgium were informed that their data could be used anonymously for research purposes through posters or leaflets displayed in practices. In Italy, patients were informed that their anonymised care-related data may be used to monitor care standard. In Spain, patients were not necessarily informed that their data will be used for research as their data were carefully anonymised.

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Supplementary table 1. List of selected and discarded quality indicators

	Palliative care domains and quality indicators	Mean score for usefulness and relevance†	Selection after the multi-step process ‡
	Domain 1: Physical aspects of care		
D1.1	Percentage of patients whose pain was known by the GP to be monitored regularly during the last three months of life.	7,5 (selected)	Selected (QI 1)
D1.2	Percentage of patients who were known by the GP to be monitored regularly for delirium during the last three months of life.	6,0	
D1.3	Percentage of patients whose symptoms were under control during the last week of life.	7,5	Not included in the questionnaire
	Domain 2: Psychological, social and spiritual treatment and care		
D2.1	Percentage of patients who were known by the GP to be receiving regular assessment for anxiety during the last three months of the patient's life.	6,5	
D2.2	Percentage of patients who were known by the GP to be monitored regularly for psychosocial problems during the last three months of the patient's life.	7,3	
D2.3	Percentage of patients who were known by the GP to be monitored regularly for religious/spiritual/existential problems during the last three months of the patient's life.	6,0	
D2.4	Percentage of patients known by the GP to have accepted that they were nearing the end of their life.	8,0 (selected)	Selected (QI 2)
	Domain 3: Information, communication, planning and decision-making with the patient		
D3.1	Extent to which patients receive information from the GP about diagnosis, prognosis, disease progression, advantages and disadvantages of treatments, palliative care options.	8,0 (selected)	Selected (QI 3.1)
D3.2	Extent to which care providers indicate that the patient has been asked how he/she feels about end-of-life decisions.	6,0	
D3.3	Number of contacts between the GP and the patient in the last 3 months of life.	7,5 (selected)	Discarded, due to lack of clarity on causal relationship
D3.4	Percentage of patients whose wishes regarding care goals have been discussed with the GP.	8,0 (selected	Selected (QI 3.2)
D3.5	Percentage of patients whose GP is aware of their wishes regarding resuscitation.	7,5 (selected)	Discarded, due to overlap with the QI for 'wishes for treatment'
D3.6	Percentage of patients whose nominated proxy decision-maker was involved when the patient became mentally incompetent.	7,8 (selected)	Discarded, due to low quality (50% missing cases) and low usability (ceiling effect)
D3.7	Percentage of patients for whom documentation is available regarding the end-of-life care and treatment that they wish to receive.	7,0	
D3.8	When a patient expressed specific wishes regarding a medical treatment that he/she does or does not want to receive towards the end of life then no further medical procedures or treatments are performed in the last week of life that are not in accordance with the wishes expressed.	7,3	
	Domain 4 Information, communication, planning and decision-making with the family and friends		
D4.1	Extent to which care providers keep the family and friends informed about the patient's condition and treatments.	6,5	
D4.2	Extent to which the family and friends are informed that the patient is nearing the end of his/her life.	7,0 (selected)	Selected (QI 4)
D4.3	Extent to which family and friends were consulted if decisions have been made about tube feeding or artificial fluids and feeding.	6,3	
	Domain 5: Information, communication, planning and decision-making with other care providers		
D5.1	Repeated (on several occasions) formal multidisciplinary consultation with and between care providers (between settings, including GP) about the patient's care goals and palliative care options.	8,0 (selected	Selected (QI 5)
	Domain 6: Type of end-of-life care		
D6.1	Percentage of patients with an acceptable time span between a new course of chemotherapy and death (according to Grunfeld, more than 2 weeks prior to death)	6,3	
D6.2	Percentage of patients for whom palliative care is started in good time.	7,5 (selected)	Selected (QI 6)
D6.3	Percentage of patients whose GP indicates that the patient has died peacefully. ¶	Discarded	Discarded

D6.4	Extent to which patients have the opportunity to be alone with close family and friends *in the last week of life.*	6,8	
D6.5	Percentage of patients for whom fluids and feeding (not including precautionary intravenous/IV line) were not started in the last month before their death.	6,3	
	Domain 7: Coordination and continuity of care		
D7.1	Extent to which information regarding care and treatment is communicated within the setting/to the next setting prior to a transfer/discharge/admission.	7,0	
D7.2	Extent to which the care goals and resuscitation status are communicated to the team at the facility to which the patient is transferred.	7,0	
D7.3	Extent to which information is noted in the medical records: the prognosis, psychosocial symptoms, functional status and symptom burden.	8,0	Not included in the questionnaire
D7.4	Percentage of patients with more than one visit to an emergency department in the last 30 days before their death.	8,0 (selected)	Discarded, low quality (26% missing cases)
D7.5	Percentage of patients who are admitted to an intensive care department in the last 30 days before their death.	7,5 (selected)	Discarded, kept the QI with the highest mean score
D7.6	Percentage of patients with more than one hospital admissions in last 30 days (according to “Earle/Peruselli”, more than one)	8,0 (selected)	Discarded, low quality (50% missing cases in Spain) and low usability (ceiling effect)
D7.7	Percentage of patients who *remained* in their preferred location in the last month before their death.	7,5 (selected)	Discarded, kept the QI with the highest mean score
D7.8	Percentage of patients who *died* in their preferred location.	8,0 (selected)	Discarded, low usability (invalid question)
D7.9	Percentage of patients who die at home.	7,5 (selected)	Selected (QI 7)
D7.10	Percentage of patients who know who the designated contact for care is according to the GP.	6,5	
	Domain 8: Support for family/friends and informal carers		
D8.1	Extent to which a regular check is kept on the resilience of the informal carers.	6,8	
D8.2	Extent to which family and friends get sufficient help with the coordination of practical problems.	6,5	
D8.3	Extent to which the family and friends get sufficient information about social services and arrangements and about financial allowances.	6,5	
D8.4	Extent to which close family and friends are advised of the possibilities of aftercare.	6,5	
D8.5	Extent to which family/friends and informal carers get support with organizing the care process.	6,5	
D8.6	Follow-up bereavement counselling offered by the physician.	8,0 (selected)	Selected (QI 8)
	Domain 9: Structure of care §		
D9.1	Percentage of GPs with training in palliative care§	8,0 (selected)	Discarded, this domain was excluded
D9.2	Percentage of GPs who work with a mobile palliative home-care team for x% of their palliative patients (percentage to be determined) §	8,0 (selected)	Discarded, this domain was excluded
D9.3	Availability of specialist palliative care at home or in a hospice if the GP should have questions when counseling patients§	8,0 (selected)	Discarded, this domain was excluded

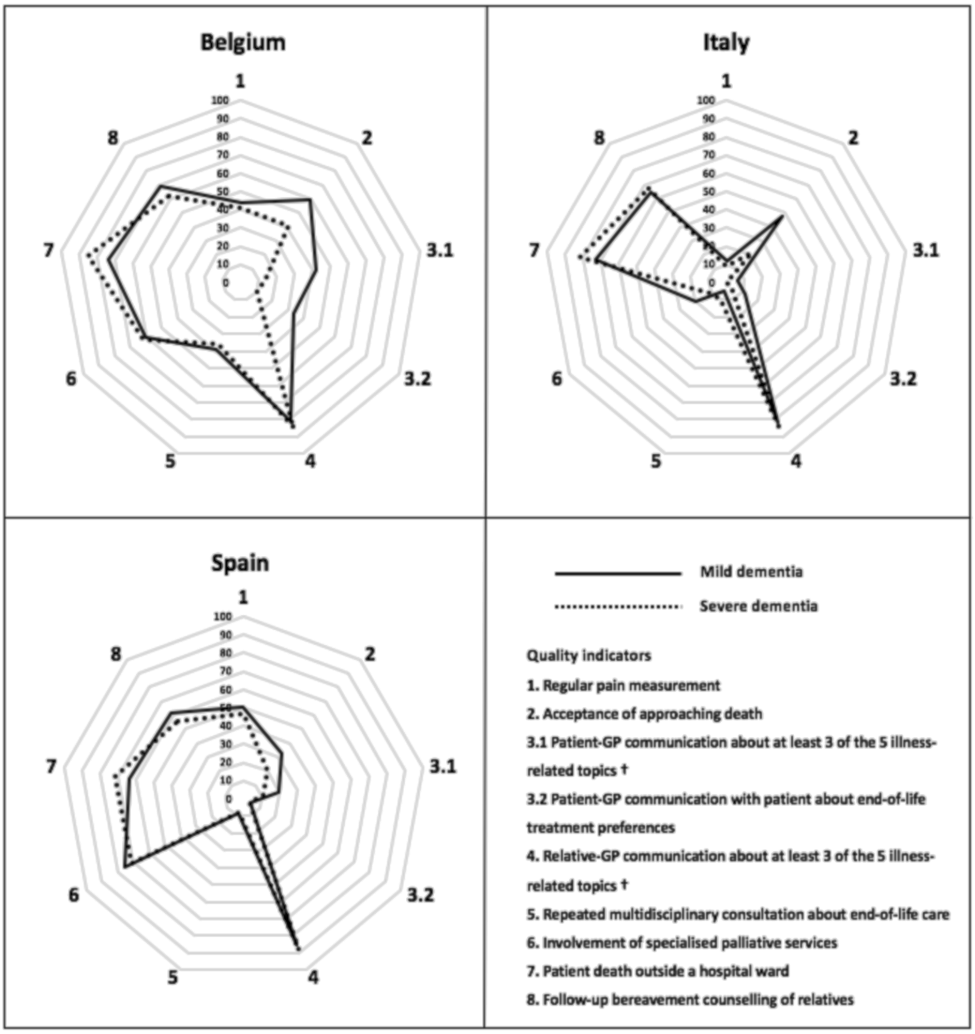
GP, General Practitioner; QI, quality indicator.

† Results of the expert consultation and steering group

‡ The remaining quality indicators were further evaluated for data quality and usability, while ensuring to keep at least 1-2 quality indicator per domain

§ Collected through yearly registration of GP Sentinel networks

¶ Quality indicator D6.3 was discarded due to the lack clarity regarding the domain into where it should be categorised (Psychosocial aspect of care rather than type of end-of-life care)



Supplementary figure 1. Overview of the nine quality indicator scores in Belgium, Italy, and Spain.

† Illness-related topics included diagnosis, course of the disease/prognosis, the approaching end of life, advantages and disadvantages of the treatments, and options in terms of end-of-life care

CHAPTER 5

Palliative care for people with dementia living at home: a systematic review of interventions

Rose Miranda, Frances Bunn, Jennifer Lynch, Lieve Van den Block and Claire Goodman

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ABSTRACT

Background. The European Association for Palliative Care (EAPC) White Paper defined optimal palliative care in dementia based on evidence and expert consensus. Yet, we know little on how to achieve this for people with dementia living and dying at home.

Aims. To examine evidence on home palliative care interventions in dementia, in terms of their effectiveness on end of life care outcomes, factors influencing implementation, the extent to which they address the EAPC palliative care domains and evidence gaps.

Design. A systematic review of home palliative care interventions in dementia.

Data sources. The review adhered to the PRISMA guidelines and the protocol was registered with PROSPERO (CRD42018093607). We searched four electronic databases up to April 2018 (PubMed, Scopus, Cochrane library and CINAHL) and conducted lateral searches.

Results. We retrieved eight relevant studies, none of which was of high quality. The evidence, albeit of generally weak quality, showed the potential benefits of the interventions in improving end of life care outcomes, e.g. behavioural disturbances. The interventions most commonly focused on optimal symptom management, continuity of care and psychosocial support. Other EAPC domains identified as important in palliative care for people with dementia, e.g. prognostication of dying or avoidance of burdensome interventions were under-reported. No direct evidence on facilitators and barriers to implementation was found.

Conclusions. The review highlights the paucity of high-quality dementia-specific research in this area and recommends key areas for future work, e.g. the need for process evaluation to identify facilitators and barriers to implementing interventions.

Key statements

What is already known about the topic?

- There is an urgent need to find effective strategies to improve home-based care for people with dementia.
- The European Association for Palliative Care (EAPC) White Paper defined optimal palliative care in dementia based on evidence and expert consensus.
- We know little about the evidence base on how to achieve optimal palliative care in dementia for people living and dying at home.

What this paper adds?

- There is evidence, albeit limited and of generally weak quality, that shows the potential benefits of home palliative care interventions in dementia in improving end-of-life care outcomes, such as the management and reduction of behavioural disturbances in people with dementia.
- The interventions focused mainly on symptom management, continuity of care and psychosocial support, with less attention paid to four other EAPC domains considered important for people with dementia, e.g. prognostication of dying or avoidance of burdensome interventions.
- The paper highlights several gaps in the evidence, including the limited evidence on facilitators and barriers to implementing the intervention and the lack of consensus on outcome measures used.

Implications for practice and research

- The EAPC's definition of optimal palliative care in dementia provided a useful framework for a systematic assessment of the range and focus of evidence of what is effective for people with dementia living and dying at home.
- The review highlights the paucity of high-quality dementia-specific research in this area and recommends key areas for future work, such as the need for process evaluations to identify facilitators and barriers to implementing interventions or for a standard outcome set to facilitate comparisons and meta-analyses.
- High-quality dementia-specific research is required to further support the evidence base for palliative care interventions to be a routine care for people with dementia living and dying at home.

BACKGROUND

Dementia is a life-limiting illness characterised by widespread physical, cognitive and behavioural impairment, resulting in severe disabilities that persist until death.(1,2) The global prevalence of dementia is projected to increase to almost 132 million by 2050.(3) The high demand for dementia care, the individual's preference to stay at home for as long as possible combined with limited supply and rising costs of institutional long-term care services highlight an urgent need to find effective strategies to improve home-based care for people with dementia, including those with advanced dementia requiring end of life care.(4–7)

To improve the quality of life of people with dementia and their families, a palliative care approach has been widely recommended.(8–10) In 2014, van der Steen and colleagues published the European Association for Palliative Care (EAPC) White Paper defining optimal palliative care in dementia based on evidence and expert consensus. These experts achieved consensus on 57 salient recommendations that fall under 11 important domains of palliative care: applicability of palliative care; person-centred care, communication, and shared-decision making; setting care goals and advance planning; continuity of care; prognostication and timely recognition of dying; avoiding overly aggressive, burdensome or futile treatment; optimal treatment of symptoms and providing comfort; psychosocial and spiritual support; family care and involvement; education of the health care team; and societal and ethical issues (Supplementary table 1).(11) The majority of this evidence draws on work in long term care and institutional settings. Less well known is the evidence on the effectiveness of palliative care interventions for people with dementia living at home.

A Cochrane review on palliative care interventions in advanced dementia found only two low quality studies, neither of which was conducted in the home setting.(12) In a systematic review that aimed to identify populations appropriate for palliative care and effective palliative care models, they found improvements in pain and depressive symptoms in people with dementia. However, this study did not indicate whether the population with dementia were living at home.(13) Another Cochrane review evaluated palliative care services for people living at home with advanced incurable illnesses, including those with dementia. They found reliable evidence that these services could reduce symptom burden and increase the chance that people with terminal diseases will die at home. However, the evaluated services were only for people with cancer and organ failure, rather than for people with dementia.(14)

In the last five years, there have been an increasing policy commitment to improving dementia care with concomitant increase in research funding.(15,16) In order to guide efforts to improve the care for people with dementia living and dying at home, we conducted a systematic review to examine evidence on palliative care interventions for this population. Our overall aim was to synthesize evidence on the effectiveness of palliative care interventions on end of life care outcomes (e.g. patient death at home or pain) for people with dementia living at home. In addition, we reviewed facilitators and barriers to implementing these interventions, assessed the extent to which the interventions reflected optimal palliative care in dementia as defined in the EAPC White Paper and identified gaps in evidence.

METHODS

Design

The systematic review adhered to the PRISMA guidelines and the protocol was registered with the PROSPERO international prospective register of systematic reviews (www.crd.york.ac.uk/prospero/ -CRD42018093607).

Eligibility criteria

We included peer-reviewed quantitative studies evaluating palliative care interventions for people with any type of dementia living at home. This included randomised controlled trials (RCTs), controlled clinical trials (CCTs), non-randomised controlled studies, controlled and uncontrolled before and after studies, interrupted time series (ITSs) and case studies published in either English or Dutch. To provide a comprehensive overview of existing research in this area, we included specialist palliative care services and non-specialist palliative care interventions, i.e. interventions that were not labelled as 'palliative care' but described as aiming to improve care at the end of life for people with dementia.

Specialist palliative care included services with the following four elements: 1) designed primarily for people with dementia living at home; 2) aim to support people outside hospital and other institutional settings for as long as possible and to enable people to stay at home; 3) be provided by specialists in palliative care or intermediate palliative/hospice care; 4) provide comprehensive care addressing different physical and psychosocial components of palliative care.(14) Non-specialist palliative care included interventions that focused either on people with advanced/severe/late stage dementia living at home or on people with dementia living at home with the potential impact on palliative care or death and dying or end of life care outcomes.

End of life care outcomes included patient death at home as the primary outcome. Secondary outcomes included time the patient spent at home, pain, dyspnoea, depressive symptoms, behavioural symptoms common at the end of life, existential or spiritual concerns, communication or care planning, experience or satisfaction, functional status, health-related quality of life, and resource use.(14) In addition to the outcomes registered in Prospero, we added institutionalisation as a secondary outcome, as it had been reported in two of the studies included. Studies that did not focus entirely on the home setting or dementia (e.g. studies on primary care or advanced incurable illnesses) were also included, provided that the majority of the participants (>50%) lived at home or had dementia.

Search strategy

The search strategy was undertaken in two phases from April to June 2018 to search for literature relating to specialist palliative care services (Phase 1) and non-specialist palliative care interventions (Phase 2). Two search strategies were developed by the research team with advice from an information specialist. In Phase 1, we used a combination of MESH headings, controlled vocabulary and free-text terms to cover palliative/end of life/terminal care, dementia, and the home setting. In Phase 2, we covered the home setting combined with either advanced/severe/late stage dementia or dementia with outcome measures relating to palliative care or death or dying. We searched four electronic databases: PubMed, Scopus, Cochrane Library, including the Cochrane Central Register of Controlled Trials (CENTRAL) and Cochrane Database of Systematic Reviews, and Cumulative Index to

Nursing and Allied Health Literature (CINAHL) (from inception to April 2018). The search strategies were validated in PubMed and translated for use in the other databases (Table 1). We also performed hand-searching of relevant journals and reference lists of included and relevant articles and citation tracking in Google Scholar). We also contacted the author of a relevant study protocol to ask for update about their study.(17)

Table 1. Search syntax for the database search

Phase 1. Specialist palliative care services	
PubMed	(((((((""Palliative care""[MESH]) OR palliative care[Title/Abstract]) OR ""Terminal care""[MESH]) OR terminal care[Title/Abstract]) OR end of life care[Title/Abstract])) AND (((""Dementia""[MESH]) OR dementia[Title/Abstract]) OR Alzheimer[Title/Abstract])) AND ((((home[Title/Abstract]) OR ""Primary health care""[MESH]) OR ""General practice""[MESH]) OR community[Title/Abstract])
Scopus	(palliative care OR terminal care OR end of life care) AND (dementia OR Alzheimer) AND (community OR home)
CINAHL	((MH "Palliative Care") OR "palliative care" OR terminal care OR end of life care) AND ((MH "Primary Health Care") OR "primary health care" (MH "Family Practice") OR "general practice" OR community OR home) AND ((MH "Dementia") OR "dementia" OR Alzheimer)
Cochrane library	"Palliative care" and "dementia" and home
Phase 2. Non-specialist palliative care interventions	
PubMed	(((((((Dementia[MeSH Terms]) OR dementia[Title/Abstract]) OR Alzheimer[Title/Abstract])) AND (((((Home health nursing[MeSH Terms]) OR Primary health care[MeSH Terms]) OR General practice[MeSH Terms]) OR home[Title/Abstract]) OR community[Title/Abstract])) AND (((((Death[Title/Abstract]) OR Die[Title/Abstract]) OR Dying[Title/Abstract]) OR Deceased[Title/Abstract]) OR "end of life"[Title/Abstract]))) OR (((((((Advanced[Title/Abstract]) OR Severe[Title/Abstract]) OR "Late stage"[Title/Abstract]) OR "Late-stage"[Title/Abstract])) AND (((Dementia[MeSH Terms]) OR dementia[Title/Abstract]) OR Alzheimer[Title/Abstract])) AND (((((Home health nursing[MeSH Terms]) OR Primary health care[MeSH Terms]) OR General practice[MeSH Terms]) OR home[Title/Abstract]) OR community[Title/Abstract]))
Scopus	(**KEY** (*dementia* OR *alzheimer*) AND **KEY** (*"Primary care"* OR *"General practice"* OR *community* OR *home* OR *"Primary health care"*) AND **TITLE-ABS-KEY** (*advanced* OR *severe* OR *"late stage"* OR *"late-stage"*) OR **TITLE-ABS-KEY** (*death* OR *dying* OR *die* OR *deceased*))
CINAHL	((MH "Dementia") OR "dementia" OR alzheimers) AND ((MH "Primary Health Care") OR "primary health care" OR (MH "Family Practice") OR "general practice" OR community OR home) AND ((Advanced OR severe OR "Late stage" OR "Late-stage") OR (Death OR Dying OR die OR deceased))
Cochrane library	((Advanced OR Severe OR "Late Stage") OR (Death OR Dying OR Die OR Deceased)) AND (Dementia OR "dementia" OR Alzheimer) AND home

Study selection

The first author (RM) removed duplicates and screened the titles and abstracts for relevance. Studies considered potentially relevant were marked as ‘include’ or ‘uncertain’. A random twenty percent of articles were independently screened by two co-authors (FB, JL). Full texts were retrieved for studies deemed as ‘included’ or ‘uncertain’. These were screened by RM against the eligibility criteria and checked by FB and JL. Discrepancies were discussed and resolved among the three authors. A PRISMA flowchart was created to describe the selection procedure and the rationale for exclusion was compiled. Mendeley citation management software was used for deduplication and management of references. Multiple reports about a similar study were collated to ensure that each study rather than each paper is the unit of interest.

Data extraction

The data were extracted to a specially-designed form in MS Excel version 16 (© Microsoft 2018). This form was pilot-tested on three articles to ensure consistency and was approved by the research team. Characteristics of the included studies were extracted by RM and checked for accuracy by FB. Study characteristics included country, study design, data collection method, research question (aim), setting, participants and intervention type. RM and FB independently extracted data on outcomes. Discrepancies were resolved by discussion and consensus between three reviewers (RM, FB, JL). Qualitative data on intervention components and potential barriers and facilitators to implementing the interventions were also extracted.

Quality appraisal

Quality appraisal was conducted by RM and FB using the "Quality Assessment Tool for Quantitative Studies" developed by Effective Public Health Practice Project.(18) Studies were rated as either strong, moderate or weak on the following components: selection bias, study design, confounders, blinding, data collection methods, withdrawals/ dropouts, intervention integrity, and appropriate data analyses used. Two authors discussed any discrepancies and reached consensus. The quality was considered as either strong (no weak ratings), moderate (one weak rating), or weak (two or more weak ratings).

Data synthesis

We described the included studies in terms of country of origin, design, data collection method, intervention components and participants. Due to heterogeneity in interventions and outcomes, data were not pooled in a meta-analysis. Instead, the outcomes of the interventions were presented separately in a table with an indication of whether the effects of the intervention were positive, negative or statistically insignificant. The available data did not allow us to calculate effect sizes. Hence, we presented data in the way it was reported in the study (e.g. P values). Qualitative data on facilitators and barriers were synthesised thematically and presented in a narrative way. We mapped the components of each of the interventions according to the 11 EAPC White Paper domains. This ensured that data synthesis was focused on aspects of care identified by international experts as important in palliative care for people with dementia. This provided insights on potential gaps and room for improvement that could better inform developers of home palliative care interventions in dementia. No subgroup analysis was conducted to look at the difference between specialist palliative care services and non-specialist palliative care interventions due to low number of articles relating to specialist palliative care.

RESULTS

In all, three articles met the inclusion criteria for specialist palliative care services and six for non-specialist palliative care interventions. The overview of the study selection is depicted in Figure 1.

General overview of the studies

We identified three studies evaluating specialist palliative care services (19–21) and five evaluating non-specialist palliative care interventions (Table 2).(22–27) One study on non-specialist palliative care intervention was reported in two articles.(22,23) Four of the studies presented evidence from the US,(19,20,24,25) two from Italy,(22,23,27) and one each from the UK (26) and Japan.(21) Of the studies, four were RCTs,(21–24) two retrospective case-control studies,(19,25) one retrospective cross-sectional study (20) and one with an unclear study design.(27) All studies used quantitative methods, one of which also used qualitative methods.(20) All studies included both male and female participants, with the majority in their eighties and women. Seven studies included people with dementia and one included terminally-ill participants, 64% of whom had dementia.(20) All interventions aimed to improve end of life care for people with dementia living at home, while one offered additional support to family caregivers.(24)

Quality of the evidence

Overall, five of the eight studies were considered of weak quality, particularly due to high risk for selection bias, inability to achieve blinding and inability to clearly measure and/or report the integrity and consistency of the intervention (Table 2).(19,20,22,23,25,27) Of these studies, three did not control for confounders and used inappropriate data analysis techniques,(20,22,23,27) while the other two studies took potential confounders into account by using propensity score matching to identify control group and analysed the data appropriately.(19,25) These five studies received moderate ratings for using health/medical records as the source of data, but the procedures for data collection were inadequately reported.

The three other studies were assessed as being of moderate quality, two received a weak rating for not achieving blinding,(21,26) while the other one received a weak rating for selection bias due to a small sample size.(24) These studies received strong ratings for study design, confounders, data collection, withdrawals/drop-outs, intervention integrity, and the data analysis techniques used. The quality of the qualitative data from the mixed-methods study was not assessed, as these data were used solely to identify potential barriers and facilitators to implementing the intervention.(20) (See Supplementary table 2 for the composite component ratings for each study).

Palliative care interventions for people with dementia living at home

Overview of specialist palliative care services

We identified three specialist palliative care services, all of which focused on educating the multi-disciplinary healthcare team (Table 2).(19–21) Transitions programme (19) and Palliative Access Through Care at Home (PATCH) (20) were specialist palliative care services delivered by trained specialist palliative care team comprising typically of geriatricians, nurses and social workers. Behaviour Analytics & Support Enhancement (BASE) is a palliative care-based psychosocial intervention delivered by trained professional home care providers, who aimed to explore unmet needs and address challenging behaviours of people with dementia in coordination with a multidisciplinary healthcare team.(21) These interventions were delivered through home visits, ranging from four to six times per week or based on patients' needs. Each intervention had multiple components, such as symptom management, medical consultation, reduction of polypharmacy, assistance with advance care planning and transitions of care, and psychosocial and spiritual support.

Overview of non-specialist palliative care interventions

Non-specialist palliative care encompassed a diverse range of interventions for people with advanced dementia (Table 2). Two studies aimed to address behavioural disturbances, one by using Multi-Sensory Stimulation (MSS) provided in day-care centres (26) and one by training and supporting primary caregivers, i.e. formal or family caregiver, to use the Comprehensive, Individualized, Person-Centred Management (CI-PCM) approach.(24) The other three studies aimed to bring care that is usually offered in institutions or hospitals to patients' homes. One of these studies evaluated the medical care offered by House Calls (25) and two evaluated the diagnostic and therapeutic treatments for acute illnesses offered by Home Hospitalisation Service.(22,23,27)

Outcomes of home palliative care interventions in dementia

The outcomes of home palliative care interventions for people with dementia are summarised in Table 3.

Patient death at home

One of the studies (retrospective cross-sectional study of weak quality) reported outcome on patient death at home.(20) This study showed that about two thirds of deceased participants with dementia who received palliative care from the trained specialist care team died at home and inpatient hospice. However, this evidence on effectiveness was inconclusive, as it relied exclusively on cross-sectional data collected through chart review and thus there was no control group or before and after data.

Institutionalisation

Two of the studies reported outcome on institutionalisation. These studies (one RCT and one unclear study design, both studies of weak quality) evaluated Home Hospitalisation Service.(22,27) They suggested that people with advanced dementia who received diagnostic and acute care at their own homes were less likely to be transferred to nursing homes and more likely to stay at home.

Functional status

One of the studies (RCT of moderate quality) evaluated functional status as an outcome.(24) This study showed that the functional status of people with dementia who received care from the trained primary caregivers on CI-PCM approach were more likely to improve than those who did not at all follow-up measurements (months 4, 12 and 28).

Behavioural symptoms common at the end of life

Four of the studies assessed behavioural symptoms, all of which suggested that home palliative care interventions are more effective than usual care in reducing behavioural disturbances.(21,23,24,26) Three studies (all RCTs of moderate quality) suggested positive effects of home palliative care interventions on behavioural disturbances of people with dementia. These interventions included the Multi-Sensory Stimulation (MSS) sessions offered in day-care centres (26) and the training courses on BASE for professional home care providers (21) and on CI-PCM approach for primary caregivers.(24) The fourth study (RCT of weak quality) reported marginally significant effect in the same direction on sleeping disorder, agitation/aggressiveness and feeding disorders.(23) However, evidence on the duration of effects was conflicting. One study found long-term positive effects of the training course on CI-PCM approach for primary caregivers on behavioural symptoms,(24) whereas another study found that behavioural symptoms deteriorated after the MSS sessions had ceased. This deterioration has been attributed to potential withdrawal effect from the one-to-one session and the appropriate stimulation.(26)

Pain

One of the studies (RCT of moderate quality) reported pain as an outcome, but results were inconclusive.(21) This study evaluated the training course on BASE, a palliative care-based psychosocial intervention offered to home care professionals who were responsible for assessing the pain of participants with dementia and discussing this assessment with the multidisciplinary team. This study suggested that compared with control group, the participants in the intervention group had significant pain reduction from baseline to follow-up assessment. However, after controlling for baseline characteristics at follow-up, no significant difference in pain was found between the two groups potentially due to the higher pain score in the intervention group at follow up. This higher pain score was attributed to the enhanced pain assessment conducted by the trained care professionals in the intervention group, whereas the care professionals who did not receive the training course may have underestimated or remained unaware of the need for pain assessment in dementia.

Satisfaction

One of the studies (retrospective cross-sectional study of weak quality) reported outcome on satisfaction. This study suggested generally high satisfaction rate of primary caregivers of people with dementia with the care provided by the trained specialist palliative care team.(20) However, this evidence was inconclusive, as it relied exclusively on a cross-sectional survey of 22 primary caregivers of deceased people with dementia who received the intervention.

Resource use

Two of the studies (both retrospective case-control studies of weak quality) reported outcomes on resource use based on estimated costs.(19,25) Compared to usual care, the Transitions programme training of specialist palliative care team resulted in lower hospital, non-hospital and all costs. It also resulted in better hospitalisation outcomes, in terms of frequency, length of stay in hospital, patient deaths in hospital, hospitalisation rates, readmission rates and admission in the intensive care unit in the final 30 days of life. They also found that in the final six months of life, resource use in the intervention group had only increased slightly, compared with a larger increase in the control group. Net cost reduction was also better in the intervention group than the control group.(19) The other study on House Calls showed that compared to control group, patients with dementia who received medical care in their own homes were more likely to have home health and hospice expenditures, but less likely to have social health expenditures. The authors attributed the relatively low social services utilization to the limited financial reimbursement available for social services.(25)

Table 2. General overview of the included studies on palliative care interventions (*n*=8).

Studies evaluating specialist palliative care services (*n*=3)				
Study	Study design	Specialist palliative care services	Study participants	Quality*
Cassel 2016 - United States of America	Observational retrospective (Case-control) Quantitative	**Transitions programme** – developed to improve palliative care for home-bound individuals with advanced chronic illness, including those with dementia. - Focused on training a specialty palliative care team comprising of doctors, nurses, spiritual care providers, and social workers. Specific interventions included in-home medical consultation, prognostication of further survival, caregiver support and advance care planning, pain and non-pain symptom management, education to promote awareness of illness trajectory and treatment choices, and psychosocial and spiritual support. - Delivered through home visits (frequency of home visits per week: 4-6 times from the registered nurses, 1-3 times from the social workers, and from the Chaplain services if needed). - When identified goals have been achieved, patients continued to receive home visits, although less frequently, supplemented with scheduled telephone calls for case management to ensure continuity of care.	Home-bound people with Medicare Advantage insurance, two years usage data, and dementia. (Case group, n=92; Control group identified using propensity score matching, n=276).	**Weak**
Holley 2009 - United States of America	Observational retrospective study (Cross-sectional) Mixed-method	**Palliative Access Through Care at Home (PATCH)** – developed to improve palliative care for vulnerable home-bound older adults with limited access to medical care, of which the majority had dementia. - Focused on training medical staff to improve a patient's quality of life, symptom management, reducing polypharmacy, supporting caregivers and assisting with advance medical planning, complex decision-making and facilitating the transitions of care. Specific interventions included medical interventions, home assessment, communication and goals of care and availability of care. - Delivered through home visits (frequency per week: 4 half-days or based on patients' needs from weekly to every 3 months) and 24-hour access to a member of the care team by telephone and on-call paging system.	**Chart review:** Home-bound people enrolled in Medicare Advantage Part B, had an existing University of Chicago affiliation, had limited life-expectancy based on primary caregiver's perception (>65 years old; 64% of the sample had dementia), n=74. **Telephone interviews,** n=22. **Face-to-face in-depth interviews,** n=13: primary caregivers.	**Weak**
Nakanishi 2018 - Japan	Randomised controlled trial Quantitative	**Behaviour Analytics & Support Enhancement (BASE) programme – developed as a** palliative care-based psychosocial intervention to explore unmet needs and address challenging behaviours of home-bound people with dementia. - Focused on a two-day training course for care professionals from local home care service providers to identify and manage unmet needs in order to reduce challenging behaviours of people with dementia. The topics addressed in the training included dementia as an illness, challenging behaviour as a communication of unmet needs, assessment of challenging behaviour and exploration of unmet needs and action plans. The training course was based on the Behavioural and Psychological Symptoms of Dementia Programme of Care, which is based on the well-developed national guidelines for dementia care. - Delivered through home visits. The care professionals also conducted ongoing assessment of challenging behaviour, multiagency discussion meetings to ensure continuity of care, monthly multiagency discussion and care managers-scheduled mandatory monthly meetings.	Home-bound patients with a diagnosis of dementia (>65 years old) of participating care professionals (Intervention group, n=141; Control group, n=142).	**Moderate**

Studies evaluating non-specialist palliative care interventions (*n*=5)

Study	Study design	Non-specialist palliative care interventions	Study participants	Quality*
Baker 2001 - United Kingdom	Randomised controlled trial Quantitative	**Multi-Sensory Stimulation (MSS) –** developed to improve behaviour and mood of older adults with moderate to severe dementia by exploring stimuli and being in a state of relaxation. MSS was added to a credible control condition of eight standardised Activity sessions. The MSS and Activity sessions had similar non-specific conditions: one-to-one attention, staff time, and number, length, frequency, location and time of sessions. - Focused on stimulating all senses, except taste, using multisensory experience, unpatterned non-sequential stimuli, nondirective enabling approach by staff and no intellectual/physical demand. - Delivered by a trained therapist at two day-centres fully equipped with MSS rooms and another room equipped with multi-sensory environments.	Home-bound people with moderate-severe dementia with a primary carer; referred to the Elderly Mental Health Service of Dorset HealthCare NHS Trust by their general practitioner, who attended at the participating day-centres for 2 or more days/week; had no other psychiatric diagnoses; and had not received more than 1 MSS session in the last 3 months. (Intervention group, n=25; Control group, n=25)	**Moderate**
Reisberg 2017 - United States of America	Randomised controlled trial Quantitative	**Comprehensive, Individualized, Person-Centered Management (CI-PCM)** – developed to complement memantine treatment in reducing behavioural disturbance among community-dwelling people with moderate to severe Alzheimer's disease. - Focused on training the primary caregivers of people with dementia to deliver care based on the universal human treatment and human rights principles, which encompassed the majority of the palliative care domains. - Delivered in New York University Langone Medical Center.	People with dementia of the Alzheimer type, who resided at the community at the time of screening, and had a family and/or professional caregiver willing and able to participate in the study. (Intervention group, n=10; Control group, n=10)	**Moderate**
Wilson 2015 - United States of America	Observational retrospective (Case-control) Quantitative	**House Calls** – developed to provide medical care to home-bound frail older people including those with Alzheimer's disease and dementia - Focused on ensuring continuity of care, integrated care based on patients' needs, coordinated team-based approaches to medical care and social work. - Delivered by a team of physicians, nurse practitioners, non-clinical care managers and social workers.	Home-bound people with Medicare Advantage insurance enrolled in the House Calls program during the study period (2004-2006). (Case group, n=144; Control group identified using propensity score matching, n=440).	**Weak**
Aimonino 2001 - Italy	Unclear† Quantitative	**Home Hospitalisation Service (HHS)** – developed to perform medical interventions, which are usually done in hospital, at home of people with severe dementia. - Intervention components and implementation unclear.	Patients with advanced dementia admitted in hospital (Intervention group, n=41; Control group, n=41)	**Weak**
Fabris 2004 and Tibaldi 2004 - Italy	Randomised controlled trial Quantitative	**Home Hospitalisation Service (HHS)** – same intervention evaluated by Aimonino et al 2001 - Focused on bringing all critical elements of hospital care to the home setting of acutely-ill patient, such as equipped physician and nursing care working together, medicines and appropriate diagnostic and therapeutic technologies. - Delivered by geriatricians, nurses, physiotherapists, social workers and counsellors. The HHS is operative for seven days during the week, starting at eight o'clock in the morning and ends at eight p.m. and there is a daily meeting for planning care management of each subject to ensure the coordination and continued provision of care.	Patients with advanced dementia admitted in hospital due to acute illness, were stable, not expected to require emergency interventions, with appropriate care supervision, had telephone connection and resided in the hospital catchment area. (Intervention group, n=56; Control group, n=53)	**Weak**

* Overall quality was considered as either strong (no weak ratings), moderate (one weak rating), or weak (two or more weak ratings) based on the rating of the integrity of each of the following components: selection bias, confounders, blinding, data collection methods, withdrawals/ dropouts, intervention integrity, and appropriate data analyses used.

† Study design is deemed unclear due to the inadequate information provided about the implementation of the study, in particular about randomisation of participants.

Table 3. Outcomes of home palliative care interventions for people with dementia

Primary outcome measure		
Patient death at home Holley 2009	**Based on chart-review of deceased PATCH participants** - More than two thirds of patients died at home and inpatient hospice - Almost a third died in hospital - Low percentage of deceased patients died in a nursing home **Based on chart-review of deceased PATCH participants with dementia** - More than half of patients with dementia died at home and inpatient hospice - More than a third of patients with dementia died in hospital - No patient with dementia died in a nursing home	 45.5% (home) and 22.7% (inpatient hospice) 27.3% 4.5% 35.7% (home) and 28.6% (inpatient hospice) 35.7% 0%
Secondary outcome measures		
Institutionalisation Aimonino 2001	**Source of data unclear** - Mortality rates - Lower percentage of patients being transferred to nursing homes Higher percentage of patients who stayed/returned at home	**HHS group vs. Control (GMW) group** 7.3% vs. 2.4%, p-value=NS 2.4% vs. 41.46, p-value<0.001 90.2% vs. 56.1%, p-value<0.001
Fabris 2004	**Source of data unclear** - Mortality rates - Length of stay - Percentage of patients transferred to nursing homes Higher percentage of patients who stayed/returned at home	**HHS group vs. Control (GMW) group** 17.8% vs. 20.7%, p-value=NS 27.6% vs. 25.1%, p-value=NS 3.6% vs.32.1%, p-value<0.001 78.6% vs. 47.2%, p-value<0.001
Functional status Reisberg 2017	**Improvement in functional status** - Based on caregiver-rated Functional Assessment Staging Disability Score (FAST-DS), with higher scores indicating greater impairment ○ Baseline (mean score) ○ Week 4 (mean score) ○ Week 12 (mean score) ○ Week 28 (mean score)	**CI-PCM group vs. control group** 6.6 vs. 6.6, p-value=NS 6.5 vs. 6.6, p-value=<0.05 6.3 vs. 6.6, p-value=<0.05 6.2 vs. 6.8, p-value=<0.05
Behavioural symptoms Nakanishi 2018	**Reduction in challenging behaviours** - Based on care professional-rated Neuropsychiatric Inventory-Nursing Home version (NPI-NH). The score for each item ranges from 0-12, with higher scores indicating worse behaviour. - Mean score in challenging behaviour at baseline - Mean score in challenging behaviours after adjusting for baseline characteristics	**BASE participants vs. Control group** 18.3 vs. 11.6, p-value<0.001 6.88, p-value<0.001 vs. 0.95, p-value=0.346
Baker 2001	**Better immediate effects on behaviour and mood 10 minutes before and after the intervention** - Based on the ratings by day hospital staff using INTERACT short - More spontaneous speech; Relating to people better; More attentive to/focused on the environment; Doing more from their own initiative; Enjoying themselves; More active or alert/less bored/inactive	**MSS group vs. control (Activity group)** Similar in both groups

	Better immediate effects on behaviour and mood during the intervention - Based on keyworker-rated 22 items INTERACT that assesses relaxation, mood and speech	
	- Talked more spontaneously	2.03 vs. 2.68, p-value=0.04
	- Talked with normal length sentences	3.71 vs. 3.04, p-value=0.05
	- Recalled more memories	2.54 vs. 1.89, p-value=0.01
	Better outcomes on behaviour and mood after 4-8 sessions - based on ratings by day hospital staff using REHAB, a widely used rating form originally designed to assess change in long-stay psychiatric patients	
	- Rehab Speech Skills (amount of speech, initiation of speech)	No change vs. Improved
	- REHAB subscales: speech disturbance (sense clarity), self-care and general behaviour	No change vs. no change
	Better outcomes on behaviour and mood after 4-8 sessions - Based on ratings by carers and aided by a research assistant using Behaviour and Mood Disturbance Scale (BMD) scale (home)	Improved vs. Deteriorated
	Better outcomes on behaviour and mood after 4-8 sessions - based on Behaviour Rating Scale (BRS), a more formal tool to assess change in behaviour, such as constant talking, making false accusations and hoarding (home)	Improved vs. No change
	Deterioration in behavioural and mood – based on REHAB subscales: speech disturbance (sense clarity), self-care and general behaviour	Deteriorated vs. deteriorated
Reisberg 2017	**Improvement in behavioural symptoms at months 12 and 28** - Based on caregiver-rated Behavioural Pathology in Alzheimer's Disease Frequency-Weighted Severity Scale assessment tool, with higher scores indicating increased magnitude and frequency of behavioural disturbances	**CI-PCM group vs. control group**
	○ Baseline (mean score)	25.1 vs. 21.6, p-value=NS
	○ Week 4 (mean score)	≈16 vs. ≈17, p-value=NS
	○ Week 12 (mean score)	11.7 vs. 19.6, p-value<0.05
	○ Week 28 (mean score)	7.2 vs. 23.7, p-value<0.05
	Improvement in behavioural symptoms at month 28 - Based on caregiver-rated Revised Memory and Behaviour Problems checklist, with higher scores indicating increased more frequent behavioural problems	
	○ Baseline (mean score)	29.9 vs. 32.7, p-value=NS
	○ Week 4 (mean score)	≈31 vs. ≈30, p-value=NS
	○ Week 12 (mean score)	≈24 vs. ≈32, p-value=NS
	○ Week 28 (mean score)	23.8 vs. 34.9, p-value<0.05
Tibaldi 2004	**Reduction in behavioural disturbances** - Source of data unclear	**HHS group vs. Control (GMW) group**
	- Sleeping disorder	9% vs. 43.3%, p-value<0.001
	- Agitation/Aggressiveness	8.9% vs. 41.5%, p-value<0.001
	- Feeding disorders	8.9% vs. 39.6%, p-value<0.001
Pain Nakanishi 2018	**Decline in pain from baseline to follow-up, but no difference in pain between the two groups after adjusting for baseline characteristics** - Based on care professional-rated Abbey Pain scale rated by the care professionals. An overall assessment of pain intensity ranges from 0-18, with higher scores indicating more pain intensity.	**BASE participants vs. Control group**
	- Mean score in pain intensity at baseline	2.4 vs. 1.0, p-value<0.001
	- Mean score in pain intensity at follow-up	1.8 vs. 0.9

	• Pain intensity at follow-up after adjusting for baseline characteristics	2.63, p-value=0.01 vs. 0.43, p-value=0.671
Satisfaction Holley 2009	**High satisfaction** - Based on telephone interviews with caregivers of deceased PATCH participants	
	• Extremely satisfied	72.7%
	• Very satisfied	18.2%
	• Satisfied	9.1%
	• Somewhat or not at all satisfied	0%
	High satisfaction - Based on telephone interviews with caregivers of deceased PATCH participants with dementia	
	• Extremely satisfied	64.3%
	• Very satisfied	21.4%
	• Satisfied	14.3%
	• Somewhat or not at all satisfied	0%
Resource use Cassel 2009	**Based on records from Sharp Administrative system**	**Transitions group vs. control group**
	Lower hospital, non-hospital and all costs	
	• Average hospital costs/month	$885 vs. 3574, p-value<0.001
	• Average non-hospital costs/month	649 vs. $1291, p-value=0.002
	• Average of all costs/month	$1534 vs. $4866, p-value<0.001
	Better hospitalisation outcomes	
	• In hospital at least once	33.7% vs. 76.1%, p-value<0.001
	• Average number of hospitalisation/month in final 30 days of life	33.7 vs. 76.1, p-value<0.001
	• Fewer hospital days/month	0.75 vs. 1.68, p-value<0.001
	• Percentage of patients admitted in hospital/month in final 30 days of life	17.4 vs. 63, p-value<0.001
	• Percentage of patients dying in the hospital	5.4 vs. 51.1, p-value<0.001
	• Average 30-day readmission rate	0.11 vs. 0.35, p-value<0.001
	• Average percentage of patients admitted in intensive care unit in final 30 days of life	8.7 vs. 34.4, p-value<0.001
	Better trends in usage in final months of life	Slight increase vs. dramatic increase
	Better cost reduction	$2690 (4.2%) vs. none
Wilson 2015	**Higher expenditures** - Based on records from JEN data management and consulting associates	**House Calls group vs. control group**
	• Percentage of patients with hospice expenditures	22.9% vs. 8.9%, p-value<0.05
	• Percentage of patients with home health expenditures	85.4% vs. 47.5%, p-value<0.05
	Percentage of patients with social service utilization	1.4% vs. 5.5%, p-value<0.05

* PATCH = Palliative Access Through Care at Home; BASE = Behaviour Analytics & Support Enhancement; MSS = Multi-Sensory Stimulation; CI-PCM = Comprehensive, Individualized, Person-Centered Management; HHS =Home Health Service; ACP = advanced care planning.

Table 4. Studies mapped according to the EAPC White Paper domains

	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Domain 6	Domain 7	Domain 8	Domain 9	Domain 10	Domain 11
	Applicability of palliative care	Person-centred care, shared-decision making	Setting care goals & ACP	Continuity of care	Prognostication, timely-recognition of dying	Avoiding futile treatment §	Optimal symptom treatment	Psychosocial & Spiritual support	Family care & involvement	Education of health care team	Societal & Ethical issues
Specialist palliative care services											
Cassel 2016 **Transitions**	✓	✓	✓	✓	✓		✓	✓	✓	✓	
Holley 2009 **PATCH**		✓	✓	✓		✓	✓	✓	✓	✓	
Nakanishi 2018 **BASE**				✓			✓	✓		✓	
Non-specialist palliative care interventions											
Baker 2001 **MSS**							✓			✓	
Reisberg 2017 **CI-PCM**		✓		✓			✓	✓	✓		✓
Wilson 2015 **House Calls**		✓		✓			✓	✓			
Aimonino 2001 **HHS**							✓				
Fabris 2004 and Tibaldi 2004 **HHS**			✓	✓			✓	✓	✓		

* PATCH = Palliative Access Through Care at Home; BASE = Behaviour Analytics & Support Enhancement; MSS = Multi-Sensory Stimulation; CI-PCM = Comprehensive, Individualized, Person-Centered Management; HHS =Home Health Service; ACP = advanced care planning.

§ Avoiding overly aggressive, burdensome and futile treatment.

Facilitators and barriers to implementing the interventions

None of the studies systematically investigated facilitators and barriers to implementing the interventions. Instead, we identified information in the discussion sections of five of the studies, which could be considered facilitators and barriers to implementation.(19–21,24,27) Some intervention components may have facilitated the implementation of the interventions, including the 24-hour access to a medical practitioner (20) and the continuing provision of tailored interventions.(21) Some formal caregiver characteristics were also discussed as facilitators to implementation, such as their active engagement,(21) reliability (24) and dedicated and highly qualified teamwork.(27) The limited time allocated to implementing the interventions was considered a barrier to implementation, because it may have hindered behavioural change and the achievement of long-term effects.(19,21)

Studies mapped according to the EAPC White Paper domains

All of the interventions aimed to optimally manage symptoms at the end of life, such as pain or acute medical illnesses (Table 4). The majority of them also ensured the continuity of care by either directly facilitating the transitions of care between settings (19,20,25) or conducting multidisciplinary discussions and collaboration (21–23,27) and caregiver support meetings.(24) They also addressed the psychosocial domain by providing psychosocial support (19,20,22,23,25,27) or managing behavioural symptoms.(21,24) Four EAPC White Paper domains were rarely addressed by the interventions: applicability of palliative care; societal and ethical issues; prognostication and timely recognition of dying; and avoidance of overly aggressive, burdensome or futile treatments. In addition, 'setting care goals and advance care planning' was addressed by only three of the eight evaluated interventions.(19,20,22,23) Compared to non-specialist palliative care interventions, specialist palliative care services focused more on training the multidisciplinary healthcare team and addressed four to nine domains at once.(19–21)

DISCUSSION

We retrieved eight studies which evaluated interventions aimed at improving end of life care outcomes for people with dementia living at home; three involving specialist palliative care services and five non-specialist palliative care interventions. None of the studies were of high quality, mostly due to high risk for selection bias and the inability to achieve blinding and to measure/report intervention integrity. We found weak evidence showing that home palliative care interventions in dementia can improve end of life care outcomes relating to institutionalisation, estimated resource use and functional status. There was moderate evidence of beneficial effects on behavioural symptoms arising from the person's cognitive and communication problems, but the evidence on whether these effects would last was contradictory. Although the evidence on pain reduction was limited and inconclusive there was some evidence of enhanced pain assessment. Evidence on facilitators and barriers was not systematically investigated and our findings are based on limited information provided in the discussion sections of the included studies. The mapping of the studies according to the EAPC domains highlighted the main preoccupations and focus of the interventions reviewed.

The existing evidence base is insufficient and generally too weak to robustly assess the effects of home palliative care interventions in dementia. Nonetheless, the potential benefits of the interventions in improving behavioural symptoms and enhancing pain assessment are consistent with earlier findings (13,14) and address key issues in dementia care.(28–30) Healthcare practitioners are often uncertain how to support people with dementia whose behaviours they find challenging.(31) Pain is also highly prevalent in older adults but poorly assessed in those with dementia,(30,32) which may result in patient distress and related behaviours.(33) Managing behavioural symptoms and assessing pain are not only important for patients with dementia. It may also contribute to reducing the burden of family caregivers who are central to enabling patients to stay at home.(34,35) While we know that promoting caregiver well-being is important,(36) it is notable that only one of the identified interventions offered additional support to address the emotional and mental needs of family caregivers.

The facilitators and barriers identified are in line with existing evidence (37,38) that highlights the importance of networks of support and easy access to tailored interventions. For example, the 24-hour access to medical practitioners and the active engagement of caregivers could enhance the accessibility of the interventions, while the tailoring of interventions based on patients' needs may increase their applicability for users.

The three most frequently addressed EAPC domains in the studies reviewed (optimal symptom management, continuity of care and psychosocial support) reflect clinician priorities and the core values of palliative care, irrespective of the reason for dying.(39) However, another EAPC priority 'person-centred care, communication and shared-decision-making' was only modestly addressed by the interventions. This is surprising when some of the most influential writing on person-centred care is situated in the dementia literature.(40) The studies failed to map according to 'applicability of palliative care' and 'societal/ethical issues' even though this is a patient population that is increasing but poorly understood by commissioners and policymakers and stigmatised in society.(41) Other domains that were under-represented in the evidence reviewed: prognostication and timely recognition of dying, avoidance of overly aggressive, burdensome or futile treatments and setting of care goals and advance care planning are similarly problematic areas in dementia care. For instance, despite the fact that most older people prefer to die at home,(7) there may still be a substantial proportion of older people with dementia dying in hospitals,(30) which is likely to occur if the palliative phase is not promptly recognised. Also, progressive cognitive decline is inherent in advanced dementia, which hinders the communication between healthcare providers and people with dementia.(1)

Implications for research and practice

The lack of evidence suggests that palliative care interventions has been given a low priority in dementia care, particularly in the home setting.(12) This may also be because most of the evidence on palliative care interventions for people with dementia is still situated in the nursing home setting,(12) where in many countries, the majority of people with dementia spend their final months or years of life.(42) Findings from the mapping of the studies according to the EAPC domains raised a question about whether research to date had given adequate attention to the specific issues and challenges experienced by people with dementia. It also highlighted the problems of transferring learnings about symptom management, continuity of care and psychosocial support from one specialty (e.g. cancer care) to the experience of dying with and from dementia. Symptom management should always be a main priority. However, the EAPC domains where there are gaps, are the domains that are very particular to the experiences of living and dying with dementia. Dementia is a socially-stigmatised condition, with a highly variable and protracted dying trajectory and one where decisions to treat and/or avoid burdensome treatments involve multiple stakeholders.(43,44) The review thus demonstrates that it may still be the early days in research for people with dementia living and dying at home. High-quality dementia-specific research is therefore required to further support the evidence base for palliative care interventions to be a routine care for people with dementia living and dying at home.(10) In designing such palliative care interventions, it is crucial to also consider strategies that would address the specific needs of home-dwelling people dying with and from dementia, e.g. prognostication of dying, avoidance of overly aggressive treatments or advance care planning, as well as interventions to assess and address the individual needs of family caregivers.

This systematic review also highlights a number gaps in the evidence. We found a lack of consensus on the outcomes used, which limited comparisons and meta-analysis. Important end of life care outcomes e.g. patient death at home and quality of life were also not consistently measured.(7,39) These issues around outcome measures may be addressed by two ongoing studies aiming to develop standard core outcome sets in dementia, one of which focuses on the home setting, while the other study involves people with dementia in research.(45,46) Although the core outcome sets to be developed can be relevant and applicable for people with dementia, it is still important to further explore the extent to which these outcomes would be relevant and applicable in evaluating home palliative care interventions in dementia. Guidelines on how to develop such core outcome sets exist, such as the handbook developed by the Core Outcome Measures in Effectiveness Trials (COMET) initiative. The COMET initiative aims to guide the development of core outcome sets by bringing together relevant key stakeholders, including patients.(47) Most of the studies were also appraised to have weak quality in part due to their inability to measure/report intervention integrity. This has been found as a persistent issue in clinical trials in palliative care,(48) which could be addressed by using standard reporting tools, e.g. CONSORT statement.(49) Evidence on cost-effectiveness is also scarce. Whilst some studies reported resource use, it was solely based on estimated costs while disregarding health benefits. Performing concurrent cost-effectiveness analysis using existing guidance could provide a better view of interventions that could potentially yield the greatest improvement in dementia care for the least resources.(50) Finally, evidence on facilitators and barriers was limited. This could be addressed by undertaking process evaluation, which is increasingly being recognised as an integral part of designing and evaluating complex interventions such as palliative care interventions. Performing process evaluations in accordance with the Medical Research Council (MRC) guidance would allow the critical exploration of factors and causal mechanisms that could explain variations in observed outcomes.(51)

Strengths and limitations

We systematically and rigorously searched the literature for existing studies on home palliative care interventions in dementia. It was a strength of the study that we drew on the EAPC White Paper to structure the data extraction and analysis. This demonstrated how the evidence was distributed according to an international consensus on what should be the key activities and focus of palliative care in dementia. However, we only found eight relevant studies, none of which were of high quality. The evidence of effectiveness therefore needs to be interpreted with caution. We adopted a broad definition of non-specialist palliative care interventions which may mean that relevant studies were missed. However, our searches were systematic and electronic database searching was supplemented with lateral searching. Our decision to only include quantitative studies, and associated process evaluations, may explain the limited evidence on facilitators and barriers to implementation. However, forward citation tracking of the included studies also did not reveal any relevant studies. To better identify studies that could yield valuable information on factors influencing the implementation of home palliative care interventions in dementia, future reviews should consider the inclusion of both qualitative and quantitative studies. We would also recommend a regular update of the systematic review, as new scientific evidence on factors influencing the implementation of home palliative care interventions emerges, such as the follow-up study of Nakanishi et al, 2018.(52) Finally, subjectivity may have been introduced in the mapping of the intervention components according to the EAPC White Paper domains. We dealt with this challenge by discussion within the research team.

Conclusion

The review offers evidence on palliative care interventions for people with dementia living at home and highlights the paucity of high-quality studies in this area. The review emphasizes the need for more rigorous and comprehensive research which considers the identified gaps in the evidence and addresses the specific issues and challenges that dying at home with or from dementia poses. The EAPC's definition of optimal palliative care in dementia provided a useful framework for a systematic assessment of the range and focus of evidence of what is effective for people with dementia living and dying at home.

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Declaration of conflicts of interest

The authors declare no conflict of interest.

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SUPPLEMENTARY FILES – CHAPTER 5

Supplementary table 1. EAPC White Paper palliative care domains and recommendations

Palliative care domains	Salient recommendations
Domain 1. Applicability of palliative care	1. Dementia can realistically be regarded as a terminal condition. 2. Improving quality of life, maintaining function and maximizing comfort, which are also goals of palliative care, can be considered appropriate in dementia throughout the disease trajectory, with the emphasis on particular goals changing over time. 3. Palliative care for dementia should be conceived as having two aspects: a palliative care approach and specialist palliative care. 4. A palliative care approach refers to all treatment and care in dementia, including adequate treatment of behavioural and psychological symptoms of dementia, comorbid diseases, and (inter- or concurrent) health problems.
Domain 2. Person-centred care, communication, and shared-decision making	5. Perceived problems in caring for a patient with dementia should be viewed from the patient's perspective, applying the concept of person-centred care. 6. Shared decision making includes the patient and family caregiver as partners and is an appealing model that should be aimed for. 7. The health care team should ask for and address families' and patients' information needs on the course of the dementia trajectory, palliative care and involvement in care. 8. Responding to the patient's and family's specific and varying needs throughout the disease trajectory is paramount. 9. Current or previously expressed preferences with regard to place of care should be honoured as a principle, but best interest, safety and family caregiver burden issues should also be given weight in decisions on place of care. 10. Within the multidisciplinary team, patient and family issues should be discussed on a regular basis.
Domain 3. Setting care goals and advance planning	11. Prioritizing of explicit global care goals helps guide care and evaluate its appropriateness. 12. Anticipating progression of the disease, advance care planning is proactive. This implies it should start as soon as the diagnosis is made with patients involved. 13. Formats of advance care plans may vary in terms of preferences, the amount of detail required, and what is available in the specific setting for the individual. 14. In mild dementia, people need support in planning for the future. 15. In more severe dementia and when death approaches, the patient's best interest may be increasingly served with a primary goal of maximization of comfort. 16. Advance care planning is a process, and plans should be revisited with patient and family on a regular basis and following any significant change in health condition. 17. Care plans should be documented and stored in a way that permits access to all disciplines involved in any stage and through transfers.
Domain 4. Continuity of care	18. Care should be continuous; there should be no interruption even with transfer. 19. Continuous care refers to care provided by all disciplines. 20. All patients should benefit from the early appointment of a central coordinator from within their care team. 21. Transfers between settings require communication on care plans between former and new professional caregivers and patient and families.
Domain 5. Prognostication and timely recognition of dying	22. Timely discussion of the terminal nature of the disease may enhance families' and patients' feelings of preparedness for the future. 23. Prognostication in dementia is challenging and mortality cannot be predicted accurately. However, combining clinical judgement and tools for mortality predictions can provide an indication which may facilitate discussion of prognosis.
Domain 6. Avoiding overly aggressive, burdensome or futile treatment	24. Transfer to the hospital and the associated risks and benefits should be considered prudently in relation to the care goals while taking the stage of dementia into account. 25. Medication for chronic conditions and comorbid diseases should be reviewed regularly in light of care goals, estimated life expectancy, and the (side) effects of treatments. 26. Restraints should be avoided whenever possible. 27. Hydration, preferably subcutaneous, may be provided if appropriate, such as in case of infection; it is inappropriate in the dying phase (only moderate consensus). 28. Permanent enteral tube nutrition may not be beneficial and should as a rule be avoided in dementia; skilful hand feeding is preferred (only moderate consensus). 29. Antibiotics may be appropriate in treating infections with the goal of increasing comfort by alleviating the symptoms of infection. Life-prolonging effects need to be considered, especially in case of treatment decisions around pneumonia.
Domain 7. Optimal treatment of symptoms and providing comfort	30. A holistic approach to treatment of symptoms is paramount because symptoms occur frequently and may be interrelated, or expressed differently (e.g., when pain is expressed as agitation). 31. Distinguishing between sources of discomfort (e.g., pain or being cold) in severe dementia is facilitated by integrating views of more caregivers.

	32. Tools to assess pain, discomfort and behaviour should be used for screening and monitoring of patients with moderate and severe dementia, evaluating effectiveness of interventions. 33. Both non-pharmacological and pharmacological treatment of physical symptoms, challenging behaviour or discomfort should be pursued as needed. 34. Nursing care is very important to ensure comfort in patients near death. 35. Specialist palliative care teams may support staff in long- term care settings in dealing with specific symptoms, while maintaining continuity of care. In managing behavioural symptoms, however, palliative care teams may need additional dementia care specialist expertise.
Domain 8. Psychosocial and spiritual support	36. In mild dementia, as also in the later stages, patients may be aware of their condition, and patients and families may need emotional support. 37. Spiritual caregiving in dementia should include at least assessment of religious affiliation and involvement, sources of support and spiritual well being; in addition, referral to experienced spiritual counsellors such as those working in nursing homes may be appropriate. 38. Religious activities, such as rituals, songs, and services may help the patient because these may be recognized even in severe dementia. 39. For dying people, a comfortable environment is desirable.
Domain 9. Family care and involvement	40. Families may suffer from caregiver burden, may struggle to combine caring with their other duties and may need social support. 41. Families may need support throughout the trajectory, but especially upon diagnosis, when dealing with challenging behaviour, with health problems, with institutionalization, with a major decline in health and when death is near. 42. Families need education regarding the progressive course of the dementia and (palliative care) treatment options; this should be a continuous process addressing specific needs in different stages, examining family receptiveness. 43. Family involvement may be encouraged; many families may wish to be involved in care even when the patient is admitted to an institution providing long-term care. 44. Families need support in their new role as (future) proxy decision maker. 45. Professional caregivers should have an understanding of families' needs related to suffering from chronic or prolonged grief. 46. Bereavement support should be offered. 47. Following the death of the patient, family members should be allowed adequate time to adjust after often a long period of caring for the patient.
Domain 10. Education of the health care team	48. The health care team in its entirety, including allied health professionals and volunteers, needs to have adequate skills in applying a palliative care approach to dementia. 49. Core competencies comprise all of the above listed domains (1 to 9). All competencies should be available within a health care team, and preferably all individual members of the team should be able to provide at least a baseline palliative care approach.
Domain 11. Societal and ethical issues.	50. Wherever patients reside, patients with dementia should have access to palliative care on the same footing as patients with other diseases which are unresponsive to curative treatment. 51. Family caregivers should have access to adequate support to combine caring for the patient with dementia with other duties. 52. Collaboration between dementia and palliative care should be promoted. 53. Curricula for training of physicians and nurses at both undergraduate and postgraduate level, as part of continuing professional education, should include palliative care for patients with illness other than cancer. 54. Professional caregivers should be motivated to work in dementia and palliative care and adequate funding for sufficient staffing is needed. 55. Economic and systemic incentives should encourage excellent end-of-life care for patients with dementia. 56. Awareness raising about palliative care in dementia is needed. 57. National strategies for dementia, for palliative care, end-of-life care, and for long-term care should each include palliative care for dementia patients. Similarly, policy making on palliative care and long-term care settings

Supplementary table 2. Composite ratings of the quality of the included studies

	Selection bias	Study design	Confounders	Blinding	Data collection	Withdrawals and Dropouts	Intervention integrity	Data analysis	Overall rating
Cassel et al 2016	Weak	Moderate	Strong	Weak	Moderate	Not applicable	Weak	Moderate	**Weak**
Holley et al 2009	Weak	Weak	Weak	Weak	Moderate	Not applicable	Weak	Weak	**Weak**
Nakanishi et al 2018	Moderate	Strong	Strong	Weak	Strong	Strong	Strong	Strong	**Moderate**
Baker et al 2001	Moderate	Strong	Strong	Weak	Strong	Strong	Strong	Strong	**Moderate**
Reisberg et al 2017	Weak	Strong	Strong	Moderate	Strong	Strong	Strong	Strong	**Moderate**
Wilson et al 2015	Weak	Moderate	Strong	Weak	Moderate	Not applicable	Weak	Moderate	**Weak**
Aimonino et al 2001	Weak	Weak	Weak	Weak	Moderate	Strong	Weak	Weak	**Weak**
Fabris et al 2004	Weak	Strong	Weak	Weak	Moderate	Strong	Weak	Weak	**Weak**
Tibaldi et al 2004	Weak	Strong	Weak	Weak	Moderate	Strong	Weak	Weak	**Weak**

CHAPTER 6

Improved quality of care and reduced healthcare costs at the end-of-life among older people with dementia who received palliative home care: a nationwide propensity score-matched decedent cohort study

Rose Miranda[a], Tinne Smets[a], Robrecht De Schreye, Kristof Faes, Nele Van Den Noortgate, Joachim Cohen[b], Lieve Van den Block[b]

[a] joint first authorship
[b] joint last authorship

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ABSTRACT

Background. While palliative home care is advocated for people with dementia, evidence of its effectiveness is lacking.

Aim. To evaluate the effects of palliative home care on quality and costs of end-of-life care for older people with dementia.

Design. Decedent cohort study using linked nationwide administrative databases and propensity score matching.

Setting/participants. All home-dwelling older people who died with dementia between 2010 and 2015 in Belgium (N=23,670).

Exposure. Receiving palliative home care support for the first time between 360 and 15 days before death.

Results. 5,637 (23.8%) received palliative home care support in the last two years of life, of whom 2,918 received it for the first time between 360 and 15 days before death. 2,839 people who received support were matched to 2,839 people who received usual care. After matching, those using palliative home care support, in the last 14 days of life, had lower risk of hospital admission (17.5% vs 50.5%; relative risk [RR]=0.21), undergoing diagnostic testing (17.0% vs 53.6%; RR=0.20) and receiving inappropriate medications, but were more likely to die at home (75.7% vs 32.6%; RR=6.45) and to have primary care professional contacts (mean 11.7 vs mean 5.2), compared with those who did not. Further, they had lower mean total costs of care in the last 30 days of life (incremental cost:−€2129).

Conclusions. Palliative home care use by home-dwelling older people with dementia is associated with improved quality and reduced costs of end-of-life care. Access remains low and should be increased.

Key words. Palliative care, terminal care, end of life care, dementia, home care services, Big Data

Key statements

What is already known about the topic?

- For a growing number of people dying with dementia, palliative care has been widely advocated.
- Evidence on the effects of palliative home care interventions in dementia is lacking, potentially due to the ethical, legal and practical challenges of conducting traditional experimental studies in this context.
- The best possible alternative is to emulate such a target trial using a matched cohort study design with a high-quality matching on the propensity of receiving an intervention.

What this paper adds

- Using linked 2010 to 2015 nationwide administrative databases in Belgium and a validated set of dementia-specific quality indicators, we were able to evaluate the effects of palliative home care support on the quality and costs of end-of-life care in dementia.
- Of all home-dwelling older people who died with dementia between 2010 and 2015, only 23.8% had access to palliative home care support at some point in the last two years of life.
- Palliative home care use by home-dwelling older people dying with dementia in Belgium is associated with improved quality and reduced costs of end-of-life care.

Implications for practice, policy and research

- Our findings offer a firmer evidence base regarding the effectiveness of palliative home care support for older people with dementia.
- Considering these clear benefits of palliative home care support in dementia, the low and considerably late uptake highlights an urgent need to further improve timely access in dementia.
- Further studies exploring strategies to improve access to palliative home care of older people dying with dementia are urgently needed.

BACKGROUND

A fast-growing number of people are dying with dementia.(1) In Europe, dementia is projected to affect about 18.8 million by 2050.(2) Palliative care has been advocated for older people with dementia, as this approach has the potential to improve their quality of life by addressing their multi-faceted physical, psychosocial and spiritual care needs for months or years until death.(3–5) Particularly in the home setting, it is important to deliver high-quality and cost-effective palliative care considering the increasing demand for care in this population combined with the shortage and rising costs of long-term institutional care services and older people's preference to live and die at home.(6–9) However, high-quality evidence on the effectiveness of home-based palliative care in dementia is lacking.

A 2016 Cochrane review on palliative care interventions in advanced dementia found only two low-quality studies, neither of which focused on the home setting.(10) A 2019 systematic review found that while palliative home care interventions in dementia could improve behavioural disturbances, enhance pain assessment and reduce costs, no robust conclusions on their effectiveness could be drawn due to the insufficient and weak evidence available.(11) This paucity of evidence may stem from the fact that conducting traditional experimental studies, such as randomised controlled trials (RCTs) in this context is difficult due to ethical, legal and practical concerns. RCTs are a strong design for providing evidence about causal relationships because they allow control over essential aspects such as temporality, confounding and experimental control.(12,13) Ethically and legally, however, we cannot randomise home-dwelling patients with dementia into receiving or not receiving palliative care (to control confounding) and prevent the latter from using palliative care when needed (to have experimental control).

The best possible alternative is to emulate the aspects of an RCT using large administrative databases and a high-quality matching on the propensity of receiving an intervention.(14–16) The use of such methodology has been made possible by advances in digitalization and data storage which substantially improve the availability and quality of routinely-collected databases.(15,16) A previously conducted matched cohort study in Belgium using such linked administrative databases and propensity score matching found that palliative home care support improves the quality of end-of-life care and reduces resource use and costs for a general palliative care population in 2012.(17) However, it remains unknown whether palliative home care could have similar effects on end-of-life care for older people with dementia. We aim to evaluate the effects of palliative home care support on the quality and costs of end-of-life care for older people who lived at home and died with dementia between 2010 and 2015 in Belgium.

METHODS

Design

We conducted a propensity-matched decedent cohort study using linked nationwide administrative databases in Belgium (2010-2015).(18) Figure 1 depicts our study methodology. We reported our study following the RECORD statement (REporting of studies Conducted using Observational Routinely-collected Data).

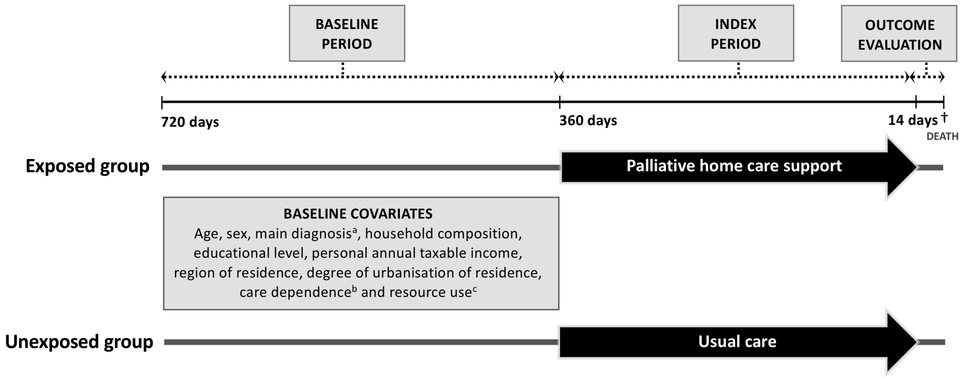

Figure 1. Time diagram describing the propensity-matched decedent cohort study methodology

[a] Main diagnosis of the person with dementia based on the recorded underlying cause of death: cancer [ICD-10 codification=C00-97] – respiratory tract [C32-C34], melanoma [C43-C46], digestive tract [C00-C21], other cancer [C22-C25, C50-C62, C64-C65, C67, C70-73, C81-C86, C88-C97]; dementia [F01-F03, G30] – Alzheimer's disease [G30], Vascular dementia [F01], and other types of dementia [F02-F03]; chronic obstructive pulmonary disease [J40-44, J47]; heart failure [I50]; other organ failure [N17-N19, I24.8, J96, K72, R09.2]; other neurodegenerative diseases [G00-G99, excluding G30] or other [all other ICD codes].

[b] Care dependence was based on receiving any of the allowance for a highly care-dependent person as judged by the GP (nomenclature=740014), for a person with handicap (740073), or for an older person (740095).

[c] Resource use included the following variables: number of hospital admission, number of emergency department admission, number of intensive care unit admission, number of general practitioner contact, number of specialist contact, length of stay in hospital and length of stay in intensive care unit.

Setting and participants

We included individuals aged 65 years and older at the time of death, who resided at home and did not have a recorded nursing home stay in the last six months of life, and died with dementia between 2010 and 2015. In Belgium, home-dwelling individuals, who are admitted in nursing homes and thus have a nursing home stay recorded in the administrative database, do not return to the home care setting. Dying with dementia was based on the underlying, intermediate and associated causes of death reported on the death certificate with ICD-10 codes (F01-F03 or G30) and whether or not they received dementia-specific medications up to ten years before death, using a medication algorithm (ATC code=N06DA01 or N06DA02 or N06DA03 or N06DA04 or N06DX01 or N06DA52). We included all deaths that occurred between 2010 and 2015 as there was no substantial change in legislation and uptake in palliative home care support in dementia within this period.(19) All participants were followed up until death and followed back up to 720 days before death.

Care for older people with dementia living at home in Belgium

Older people with dementia living at home typically receive care from health and social care workforce in primary care and specialist care services, e.g. neurologists. In Belgium, the primary care workforce essentially comprises general practitioners (GPs) together with community nurses, who deliver personal care, technical nursing procedures and psychosocial care, and social care workers, who deliver social support.(20) All specialist care services are accessible for patients without referral from GPs, while the written permission of GPs is needed to initiate palliative home care support for all health-insured people, who are seriously ill, have a short life expectancy (defined by law as 'more than 24 hours and less than three months') for whom curative treatment is no longer an option and have an intention to receive end-of-life care and die at home (Table 1).(17,21-23)

Palliative home care support aims to address the multi-faceted care needs of this population in need of palliative care, including those with dementia. Ideally, the use of palliative care is progressive in nature and depends on the increasing needs of patients. Palliative home care measures include home visits by a multidisciplinary palliative home care team; home visit by a palliative care nurse or physiotherapist, or receiving financial allowance for palliative patients.(17,19,21)

Table 1. Description of palliative home care support in Belgium

Background. Since 1985, palliative home care support in Belgium includes measures to support palliative care patients living at home.(21) In 2002, a legislation has been passed to recognise the right of all Belgian citizens for receiving palliative care. Since then, all health-insured people in Belgium have the legal right to access palliative home care support. Seriously ill individuals with a short life expectancy (defined by law as 'more than 24 hours and less than three months') for whom curative treatment is no longer an option and have an intention to receive end-of-life care and die at home are eligible to receive specific support measures from the Belgian government. Palliative care aims to guarantee the highest possible quality of life and maximum autonomy of patients and their relatives.(22) In 2016, this legislation has been amended to extend the scope of palliative care to individuals who are identified to be in the advanced or terminal stage of a severe progressive and life-threatening disease, regardless of their life expectancy. Ideally, the use of palliative care is progressive in nature and depends on the increasing needs and wishes of patients.(23)

Current study. The 2002 palliative care legislation is applicable, because our linked data included information on palliative home care support that had been delivered to individuals who died between 2010 and 2015.

Point of entry. General practitioners (GPs) are the gatekeepers for home care and their written permission was required to initiate palliative home care support in Belgium.(17)

Support measures	Components of palliative home care support measures
1) **Multidisciplinary palliative home care team**	- Includes at least one GP, two nurses and an administrative assistant - Main goal: to advise GPs, health professionals, counsellors, informal caregivers and volunteers involved in the provision of palliative home care of a patient and to organize and coordinate the provision of that palliative care at home between different care providers - Free of charge for the patient with no time limit
2) **Palliative home care nursing or physiotherapy**	- A type of nursing care or physiotherapy at home, which is different from standard nursing care or physiotherapy at home for heavily dependent home-patients in the number of caring tasks provided and round-the-clock availability - Free of charge for the patient
3) **Allowance for palliative patients living at home**	- A lump sum of €594.79 in 2010 to €647.16 in 2015 - Can be obtained twice (possibility to claim a second after 1 month) - Aimed to cover non-reimbursed or partially reimbursed costs related to the provision of palliative care at home (e.g. certain medicines, care materials/tools)

Exposed group

Exposure was defined as receiving at least one type of palliative home care support measure for the first time between 360 and 15 days before death. Receiving any or the combination of the three measures was chosen as exposure, as we considered the different types of support to be the same intervention: initiation of palliative home care, and this operationalization of palliative home care support had also been used in previous studies.(17,19,21) We excluded those who received palliative home care support for the first time either between 720 and 361 days before death to avoid an overlap in the period used for the propensity score matching or in the last 14 days to avoid an overlap in the timing between exposure and outcome (temporality criterion). Using nomenclature codes and corresponding dates (coded in days before death), we identified the delivery and timing of a specific measure. Multiple measures were often delivered; hence, we identified the earliest initiation of the measure.

Unexposed group

The unexposed group included individuals who did not receive palliative home care support in the last twoyears of life, matched to people who received it.

Data sources

We used linked data from eight routinely-collected nationwide administrative databases in Belgium, including socio-demographic, healthcare, pharmaceutical, cancer registry, death certificate, population registry, census and fiscal databases. The Belgian healthcare system is funded through social security contributions and taxation, with a mandatory national health insurance covering the total population, combined with a private system of healthcare delivery based on independent medical practice, free choice of service provider and mainly fee-for-service payment. Health insurance reimburses healthcare costs directly to the patient and all reimbursements are registered. Hence, the databases included data of all individuals registered with a Belgian sickness fund at the time of death (98.8% of all deaths).(18)

After obtaining approval from all relevant data protection agencies, data linkage was securely and ethically performed to guarantee anonymity of the individuals by a third party officially responsible for data protection and linkage in Belgium. Data were linked at individual level using a unique identifier and included person-level reimbursed healthcare use in the last twoyears of life (recorded as nomenclature codes), including dispensed medication in the hospital and community pharmacy (recorded as Anatomical Therapeutic Chemical Classification System codes). For all healthcare data, the exact delivery date is recorded (coded as number of days before death). We also have demographic, fiscal and death certificate data, including cause of death, coded using International Statistical Classification of Diseases, Tenth Revision (ICD-10) codification).(18,24)

Outcomes

Outcomes to determine quality of end-of-life care were based on a validated set of 28 quality indicators measuring the prevalence of specific healthcare interventions in the last 14 days of life and indicating appropriateness or inappropriateness of end-of-life care in dementia on an aggregated level (see quality indicators in Supplementary Table 1).(25,26) This indicator set was developed for people with dementia using the RAND/UCLA Appropriateness method, involving literature review and expert consensus.(30) We used 22 of the 28 outcome measures, four of which indicate appropriate care. We excluded three indicators that overlapped with the exposure, one that could not be measured on an individual level and two that relate to individuals who permanently resided in nursing homes.(26) Based on specific healthcare consumption data, total direct medical costs of end-of-life care were calculated from a third-party and patient co-payment perspective, including inpatient, outpatient and total costs. Based on the exact dates of delivery, costs of care were calculated in the last 30 days of life and actualized to 2017.

Statistical analysis and propensity score matching

We used descriptive statistics to describe the characteristics of the cohort, stratified by exposed and unexposed groups. An included individual who received palliative home care support was matched to one who did not, based on an estimation of their propensity for receiving the support (Figure 1). To calculate propensity scores, predictors for receiving the exposure, identified as relevant based on clinical knowledge and previous studies, were considered as baseline covariates.(17,27-31) These included age, sex, main diagnosis of the person with dementia based on the recorded underlying cause of death, household composition, education, annual income, region and degree of urbanisation of residence, care dependence and resource use. For temporality purposes, baseline was considered as the period between 720 and 361 days before death, except for cause of death. Because no information about main diagnoses is available for this period and different diagnostic groups were expected to differ strongly in terms of propensity for exposure, we assumed that the underlying cause of death category was indicative of a condition present in the baseline period.

For the propensity score matching we used a greedy 1:1 exposure–control propensity scores matching algorithm.(32) For every case, the best match was made first and a next-best match next, in a hierarchical sequence until no more matches could be made. Best matches are those with the highest digit match on propensity score. The algorithm proceeds sequentially to the lowest digit match on the propensity score (eight digit to one digit). No trimming was performed. Data on population characteristics, quality of care outcomes and costs were analysed using descriptive statistics. Risk ratios were calculated to measure the differences in outcomes between the exposed and unexposed groups. Costs for the matched exposed and unexposed groups were presented as estimated means along with the corresponding 95% confidence interval and standard error. All analyses were conducted using SAS Enterprise Guide, V9.4.

Ethics

Ethics approval was provided by the Committee for Medical Ethics of the University Hospital Brussels (UZ Brussel) (B.U.N. 143201627075) and the ethics committee of the Ghent University Hospital (B670201422382). The administrative data-linkage was approved by the national Belgian Data Protection Authority (project SA1/STAT/MA-2015-026-020-MAV) and by the Statistical Monitoring Committee (project STAT-MA-2015-026).

RESULTS

Characteristics of study population

There were 634,445 deaths in Belgium between 2010 and 2015, of whom 529,534 individuals (83.5%) were aged 65 years and older at the time of death. Of these older people, 59,407 individuals (11.2%) died with dementia, of whom 23,670 individuals (39.8%) resided at home in the last six months of life and thus were included in the study (Figure 2). In the last two years of life, 5,637 individuals (23.8% of the included population) received palliative home care support, of whom 1,720 (30.5%) received it for the first time within 14 days before death and 999 (17.7%) received it for the first time between 720 and 361 days (both excluded from the propensity score matching). Our final unmatched study population comprised 20,951 individuals, of whom 2,918 received palliative home care support for the first time between 360 and 15 days before death. Before matching, the exposed group differed considerably from the unexposed group in underlying cause of death, household composition, urbanization and care dependence (Table 2). For instance, compared to the unexposed individuals, the exposed individuals died considerably more often from cancer (8.1% vs. 29.7%) and were more care dependent (43.3% vs. 77.2%), which could have influenced both the exposure and the outcome. After matching of 2,839 exposed individuals to as many unexposed individuals with a corresponding propensity score, patient characteristics were balanced (Table 2 – "After matching columns"). For more information on the frequencies of the specific delivered measures that compose the exposure, please Supplementary Table 2.

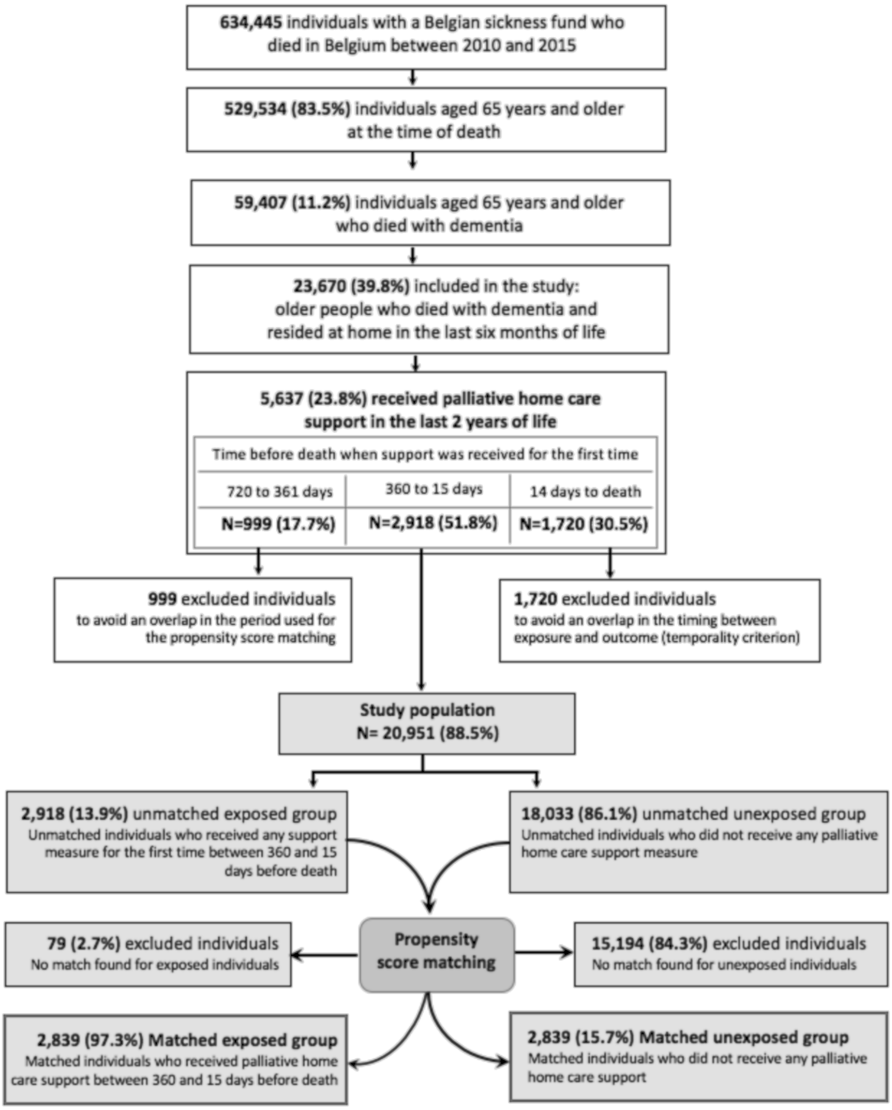

Figure 2. Flowchart of selecting the matched exposed and unexposed groups

Table 2. Characteristics of study population before and after propensity score matching

	Before matching (N=20,951)		After matching (N=5,678)	
	Exposed	Unexposed	Exposed	Unexposed
Number of patients (%)	**2,918**	**18,033**	**2,839**	**2,839**
Earliest initiation of any supportive measure in days, median (95% CI)	103 (99-105)	0 (0)	103 (99-106)	0 (0)
Age at time of death, mean (standard deviation [SD])	83.4 (6.4)	83.8 (6.2)	83.4 (6.5)	83.5 (6.2)
Sex – Women, n (%)	48.7	50.4	48.7	47.5
Underlying cause of death, %				
- Cancer (all types)	29.7	8.1	28.3	27.2
o Respiratory tract	5.4	1.5	5.0	5.2
o Melanoma	1.3	0.2	1.0	0.9
o Digestive tract	6.1	1.6	5.9	5.6
o Other cancer	17.0	4.8	16.4	15.5
- Chronic obstructive pulmonary disease	2.0	3.0	2.1	2.3
- Dementia (all types)	31.3	25.0	31.7	32.9
o Alzheimer's disease	14.5	8.0	14.8	14.7
o Vascular dementia	2.0	2.0	2.0	1.7
o Other types of dementia	14.8	15.0	14.9	16.5
- Heart failure	3.5	4.2	3.6	3.4
- Other organ failure	1.7	2.6	1.8	1.7
- Other neurodegenerative diseases	8.1	5.4	8.2	8.7
- Other	23.7	51.8	24.2	23.9
Household composition, %				
- Living together, with children	10.2	8.0	10.3	10.6
- Living together, without children	58.0	51.9	57.8	57.7
- Single person household	17.1	28.2	17.4	17.8
- One-parent family	8.2	6.8	8.0	7.9
- Other	4.2	3.3	6.5	6.1
Educational level, %				
- No education	8.6	7.5	8.6	8.7
- Primary school education	31.4	30.7	31.5	31.6
- Secondary school education	18.9	17.3	18.7	17.8
- Post-secondary school education	16.5	16.4	16.4	15.7
Personal annual taxable income in decile, %				
- Lowest income decile	0.4	0.4	0.4	0.5
- Second income decile	0.1	0.4	0.1	0.1
- Third income decile	1.67	0.9	1.7	1.6
- Fourth income decile	19.5	15.7	19.3	19.6
- Fifth income decile	22.0	20.0	22.2	22.4
- Sixth income decile	28.9	30.5	29.0	29.3
- Seventh income decile	15.4	18.3	15.3	14.6
- Eighth income decile	5.5	6.7	5.4	5.1
- Ninth income decile	3.7	4.1	3.7	3.6
- Highest income decile	2.9	3.0	2.9	3.1
Region of residence, %				
- Flemish region	62.0	61.4	62.1	61.8
- Walloon region	34.1	31.6	34.0	34.7
- Brussels Capital region	3.9	7.02	3.9	3.5
Degree of urbanization of residence, %				
- Very high	23.6	30.7	23.9	23.3
- High	28.6	27.8	28.6	28.4
- Average	32.3	27.5	32.5	32.9
- Low	14.9	13.0	14.9	15.4
Care dependence, %	77.2	43.3	76.8	78.1
Resource use, mean (SD)				
- Number of hospital admission	0.7 (1.1)	0.6 (1.0)	0.7 (1.1)	0.6 (1.1)
- Number of emergency department admission	0.5 (0.9)	0.4 (0.8)	0.5 (0.9)	0.5 (0.9)
- Number of intensive care unit admission	0.04 (0.3)	0.1 (0.3)	0.0 (0.3)	0.0 (0.3)
- Number of general practitioner contact	14.2 (12.7)	12.7 (12.0)	14.1 (12.4)	14.1 (14.7)
- Number of specialist contact	3.3 (4.1)	3.3 (4.2)	3.3 (4.1)	3.3 (4.1)
- Length of stay in hospital	9.3 (19.4)	7.4 (17.6)	9.3 (19.4)	8.9 (20.3)
- Length of stay in intensive care unit	0.1 (1.1)	0.1 (1.1)	0.1 (1.0)	0.1 (1.0)

Missing cases before matching, %: household composition, exposure=0.1; non-exposure=0.4 | education level, exposure=24.6; non-exposure=27.9 | income in decile, exposure=0.1; non-exposure=0.4 |urbanisation, exposure=0.7; non-exposure=1.0 | Missing cases after matching, %: education level, exposure=22.5; non-exposure=21.8.

Effects on inappropriate end-of-life care in dementia

In the last 14 days of life, compared to the unexposed group, the palliative home care support group less frequently received inappropriate medications, e.g. statins with no decline in use (2.1% vs 6.9%; Risk ratio[RR]=0.29) or anti-hypertensives (22.7% vs 38.5%; RR=0.47), and underwent less surgery (0.2% vs 1.2%; RR=0.17) (Table 3). Compared with the unexposed group, fewer people in the exposed group were admitted to a hospital (17.5% vs 50.5%; RR=0.21).

Effects on appropriate end-of-life care in dementia

In the last 14 days of life, 75.7% of people exposed to palliative home care support died at home, compared with 32.6% of the unexposed individuals (RR=6.45; Table 3). People in the exposed group also had more contacts with GPs and other primary care professionals (mean 11.7 vs mean 5.2) than those in the unexposed group.

Costs of care

In the last 30 days of life, compared with the unexposed group, the group exposed to palliative home care support had lower mean total inpatient costs of care (€2156 vs €6269) but higher mean total outpatient costs of care (€3007 vs €1024) (Table 4). Mean total direct medical costs of care for people in the exposed group were lower than for people unexposed (€5164 vs €7293).

DISCUSSION

Main findings

We found that of the 23,670 home-dwelling older people who died with dementia between 2010 and 2015 in Belgium, only 23.8% received palliative home care support in the last two years of life (N=5,637), 30.5% of whom received it for the first time within only 14 days before death (N=1,720). In the propensity-matched population, people who used palliative home care support received less inappropriate and more appropriate care in the last 14 days of life and had lower mean total costs of care in the last 30 days, compared with those who did not use any palliative home care support.

Strengths and weaknesses

Because it is difficult to conduct traditional experimental studies that allow the making of causal inferences by controlling temporality, exposure and confounding,(33) most evidence on the effects of palliative home care in dementia comes from observational studies known to have different sources of bias.(11,34) Using large administrative databases, a validated set of dementia-specific end-of-life care quality indicators, and high-quality propensity score matching, our study is the first to offer a firmer evidence base on the effects of palliative care for home-dwelling older people with dementia. Using nationwide administrative databases on all deaths over a six-year period, our findings are generalisable to all older people with dementia in Belgium.(15) This study is also largely reproducible in countries that use comparable databases and have similar types of services and healthcare systems.

Table 3. Effects of palliative home care support on the quality of care in the last 14 days of life in older people dying with dementia (N=5,678)

	Palliative home care support		Risk ratio
	Exposed (N=2,839)	**Unexposed** (N=2,839)	
Inappropriate end-of-life care in dementia			
1. Received statins and did not have declining use	2.1	6.9	0.29
2. Received two or more gastric protectors[a]	12.6	26.6	0.40
3. Received anti-hypertensives	22.7	38.5	0.47
4. Received calcium or vitamin D	1.5	6.0	0.24
5. Received a prescription for novel oral anticoagulants or vitamin K antagonists	18.6	37.6	0.38
6. Received a prescription for prophylactic gout medication	0.7	1.9	0.38
7. Received serotonin reuptake inhibitors	3.9	6.1	0.62
8. Received treatment from a neurologist	0.1	0.5	0.14
9. Received surgery	0.2	1.2	0.17
10. Had a cancer diagnosis and received chemotherapy[b]	1.6	2.7	0.59
11. Had diagnostic testing[c]	17.0	53.6	0.20
12. Had a port-a-catheter installed	0.0	0.1	0.50
13. Received blood transfusion	0.9	1.2	0.71
14. Were reanimated	0.0	1.1	–
15. Had one or more emergency hospital visits	10.3	23.9	0.37
16. Had one or more admissions to the intensive care unit	0.5	4.4	0.12
17. Had one or more hospital admissions	17.5	50.5	0.21
18. Died in hospitals	24.3	67.5	0.15
Appropriate end-of-life care in dementia			
19. Died at home	75.7	32.6	6.45
20. Received neuropathic medication when receiving morphine	2.0	1.9	1.07
	Mean	Mean	Mean incremental
21. Average number of general practitioner contact	3.1	1.1	+2.0
22. Sum of the number of contacts with a general practitioner or primary care professionals	11.7	5.2	+6.5

Abbreviations. CI=confidence interval; SE=standard error

[a] Two or more prescription of gastric protectors.

[b] The denominator used was the total number of people with cancer.

[c] Diagnostic testing includes spirometry or radiography or blood drawn or electrocardiogram.

Table 4. Effects of palliative home care support on direct medical costs of care in the last 30 days of life in older people dying with dementia (N=5,678)

	Palliative home care support				Mean incremental
	Exposed (N=2,839)		**Unexposed** (N=2,839)		
	Mean (95% CI)	**SE**	**Mean (95% CI)**	**SE**	
Total inpatient costs [a]	2156 (2002-2310)	78.6	6269 (6054-6483)	109.4	+4113
Total outpatient costs [b]	3007 (2953-3062)	27.9	1024 (988-1060)	18.3	+1983
Total costs	5164 (5027-5300)	69.7	7293 (7091-7496)	103.1	-2129

All costs are expressed in 2017 euros. Abbreviations. CI=confidence interval, SE=standard error.

[a] Inpatient costs are incurred after receiving a medical service or an act that requires hospitalization and at least one overnight stay in a hospital under a physician's care.

[b] Outpatient costs include all medical costs that do not require an overnight stay in a hospital or medical facility, are administered in a medical office, hospital, nursing home or at home and are incurred by using outpatient/ambulatory care.

Nevertheless, our study has limitations. The most important one is probably a possible problem of residual confounding and confounding by indication. With the propensity score matching, we could eliminate confounding due to measured covariates but not for unmeasured covariates,(35) such as differing preferences and attitude towards care of patients and caregivers, their subjectively experienced symptom or caregiving burden or personality traits, which can affect both the exposure and outcomes.(36,37) Secondly, because we did not have diagnostic or comorbidity data, we had to rely on underlying cause of death for the matching procedure. Although we were able to match the exposed and unexposed groups based on their level of care dependence, we still lack information on other potential confounders, such as frailty and severity and aetiology of dementia, which could also affect the exposure and outcome. If such data would become available or other matching procedures are used (e.g. a difference-in-differences cross-temporal matching design instead of cross-sectional matching), this could limit residual confounding in future comparable studies.(38) Thirdly, because only the 30-day cost calculation was possible with our data, it does not strictly comply with the temporality criterion, though the potential corresponding bias is likely to be limited. Fourthly, the quality indicators on which we based our outcomes are not developed to express quality of care for individual patients.(26) Our study should therefore be considered as an evaluation of palliative home care support in dementia on an aggregated level, providing relevant information for commissioners and policymakers. Finally, although we combined all-reported causes of death and the medication algorithm to identify older people who died with dementia, a substantial proportion of older people with dementia might have still been excluded due to potential underdiagnosis of dementia in primary care.(39,40)

What this study adds

We showed that compared with the unexposed group, the group exposed to palliative home care support received better quality of end-of-life care in the last 14 days of life. In particular, we found that people with dementia who used palliative home care support had lower risk of receiving inappropriate medications, undergoing surgery and being hospitalised; had considerably more contacts with healthcare professionals in primary care; and had a higher chance of dying at home. These positive findings concur with an earlier study suggesting similar positive effects of palliative home care support for a general palliative care population and with other previous studies focused on palliative home care interventions in dementia.(11,17,34) Nonetheless, to our knowledge, ours is the first to confirm such positive findings for home-dwelling older people with dementia. A causal relationship between palliative home care support use and better quality of end-of-life care is plausible given that palliative care is aimed at improving the quality of life of patients and families facing problems associated with life-threatening illness, through prevention and relief of physical, psychosocial and spiritual suffering.(41) It also uses a multidisciplinary team approach, facilitating active care coordination between all involved caregivers, which contributes to enabling patients to stay at home for as long as possible and to preventing unnecessary hospital admissions.(4) Further, eliciting patient preferences is an essential part of palliative care, making it more likely that patient preferences are taken into account when end-of-life care treatment decisions are made.(4) Finally, our findings showed that palliative home care support reduced total direct medical costs of care in the last month of life in older people with dementia. This also confirms previous findings suggesting that palliative home care can reduce resource use and estimated costs.(11,17,34)

Because our evidence suggests the effectiveness of palliative home care support in dementia, it is concerning that three out of four people with dementia who could potentially use palliative home care support did not do so, and of those who did use it, one in three received it for the first time only within 14 days of death. This concurs with widespread reports of suboptimal access to palliative care for people with dementia.(5) Potentially, GPs in Belgium, who like in many countries are gatekeepers for initiating palliative home care support, are not always aware that palliative care is appropriate for people living with dementia or are reluctant to initiate conversations on palliative care due to its connotation with dying.(42,43) Considering the protracted and unpredictable disease trajectory of dementia,(44,45) it is difficult, even for GPs, to identify when certain palliative care support measures might be appropriate, further hindering access.(36,46) Interestingly, about one in three of those who received palliative home care support died of cancer. Hence, having cancer might have been an important 'trigger' to initiating such support, which further highlights the difficulty of accessing such support for those with dementia.

Implications for practice, policy and research

Considering the progressive and terminal nature of dementia (44,45) combined with previous reports of suboptimal end-of-life care for this population,(47-49) our study highlights an urgent need to increase timely access to palliative home care support for older people with dementia. Strategies to achieve this might include active screening of people with dementia in primary care using pre-defined criteria based on patient needs and preferences rather than prognosis to 'trigger' the initiation of palliative home care support; raising awareness about the benefits of palliative care in dementia among primary care and secondary care professionals involved in dementia care; improving professionals' communication skills to introduce such sensitive topics; and introducing financial or other incentives to increase uptake.(4,7,31) Nevertheless, providing high-quality and comprehensive palliative care to improve the quality and reduce the costs of end-of-life care for more older people with dementia living at home is a highly demanding and complex work for the palliative care professionals in primary care.(50) In order to support these palliative care professionals in delivering palliative care to this population, there is an urgent need for continued and stronger public health investments in this sector. Because there is still no known care approach that aims to improve the access of older people with dementia living at home to palliative care services,(11) further work is needed to develop and evaluate a care approach that for example could comprehensively address all factors that might play a role in the access to palliative home care support of older people with dementia living and dying at home.(36,51)

Conclusion

Palliative care has been widely advocated to improve the quality of life and dying for older people with dementia, but there has been limited evidence of its effectiveness in this population so far. Our study suggests that palliative home care support improves quality and reduces total direct medical costs of end-of-life care in dementia. Despite these clear benefits, uptake in this population is low and late. Further studies exploring strategies to improve timely access to palliative home care for older people dying with dementia are urgently needed.

Declarations

Authorship

RM, TS, JC and LVDB made equal substantial contribution to conceptualising the design of the work. JC, RDS and KF acquired the data. RM and TS supervised data analyses. RDS and KF performed propensity score matching. RDS performed all other data analyses, except for cost evaluation which was performed by KF. RM and TS drafted and revised the manuscript critically for important intellectual content. NVDN substantially contributed to interpreting data from a clinical perspective. All authors made substantial contribution to interpreting the data and revising the manuscript critically; have given the final approval of the manuscript to be submitted for publication; and have participated sufficiently in the work to take responsibility for appropriate portions of the content.

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Declaration of conflicts of interest

The authors have no conflicts of interest to declare.

Research ethics (also to be found in the Methods section)

Ethics approval was provided by the Committee for Medical Ethics of the University Hospital Brussels (UZ Brussel) (B.U.N. 143201627075) and the ethics committee of the Ghent University Hospital (B670201422382). The administrative data-linkage was approved by the national Belgian Data Protection Authority (project SA1/STAT/MA-2015-026-020-MAV) and by the Statistical Monitoring Committee (project STAT-MA-2015-026).

Data management and sharing

In accordance with Belgian law, approvals for access to the administrative databases and the database integrating all databases were obtained from two separate national sectoral committees for privacy protection. As stated by the Sectoral Committee of Social Security and Health – Department Health and the Data Protection Authority (subcommittees of the Belgian Commission for the Protection of Privacy), we could not make the supporting data openly available due to ethical concerns regarding sensitive and potentially-identifying data. Additional information about the data, codes, syntaxes and access regulations are available upon request.

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SUPPLEMENTARY FILES – CHAPTER 6

Supplementary table 1. The quality indicators used as outcomes and excluded in the present study

QUALITY INDICATORS USED AS OUTCOMES IN THE PRESENT STUDY	
Quality indicators	**Numerators (Number of people who died from dementia who*)[a]**
Inappropriate end-of-life care in dementia	
1. Statins[a]	*received statins and did not have declining statin use
2. Neurologist visit	*received treatment from a neurologist
3. Gastric protectors	*received two or more prescriptions of gastric protectors
4. Anti-hypertensives	*received antihypertensives
5. Calcium vitamin D	*received calcium or vitamin D
6. Novel oral anticoagulants or vitamin K antagonists	*received a prescription for novel oral anticoagulants OR vitamin K antagonists
7. Prophylactic gout medication	*received a prescription for prophylactic gout medication
8. Serotonin reuptake inhibitors	*received serotonin reuptake inhibitors
9. Surgery	*received surgery
10. Chemotherapy[c]	* had a cancer diagnosis and received chemotherapy
11. Diagnostic testing	*had diagnostic testing (spirometry OR radiography OR blood drawn OR electrocardiogram)
12. Received a port-a-catheter instalment	*had a port-a-catheter installed
13. Blood transfusion	*received blood transfusion
14. Reanimation	*were reanimated
15. Emergency department admissions	* had one or more emergency hospital visits
16. Intensive care unit (ICU) admission	*had one or more admissions to the intensive care unit
17. Hospital admissions	* had one or more hospital admission
18. Hospital death	*died in hospital
Appropriate end-of-life care in dementia	
19. Home death	*died at home
20. Morphine and neuropathic medication	*received neuropathic medication when receiving morphine
21. General practitioner (GP) contact	*had an increase in average number of contacts with a GP
22. Primary caregiver contact	*Sum of number of contacts with a general practitioner or other primary care professional
EXCLUDED QUALITY INDICATORS	
Quality indicators	**Numerators (Number of people who died from dementia who*)**
23. Specialized palliative care[d]	*received specialized palliative care (hospital palliative unit OR palliative daycare centre OR multidisciplinary home care)
24. Official palliative care status[d]	* received official palliative care status, enabling financial government support for palliative care
25. Late initiation of palliative care[d]	* had a first referral to specialized palliative care OR received official palliative status
26. Tube feeding or intravenous feeding[e]	*received tube feeding or intravenous feeding
27. ICU admissions from nursing home[f]	*lived in a nursing home and had one or more ICU visits
28. Home death or death in nursing home of residence[f]	*lived and died in a nursing home

[a] The denominators are the number of older people who died from cancer, unless otherwise indicated.

[b] The denominator was the number of people who used statins.

[c] The denominator was the number of people who died from dementia and had a diagnosis of cancer.

[d] Excluded because it overlaps with palliative home care support (exposure).

[e] Excluded because it is reimbursed as a package in hospitals and could therefore not be measured on an individual level.

[f] Excluded because they relate to individuals who permanently resided in a nursing home.

Supplementary table 2. Frequencies of delivered palliative home care support measures (N=2,839)

Matched individuals who received palliative home care support	Frequencies (%)
Received support measure 1	2,792 (98.3)
Received support measure 2	1,010 (35.6)
Received support measure 3	1,211 (42.7)
Received combined support measures 1 and 2	988 (34.8)
Received combined support measures 1 and 3	1,196 (42.1)
Received combined support measures 2 and 3	423 (14.9)
Received all three support measures (1, 2 and 3)	418 (14.7)

Support measure 1= Allowance for palliative patients living at home; Support measure 2= Multidisciplinary palliative home care team; Support measure 3=Palliative home care nursing or physiotherapy.

General Discussion

Discussion

This part of the dissertation discusses the main findings of the six studies aiming to describe palliative care and to study how it can be improved for older people with dementia living in nursing homes (**Research Aim 1**) and at home (**Research Aim 2**). To realise Research Aim 1, we described how many people with dementia die in nursing homes, how these residents die in relation to their palliative care service use and comfort in the last week of life, and if there are changes over time, as well as evaluated whether a generalist palliative care programme for nursing homes affects comfort at the end of life and quality of care and dying of residents with dementia differently than those without dementia (**PART I of this dissertation**). To realise Research Aim 2, we described the current quality of primary palliative care and the current evidence on palliative home care interventions for older people with dementia living at home, as well as evaluated the effects of palliative home care support on quality and costs of end of life care for people with dementia in Belgium (**PART II of this dissertation**). The main findings will be summarised, followed by a discussion of the methodological considerations of the research design and methods used. Further, a general discussion will reflect on the findings in relation to previous research. Finally, the implications of the findings for practice, future research and policy will be provided.

1.1. Summary of main findings

The first three Chapters focused on palliative care for nursing home residents with dementia (Research Aim 1 – PART I). **Chapter 1**, we examined the differences between 2010 and 2015 in the prevalence and characteristics of residents with dementia in nursing homes in Flanders and their palliative care service use and comfort in the last week of life. Between 2010 and 2015, there was a 15%-point increase in the prevalence of dementia in the nursing homes. Almost all residents' characteristics did not change, except for the level of cognitive impairment in the last month of life based on the Cognitive Performance Scale (CPS), with a total of 11%-point decrease in residents with severe and very severe cognitive impairment (i.e. CPS scores 5-6), and the level of cognitive and functional impairment based on the Global Deterioration Scale (GDS), with a total of the 14%-point increase in residents who lost all verbal abilities, was incontinent/required assistance with eating and toileting and lost basic psychomotor skills (i.e. GDS stage 7). Among residents in both years, about half died with advanced dementia, more than 90% developed clinical complication in the last month of life, and the majority stayed in nursing homes for about two years. Pain assessment in the last week of life was performed proportionally more often for residents in 2015 than in 2010 (83% vs. 63%). However, in both years, between 37% and 52% of residents neither received psychosocial intervention in the last month of life nor spiritual care shortly before death. We found no change in residents' total comfort in the last week of life.

In **Chapter 2**, we investigated the occurrence rates of clinical events in the last month of life and their associations with comfort in the last week of life of nursing home residents with advanced, non-advanced and no dementia in six EU countries. We found that in the last month of life, about a quarter of nursing home residents developed pneumonia across the three groups of residents. Febrile episodes and intake problems were more common, but occurrence rates differed between groups; those with advanced dementia more frequently developed febrile episodes and intake problems. Overall, developing these three major clinical events was associated with less comfort, but this varied according to the presence and severity of dementia. While the presence and severity of dementia did not moderate a consistently negative association between pneumonia and comfort across the three groups, it did moderate the association between intake problems and comfort. In short, less comfort was observed in residents with advanced, non-advanced and no dementia who developed pneumonia. Among residents who developed intake problems, less comfort was observed only in residents with non-advanced dementia and no dementia. Developing 'other clinical events' was not associated with comfort in any of the groups.

In **Chapter 3**, we assessed whether the effects of PACE Steps to Success palliative care programme on comfort in the last week of life and quality of care and dying in the last month of life differ between residents with advanced, non-advanced, and no dementia in seven European countries. PACE Steps to Success is a multi-component train-the-trainer programme aiming to integrate generalist and non-disease-specific palliative care for the nursing home population. We found that the effects of PACE Steps to Success on both outcomes did not differ between the three subgroups.

The following Chapters focused on palliative care for older people with dementia living at home (Research Aim 2 – PART II). In **Chapter 4**, we systematically investigated the overall quality of primary palliative care for older people with dementia in Belgium, Italy and Spain. This study showed considerable cross-country differences on regular pain measurement, acceptance of approaching death, patient-GP communication about illness and medical treatments, involvement of specialist palliative care services, and repeated multidisciplinary consultations about end-of-life care. Quality indicator scores in Belgium were higher than Italy, but not appreciably higher than Spain. For instance, repeated multidisciplinary collaborations about end-of-life care were conducted significantly more often in Belgium than in Spain and Italy. Nevertheless, in the three countries, regular pain assessment was performed in not more than half of the patients. More than two-thirds of the patients had poor communication with GPs. The countries did not differ on scores for relative-GP communication, which ranged from 81% to 88%, and for dying in hospitals. In particular, about a third of the patients across the three countries died in a hospital.

In **Chapter 5**, we systematically reviewed the international evidence on specialist and non-specialist palliative home care interventions in dementia. We retrieved eight studies evaluating interventions aimed at improving end of life care outcomes for people with dementia living at home. None of the studies were of high quality, mostly due to the inability to achieve blinding and to measure/report intervention integrity. We found weak evidence showing that palliative home care interventions in dementia can improve end of life care outcomes relating to institutionalisation, estimated resource use and functional status. There was moderate evidence of beneficial effects on behavioural symptoms arising from the person's cognitive and communication problems, but the evidence on whether these effects would last was contradictory. Although the evidence on pain reduction was limited and inconclusive there was some evidence of enhanced pain assessment. Evidence on facilitators and barriers was not systematically investigated and our findings are based on limited information provided in the discussion sections of the included studies. The mapping of the studies according to the European Association for Palliative Care (EAPC) domains highlighted the main preoccupations and focus of the interventions reviewed.

In **Chapter 6**, we aimed to fill some of the gaps related to the lack of evidence for palliative care effects in dementia. Using linked population-level administrative databases in Belgium, we found that of the 23,670 home-dwelling older people who died with dementia between 2010 and 2015 in Belgium, only 23.8% received palliative home care support in the last two years of life, 30.5% of whom received it for the first time within only 14 days before death. In the propensity score-matched population, people who used palliative home care support in the last 14 days of life less frequently received inappropriate care, such as inappropriate medications (e.g. statins with no decline in use or anti-hypertensives) or underwent surgery, while they received more appropriate care. In particular, 75.7% of people who received palliative home care died at home, compared with 32.6% of the individuals who did not receive it. People who received palliative home care also had more contacts with GPs and other primary care professionals than those who did not receive it. In the last 30 days of life, the group who received palliative home care, compared to those who did not, had lower mean total inpatient costs of care but higher mean total outpatient costs of care. Mean total direct medical costs of care for people who received palliative home care were lower than for people who did not.

1.2. Methodological considerations, strengths and limitations

To realise Research Aim 1, we used two epidemiological studies in nursing homes (i.e. the Dying Well with Dementia study (2010) and the PACE study (2015)) – and performed a subgroup analysis of a cluster-RCT (investigating the effect of the PACE Steps to Success training programme). To realise Research Aim 2, we used a mortality follow-back study using existing GP Sentinel Networks (EUROSENTIMELC), a systematic review of interventions, and a nationwide propensity score-matched decedent cohort study. In this section, the methodological considerations of these studies, including their strengths and limitations, are described.

1.2.1. The Dying Well with Dementia study and the PACE study (Chapters 1 and 2)

The Dying Well with Dementia and PACE studies allowed us to investigate changes between 2010 and 2015 for nursing home residents with dementia in Flanders, Belgium in relation to their demographic and clinical characteristics, palliative care service use and comfort in the last week of life (**Chapter 1**). Although these were two separate studies, both utilised similar study designs, and all variables of interest were measured in the same way. However, these studies have a number limitations that should be taken into account in interpreting the results. More specifically, because they remain separate studies, the variables that could be explored and compared between the years were limited. For instance, the palliative care services that could be explored are limited to services measured in both studies. Nevertheless, the services investigated comprise important components of palliative care in dementia, e.g. comprehensive delivery of physical, psychosocial, or spiritual support.(1) The Dying Well with Dementia study has limited data on nursing home characteristics that might have influenced palliative care service use or comfort at the end of life. Although we accounted for the clustering of data within nursing homes in the analyses, which could partly mitigate this limitation, our inability to control for unmeasured variables that could influence palliative care service use or comfort remains a clear limitation of this method.

The PACE study provided a better understanding of the associations between the most common clinical events, such as pneumonia and intake problems, and comfort in dying residents with varying stages of dementia in six EU countries (**Chapter 2**). One of the main limitations of both epidemiological studies is their cross-sectional nature. In particular, it is not possible to establish causality between multiple events or between events and outcomes. In Chapter 1, we could not explore whether the extent of residents' palliative care service use related to the identified lack of change in their total comfort in the last week of life (i.e. temporal relationship). In Chapter 2, we could not explore whether the timing of the occurrence of intake problems relate to the observed discomfort in residents with advanced dementia (i.e. temporal relationship). Hence, we could not make causal inferences between the occurrence of clinical events and comfort at the end of life.

1.2.2. The subgroup analysis of the PACE cluster-RCT (Chapter 3)

This subgroup analysis offers the very first insight in the extent to which the effects of a generalist, non-disease-specific palliative care programme, which was designed to train nursing home staff in delivering high-quality palliative care, varied between residents with advanced, non-advanced and no dementia. One of the major strengths of this subgroup analysis was the relatively large sample size per subgroup for whom the severity of dementia was determined using validated instruments. Further, this subgroup analysis was pre-planned and used statistical tests of interactions, which enhance the validity of study results. Nonetheless, findings should be interpreted in light of this study' limitations. Because power calculation was not conducted for this subgroup analysis, our study might not have detected potentially important but small subgroup difference in programme effects. For instance, although we found a 2.7 CAD-EOLD score point difference between residents with non-advanced and no dementia, which is close to what we considered as a clinically-important effect (i.e. CAD-EOLD score of 3 points),(2,3) the limited power might not have allowed us to detect statistically significant differences. This is also the reason why we only interpreted the differential effects between the subgroups, and not the programme effects in the individual subgroups.

Determining the presence and severity of dementia for Chapters 1 to 3

The presence of dementia relied on the estimation of the nursing home staff and/or the GP and not of specialists. The GP's specificity in diagnosing dementia is good, which makes false positives less likely to occur.(4) Further, a previous study shows that nurses could detect dementia with 94% accuracy (with 92% sensitivity and 96% specificity), which suggests the nurses' capabilities to determine the presence of dementia.(5,6) While this can be considered a feasible method to determine the presence and severity of dementia in such large epidemiological studies, there might still be limited misclassifications, especially among residents with difficult-to-observe mild dementia symptoms.(7) Moreover, about 10% of the nursing home staff respondents were care assistants, who thus determined the presence and severity of dementia and might have led to limited misclassifications. In Chapter 1, only the Dying Well with Dementia study used the Katz-scale criteria to exclude residents without dementia before data collection.(8) Nevertheless, such residents without dementia would have also been identified by the nursing home staff and/or the GPs in the PACE study, as they could detect dementia rather accurately.(6,9) Moreover, for a few residents in the Dying Well with Dementia and PACE studies, we could not determine the presence or absence of dementia due to non-response, which might have influenced the calculation of the prevalence of dementia in Chapter 1.

To compare with earlier findings,(10,11) the severity of dementia has been determined using the combination of two highly discriminatory nursing home staff-reported instruments – CPS and GDS, both of which were developed to measure the cognitive and functional status of residents.(12,13) However, for the purpose of this study, we used the GDS only as an additional layer of assessment in order to increase the validity of the dementia severity variable. More specifically, in the after-death questionnaire, we only asked the nursing home staff whether or not a resident fulfilled all the criteria based on GDS stage 7 (severe impairment): "*Did the resident fit all 3 criteria of the following description 1 month before death?": 1) all verbal abilities are lost over the course of this stage; 2) incontinent; requires assistance with toileting and feeding; and 3) basic psychomotor skills are lost with the progression of this stage (e.g. ability to walk)*. Because of the wordings, such as toileting or ability to walk, the 'binary' GDS might have been interpreted as related to the functional status of the residents. Because of this limitation of GDS, we did not use the GDS scores to describe the cognitive and functional status of residents, but we only showed these data to provide an underlying reason for the seemingly contradictory findings in Chapter 1. More specifically, between 2010 and 2015, we found a somewhat lower percentage of residents who died with severe cognitive impairment (i.e. CPS scores 5-6) but a higher percentage of residents who lost all verbal abilities, was incontinent/required assistance with eating and toileting, and lost basic psychomotor skills (i.e. GDS stage 7). These findings might explain the slightly higher but non-statistically significant difference in the proportion of residents with advanced dementia in 2015 than in 2010 in this chapter.

1.2.3. Mortality follow-back study using existing GP Sentinel Networks (EUROSENTIMELC) (Chapter 4)

This mortality study is the first to systematically measure the quality of palliative care for older people with mild or severe dementia using a limited set of quality indicators for primary care, which could guide efforts to improve primary palliative care for this population. The GP Sentinel Networks are nationwide networks of GPs, which provide a representative sample of both GPs and the general population in Belgium, Italy and Spain (Castille y Léon and Valencia regions in Tuscany). This representativity of the networks means that the findings are generalisable to the general population. This study also includes people with dementia who had and had not received specialised palliative services. The inclusion of all non-sudden deaths in our study also enabled us to assess the quality of care delivered in the context of dying. Nevertheless, one of the limitations of this method is that data only provide the GP's perspectives of the situation. While GPs have a pivotal role in providing care to older people with dementia living at home, there can be situations when GPs are not informed about patient care, for instance if patients were hospitalised and died there. This limitation is relevant for about 15 to 34% of the sample who died in hospitals. Further, the presence and severity of dementia is based on the estimation of the GPs, and not of specialists. The GP's specificity in diagnosing dementia is good, which makes false positives less likely to occur.(4) Nevertheless, there remains a chance for limited misclassification, especially for those with mild dementia symptoms.

Retrospective research methods used for Chapters 1 to 4

To collect data, after-death questionnaires about residents and people with dementia were used in the Dying Well with Dementia study, the PACE study, the PACE cluster-RCT and EUROSENTIMELC. These questionnaires were distributed and completed by the nursing home staff most closely involved in resident care, GPs, and nursing home managers/administrators. The use of retrospective methods is well-established in the field of social science research and large-scale population-based epidemiological end-of-life studies.(14–17) This limits potential bias in prospective sampling related to the underrepresentation of people who live longer than the study follow-up period or who have dementia for whom the terminal phase is difficult to predict. The use of retrospective data collection also allowed us to select a population-based sample in order to obtain a better view and description of nursing home residents with dementia, in terms the prevalence of dementia, demographic and clinical characteristics including the occurrence of acute clinical events, palliative care service use, comfort at the end of life. Finally, the method also allowed us to include both residents with advanced dementia and non-advanced dementia, a population that is often excluded from palliative care and end-of-life care research.

Nevertheless, retrospective methods have limitations.(15,18) Because data were collected after death, proxy respondents – namely nursing staff, GPs, and nursing home administrators – were the ones who provided the data and not the resident or patient. The use of proxy respondents is widely used in research for older people, including those with dementia, and palliative care.(19–22) It has been reported that proxy reports are most reliable in terms of being in line with patients' own judgment regarding observable symptoms and quality of care and services received. However, it might be less reliable with subjective aspects of patient's experiences, such as the level of pain or emotional distress.(23) Nonetheless, for difficult to observe outcomes, such as the comfort while dying due to relief from pain or emotional distress, we used validated instruments that can be used by nursing home staff (i.e. CAD-EOLD scale). The CAD-EOLD scale has been shown to be valid in advanced dementia, less advanced dementia and mixed nursing home population.(24,25) While the use of proxy respondents has inherent limitations, it can be considered a fair substitute for residents' response for the aspects and circumstances studied in this dissertation.

Another limitation of retrospective methods is the possibility for recall bias. Especially for emotionally-loaded or burdensome events, such as the occurrence of acute clinical events or the dying phase of a resident, respondents might recall events inaccurately or incompletely, or they might change the sequence of events.(26) The longer it has been since the event happened, the more difficult it is for respondents to recall it vividly. Hence, explicit efforts had been taken to limit this limitation; though recall bias is still possible. In particular, the data were collected within three months in the epidemiological studies, within four months in the PACE cluster-RCT and within seven days for EUROSENTIMELC. In completing the after-death questionnaires, the respondents were also requested to use medical files and other memory supports.

1.2.4. Systematic review of interventions (Chapter 5)

It was a strength of the systematic review that we drew on the EAPC White Paper to structure the data extraction and analysis. This demonstrated how the evidence was distributed according to an international consensus on what should be the key activities and focus of palliative care in dementia. However, we only found eight relevant studies, none of which were of high quality. The evidence of effectiveness therefore needs to be interpreted with caution. As we adopted a broad definition of non-specialist palliative care interventions, which in itself is a strength of this review, this may mean that relevant studies were missed. However, our searches were systematic and electronic database searching was supplemented with lateral searching. Our decision to only include quantitative studies, and associated process evaluations, may explain the limited evidence on facilitators and barriers to implementation. However, forward citation tracking of the included studies also did not reveal any relevant studies. Finally, subjectivity may have been introduced in the mapping of the intervention components according to the EAPC White Paper domains, which we tried to limit through discussion within the research team.

1.2.5. Nationwide propensity score-matched decedent cohort study (Chapter 6)

Most evidence on the effects of palliative home care in dementia comes from observational studies known to have different sources of bias. Using large administrative databases, a validated set of dementia-specific end-of-life care quality indicators, and high-quality propensity score matching, this study is the first to offer a firmer evidence base on the effects of palliative care for older people with dementia living at home. Using nationwide administrative databases on all deaths over a six-year period, findings are generalisable to all older people with dementia in Belgium. This study might also be reproducible in countries that use comparable databases and have similar types of services and healthcare systems. Nevertheless, our study has limitations. The most important one is probably a possible problem of residual confounding and confounding by indication. With the propensity score matching, we could eliminate confounding due to measured covariates but not for unmeasured covariates,(27) such as differing preferences and attitude towards care of patients and caregivers, their subjectively experienced symptom or caregiving burden or personality traits, which can affect both the exposure and outcomes.(28,29) Secondly, because we did not have diagnostic or comorbidity data, we had to rely on underlying cause of death for the matching procedure. Although we were able to match the exposed and unexposed groups based on their level of care dependence, we still lack information on other potential confounders, such as frailty and severity and aetiology of dementia, which could also affect the exposure and outcomes. If such data would become available or other matching procedures are used (e.g. a difference-in-differences cross-temporal matching design instead of cross-sectional matching), this could limit residual confounding in future comparable studies.(30) Another limitation of this method is that it does not strictly comply with the temporality criterion because only the 30-day cost calculation was possible with our data; though the potential corresponding bias is likely to be limited. The quality indicators on which we based our outcomes are not developed to express quality of care for individual patients.(31) Our study should therefore be considered as an evaluation of palliative home care support in dementia on an aggregated level, providing relevant information for commissioners and policymakers. Finally, although we combined all-reported causes of death and the medication algorithm to identify older people who died with dementia, a substantial proportion of older people with dementia might have still been excluded due to potential underdiagnosis of dementia in primary care.(32,33)

1.3. General discussion

In-depth discussions and reflections are presented according to the two parts of this dissertation. Part I discusses three overarching themes regarding palliative care for nursing home residents with dementia, including the increasing demand for palliative care to promote comfort at the end of life of residents with dementia; potential ways to promote comfort at the end of life of this population; and the effects of a generalist palliative care training programme on comfort at the end of life of residents with dementia. In Part II, three overarching themes related to palliative care for older people with dementia living at home are discussed, including several crucial aspects of palliative care where improvements can be made for this population, the effects of palliative home care interventions in dementia and the ways to improve the evidence-building on this very important topic.

PART I. Palliative care for nursing home residents with dementia

Increasing demand for palliative care to promote comfort at the end of life of residents with dementia

There are strong calls for more research and action to improve palliative care for people with dementia, especially in the nursing home setting.(34–37) The importance of these calls is further illuminated by the three main findings from this dissertation. First, using the context of Flanders, Belgium, Chapter 1 described a substantially ***higher prevalence of dementia in nursing homes between 2010 and 2015***, and this is in spite of the growing number of policies that support older people with dementia to stay at home for as long as possible. Over this relatively short period, almost an additional 15% of the residents died with dementia, of whom about half died before they reached the advanced stage. Perhaps, this is because such increase in the prevalence of dementia also occurred in the home setting, as the 2016 estimates in Flanders suggest that there were 15,855 more people with dementia in 2015 than in 2010,(38) which is congruent with the current trends in dementia prevalence in other countries in Europe.(39) People with dementia often have multi-faceted physical, psychosocial, and spiritual care needs that could become increasingly complex over months or years until death. In addition to these complex care needs is another layer of complexity posed by the specific disease trajectory and symptoms of dementia, such as its prolonged and highly variable disease trajectory or the associated cognitive impairment, which might impact health service use and provision. In a 4-year prospective cohort study published in 2013, Eska and colleagues found that the risk of institutionalisation of people with dementia increased significantly with older ages of patients and caregivers, greater use of community health services and greater caregiver burden.(40) Hence, the increase in dementia prevalence, together with their increasingly complex care needs that might become unmanageable for their family carers at a certain moment, might have led to an increased number of people with dementia transferred to nursing homes.

Second, Chapter 1 showed that ***demographic and clinical characteristics of residents with dementia in 2010 and 2015 remained almost similar.*** In both years, a sizable proportion of the residents died with advanced dementia, developed clinical complications as they approached death, and stayed in the nursing homes for about two years. These findings suggest that the prolonged and complex palliative care needs of nursing home residents with dementia still seem to persist over the years.(41,42) Further, based on CPS scores, we found a lower proportion of residents who died with severe cognitive impairment in 2015 than in 2010. This finding suggests that the residents in 2015 may have died more often with other diseases that do not necessarily result in cognitive impairment. For instance, in 2015, cardiovascular diseases were reported to be the main cause of death in the EU for people aged 65 years and over.(43) Comorbidities, which often occur alongside old age and dementia, pose an additional complexity in addressing the care needs of residents with dementia.(44)

Third, Chapter 1 revealed that ***the total comfort in the last week of life of residents with dementia did not change between 2010 and 2015***. The scores on the validated scale EOLD-CAD measuring comfort at the end of life in this population showed a room for improvement in both years. The observed evolution related to the prevalence of nursing home residents with dementia and their clinical characteristics and comfort while dying is likely to continue in the future, as the prevalence of dementia in Flanders has been projected to almost double by 2060.(38) Further, although this evolution has been identified in the specific context of Flanders, Belgium, comparable trends might have also occurred in other countries that implemented similar dementia and palliative care policies and initiatives and have similarly increasing prevalence of dementia.(39,45–48) Overall, these three main findings suggest the increasing demand for palliative care in dementia in nursing homes in the future.

How can we promote comfort at the end of life of nursing home residents with dementia?

To promote comfort at the end of life of residents dying with varying stages of dementia, findings from this dissertation also shed light on the aspects of palliative care where improvements can be made. ***The first room for improvement concerns the need for a more comprehensive palliative care approach encompassing physical, psychosocial and spiritual support****,* which is paramount to improving residents' overall comfort at the end of life.(1) Our findings concur with other reports arguing that there remains to be an "*over-reliance on the medical model*", primarily on the provision of physical care in this setting.(49) In particular, Chapter 1 showed that of the investigated physical, psychosocial and spiritual care services used by nursing home residents with dementia, only one increased between 2010 and 2015. More specifically, the proportion of residents for whom pain assessment has been conducted increased over the years, which relates to the physical aspect of care. While there was no change in their use of psychosocial interventions nor spiritual care at the end of life, there remained a substantial proportion of residents with dementia, who did not receive psychosocial and spiritual support.

Nonetheless, the identified increase in pain assessment is encouraging,(50) as about 60 to 80% of residents with dementia regularly experience pain, potentially due to many different causes, such as musculoskeletal, gastrointestinal and cardiac conditions, but also genitourinary infections and wounds (e.g. pressure ulcers).(51) In 2004, a guideline for pain control has been launched for nursing homes in Flanders.(52) Since then, pain control in dementia has also received relatively adequate attention in many other regional initiatives.(53–55) Pain control is also a major component in the palliative care guideline for nursing homes and the dementia policy, both launched in 2010.(56,57) We can thus argue that the encouraging improvement in pain assessment identified in 2015 might have been the outcome of these earlier initiatives. This implies that to achieve positive change in nursing homes, long-term, continuous and consistent efforts seem crucial.

Despite this increase in pain assessment, our findings in Chapter 1 still showed no apparent change in residents' comfort due to relief from pain. Earlier studies point toward an underuse of pain medication in cognitively impaired residents, especially those unable to communicate pain verbally.(58) Pain, if not treated promptly and adequately, can cause patient distress and discomfort. It might also underlie other symptoms or behavioural disturbances, such as agitation, aggression and depression,(59) which could result in poorer quality of life and could further complicate the delivery of dementia care.(60,61)

The second room for improvement relates to the major clinical events that were found to be associated with discomfort at the end of life (Chapter 2). More specifically, we found that the associations between these clinical events (i.e. pneumonia and intake problems) and comfort varied according to the presence and severity of dementia. Pneumonia, in particular, affects about a quarter of the nursing home population regardless of the presence and severity of dementia. Its negative association with comfort also did not differ between residents with advanced, non-advanced and no dementia, which is contrary to earlier studies suggesting that pneumonia is a hallmark of advanced dementia.(62,63) Potentially, the distressing respiratory symptoms of pneumonia, such as dyspnoea, laboured/rapid breathing or dry/hacking cough, may be perceived as profoundly uncomfortable for affected residents.(64–67) Further, even among cognitively-impaired residents who could not communicate, such as those with moderate to advanced dementia, breathing difficulties remain easily observable for healthcare professionals.(67–69) The discomfort associated with pneumonia has also been observed widely in previous months due to recent events related to the COVID-19 pandemic.(70) Contracting the corona virus can result in pneumonia, especially among nursing home residents who are often frail and have dementia.(71–73) Therefore, preventing pneumonia and addressing its symptoms emphasise an opportunity for improvement in comfort in dying residents with advanced and non-advanced dementia.

In addition, compared with residents with non-advanced and no dementia, intake problems were more likely to occur but remarkably less likely to be negatively associated with comfort in residents with advanced dementia (Chapter 2). Generally, these findings concur with earlier studies suggesting that intake problems are specific in advanced dementia (62,63) and suggest that the cause and origin of intake problems in those with advanced dementia, which can be multifactorial, might differ from those with non-advanced and no dementia. Residents with advanced dementia often develop intake problems gradually, whereas in frail residents without dementia, intake problems may develop more suddenly secondary to acute infections or other conditions.(74–76) Nonetheless, to promote comfort at the end of life, this finding supports current recommendations to forego tube feeding in residents with advanced dementia, as it may be burdensome and lack clinical benefit in ameliorating malnutrition, maintaining skin integrity or preventing aspiration pneumonia.(76) A prospective cohort study in the US suggests that tube feeding-related complications were also found to account for about half of all emergency department visits in residents with advanced dementia.(77) Potentially-avoidable hospitalisations pose inherent risks to nursing home residents, including discomfort, increased morbidity and mortality and hospital-related complications, such as infections, delirium, polypharmacy and related adverse drug reactions.(78,79) It may also cause anxiety and low satisfaction with care among residents and their families and is expensive for the health and social care system.(78–80)

Effects of a generalist palliative care training programme on comfort at the end of life of residents with dementia

In Chapter 3, we assessed whether the effects of a multi-component generalist, non-disease-specific palliative care training programme (i.e. PACE Steps to Success) differed between residents with advanced, non-advanced and no dementia. The primary trial analyses of the PACE cluster-RCT revealed that PACE Steps to Success did not improve comfort in the last week of life of residents (primary outcome), but it appeared to improve their quality of care and dying in the last month of life (secondary outcome).(3) Further, the cost-effectiveness analysis embedded in the PACE cluster-RCT suggested substantial medical cost savings after implementing PACE Steps to Success while retaining quality of care, primarily due to lower hospitalisation costs of approximately €1000.(81)

Because nursing homes offer round-a-clock care services to a mixed nursing home population dying with and without dementia,(82) PACE Steps to Success comprised essential domains of palliative care that have been widely recommended for both residents with and without dementia (i.e. advance care planning, optimal symptom assessment and management of pain and depression until the end of life, education of and support for healthcare providers, and support for family).(36,83,84) The majority of programme elements were therefore generic for all nursing home residents and only three elements were dementia-specific, i.e. communication training in advanced dementia for the PACE coordinators in the nursing homes, and two elements integrated into the training for all nursing home staff which emphasised dementia as a terminal illness (as part of Step 2) and offered symptom control strategies for residents with and without dementia (in Step 4).(3,85) Hence, we hypothesised a priori that the effects of this programme might differ between those with and without dementia in favour of those with mild/moderate or no dementia compared with advanced dementia.

Contrary to this hypothesis, we found that the effects of PACE Steps to Success did not differ between residents with advanced, non-advanced and no dementia. For the primary outcome – comfort in the last week of life – PACE Steps to Success did not achieve better outcomes for residents without dementia or with non-advanced dementia than for those with advanced dementia. Hence, the stepwise training of nursing home staff over a one-year period was not sufficient to improve comfort in the final days of life in nursing home residents without dementia, nor in those with different stages of dementia. This finding confirmed the negative results of the primary trial analyses on comfort at the end of life.(3) Nevertheless, for the secondary outcome, our analyses showed that the PACE Steps to Success programme improved quality of care and dying in the last month of life equally for those with dementia (regardless of the stage) and those without dementia. Although this finding needs to be interpreted cautiously as this is a secondary outcome and the effect is only medium-sized, they are remarkable, as this palliative care programme only had a limited number of dementia-specific elements as part of the training.(85) In particular, it is remarkable that the Quality of Dying in Long Term Care (QOD-LTC) subscale 'preparatory tasks' differed between the intervention and control groups, including items such as 'residents had treatment preferences in writing', 'residents' funeral was planned' and 'residents had named a decision-maker'.(3) These items are related to the process of advance care planning, which appears to be equally improved by the PACE program. As the process evaluation showed, 'advance care planning with patients and family' was also the first and best implemented step in the PACE program.(87)

The primary analyses combined with the process evaluation of the PACE cluster-RCT discussed a number of potential factors that can explain why PACE Steps to Success did not affect the primary outcome – comfort at the end of life.(3,87) These factors include 1) the content of the intervention itself, 2) the quality of its implementation in several nursing homes, 3) a possible mismatch between the intervention and the primary outcome, or 4) a combination of these factors.(3) In order to improve palliative care for nursing home residents with dementia, future development and evaluation of such palliative care interventions in nursing homes should target these factors while taking the specific care needs of people with dementia into account.

PART II. Palliative care for older people with dementia living at home

How can we improve palliative care for older people with dementia living at home?

Findings from this dissertation also bring light to aspects of palliative care where improvements can be made for older people with dementia living at home. Chapter 4 suggests considerable differences and similarities between Belgium, Italy and Spain in the overall quality of primary palliative care for older people with dementia, potentially as a result of different national health systems (e.g. palliative care resources and focus on dementia) and healthcare cultures.(46) Although these countries have national palliative care legal frameworks and have integrated it into their health systems,(88,89) our findings suggest that the overall quality in Belgium is higher than in Italy, but not appreciably higher than in Spain. This may be because Belgium has the highest ratio of palliative care resources per million inhabitants,(88,89) which is a critical facilitator to delivering palliative care services to older people with dementia.(28) Belgium also provides detailed guidelines for palliative home care teams and networks,(90) which could promote collaborative practice and reciprocal sharing of knowledge, expertise and information with GPs. This collaborative practice may also explain our findings regarding the significantly higher multidisciplinary end-of-life care consultations in Belgium than in Italy and Spain, which is another vital element of optimal palliative care in dementia.(1)

The comparable quality for Spain and Belgium may have resulted from their efforts to expand palliative care from cancer patients to older people and those with dementia.(88,91) More concretely, in Belgium for instance, several workgroups of the Federation of Palliative Care focus specifically on topics, such as "Palliative Care for Older People". Furthermore, the broadening of palliative care to include non-cancer patients is one of the topics addressed in the workgroup Palliative Support Teams. The Pathway of Palliative Care in the Primary Care Setting explicitly aims to improve palliative care for patients in the primary setting, and the definition of palliative care patients explicitly uses frailty parameters that go beyond patients with cancer.(88) Since 2003 in Spain, all terminally-ill patients have the right to receive palliative care, and in their 2010 to 2014 Palliative Care Strategy of the National Health System, they explicitly targeted palliative care for older people and those with dementia.(88,91) In contrast, in Italy, palliative care remained focused on the needs of cancer patients and those with Amyotrophic Lateral Sclerosis but not for older people nor for those with dementia.(88) This may explain why Italy seems to have the lowest scores in the overall quality of primary palliative care. While Italy currently has a National Dementia Plan that mentions the importance of palliative care in dementia, this plan has only been approved in October 2014.(92) Hence, it may not have been fully implemented yet during the study period in Italy, which was between June 2013 and May 2015. Based on these findings, we argue that incorporating palliative care in national or regional policies with a concomitant increase in resources, especially for older people with dementia, and enhancing multidisciplinary collaboration among GPs, palliative home care teams and other healthcare networks seem imperative in improving the quality of palliative care for older people with varying stages of dementia who live at home.

Chapter 4 also highlights similar opportunities for improvement in primary palliative care in dementia across the three countries, including pain assessment, communication with patients, and prevention of avoidable hospitalisations. First, the pain of more than half of patients across the countries was not regularly measured in the last three months of life according to the GPs. Such suboptimal pain assessment in dementia is in line with earlier reports, and there is consensus within the literature that the underlying reason for sub-optimal pain management in dementia is the challenge of accurately identifying pain in these individuals.(50,93) The gold standard for assessing pain is through self-report due to its subjective nature.(50,93) People could report their experience of pain, including its intensity, duration, quality and location through a number of existing visual and numerical scales. However, as these scales rely on an individual's memory, verbal capacity, expectations and emotions, these scales lack utility in people with dementia. Problems with communication and abstract thinking that is inherent in the advanced stage of dementia severely limits the extent of self-report that is possible. It is also complex for healthcare professionals to determine whether behavioural disturbances of people with dementia are due to pain or the dementia itself; thus further complicating pain assessment.(94–96) Finally, misconceptions about pain in older people cease to exist, such as that pain is a natural part of ageing; that the inability to deal with pain is a sign of weakness; or that pain medication can cause addiction and should best be provided only when needed.(97)

Second, we found that more than two thirds of the patients, particularly in Italy and Spain, appeared to have poor communication with GPs. The relatively higher score for patient-GP communication in Belgium may be due to their continued efforts in advance care planning (88,98) and the culture of wanting to be informed about health-related issues.(99) The identified scores for communication between GPs and patients with dementia in this dissertation also appear to be generally lower than in other disease groups, such as in cancer or even in frailty.(98,100,101) While this less frequent communication with patients may be understandable due to cognitive decline inherent in dementia, our study suggests that this is an apparent problem even for people with mild dementia. In line with existing evidence in other disease groups,(98,100) we found high levels of relative-GP communication across the three countries, implying that GPs communicate more often with relatives than with patients (Chapter 4), which seems to be an alternative to the poor communication with patients. While it is crucial to communicate with family and family carers of people with dementia, recommendations in dementia consistently place emphasis on person-centred care,(1,102) and to realise this, people with dementia should be involved as much as possible in deciding for their own care.

Finally, although most older people with dementia prefer to die at home,(103,104) about a third of people with dementia still died in a hospital. Admission to hospital is frequent among people with dementia, especially among those living in the community, and hospitalisations at the end of life are the most common type of transfer among older people.(105–107) While some hospitalisations are appropriate and necessary, unnecessary hospitalisation at the end of life should best be avoided. In line with the impact of hospitalisations from nursing homes, hospitalisations at the end of life from the community setting can also result in physical discomfort, psychological distress, burdensome medical treatments, functional decline and mortality; and can also impose a remarkable economic burden.(106,108) Further, at each transition, the chance of miscommunication or the lack hereof between various care providers exists. In such cases, the wishes and preferences of patients for their care might not be congruent with the care they receive, and medical errors may also occur due to discontinuity of care.(109,110) GPs also consider hospitalisation at the end of life inappropriate and/or potentially-avoidable in about 20% of non-sudden deaths in Belgium and about 25% of deaths in the Netherlands.(111–113) The previously-identified lack of communication with patients with dementia regarding their wishes and preferences might have contributed to this problem, which underscores another reason why the communication with patients needs to be enhanced. Other issues, such as problems in communication between healthcare professionals and an inability to provide continuous high-quality palliative care in the home setting, might have also contributed to this finding, which may thus need to be addressed as well.(106,107)

Effects of palliative care interventions for older people with dementia living at home

Findings from the systematic review suggest the potential benefits of palliative home care interventions in improving behavioural symptoms and enhancing pain assessment in older people with dementia living at home (Chapter 5). These findings are consistent with earlier studies (114,115) and address key issues in dementia care that have also been identified throughout this dissertation.(101,116,117) Healthcare professionals are often uncertain how to support people with dementia whose behaviours they find challenging.(118) Managing behavioural symptoms and assessing pain are not only important for patients with dementia, but it may also contribute to reducing the burden of family carers who are central to enabling patients to stay at home for as long as possible.(40,119)

While this systematic review suggests patient care benefits of palliative home care interventions in dementia, the identified evidence base is insufficient and generally too weak to robustly assess their effects. As explained in detail in the Introduction section of this dissertation, this paucity of evidence may stem from the fact that conducting traditional experimental studies, such as RCTs in this context is difficult due to ethical, legal and practical concerns. In response, we evaluated the effects of palliative home care support on the quality and costs of end of life care for older people with dementia living at home (Chapter 6). We used linked routinely-collected nationwide administrative databases and decedent cohort study design with a high-quality matching on the propensity of receiving an intervention, which can be considered as the best possible alternative to emulate the aspects of an RCT. To measure the outcome of this palliative home care support on the quality of end of life care, we used a set of quality indicators specifically validated for people with dementia.(31)

Findings from this evaluation study showed that compared with those who did not receive palliative home care support, those who received it had better quality of end-of-life care in the last 14 days of life. In particular, we found that people with dementia who used palliative home care support had lower risk of receiving inappropriate medications (e.g. anti-hypertensives, calcium or vitamin D), undergoing surgery and being hospitalised; had considerably more contacts with healthcare professionals in primary care; and had a higher chance of dying at home. These findings concur with an earlier study suggesting similar positive effects of palliative home care support for a general palliative care population and with other previous studies focused on palliative home care interventions in dementia.(120,121) Nonetheless, to our knowledge, ours is the first to confirm such positive findings for older people with dementia living at home. A causal relationship between palliative home care support use and better quality of end-of-life care is highly plausible given that palliative care is aimed at improving the quality of life of patients and families facing problems associated with life-threatening illness, through prevention and relief of physical, psychosocial and spiritual suffering.(122) It also uses a multidisciplinary team approach, facilitating active care coordination between all involved caregivers, which contributes to enabling patients to stay at home for as long as possible and to preventing unnecessary hospital admissions.(1) Further, eliciting patient preferences is an essential part of palliative care, making it more likely that patient preferences are taken into account when end-of-life care treatment decisions are made.(1) Finally, findings from this study showed that palliative home care support reduced total direct medical costs of care in the last month of life in older people with dementia. This also confirms previous findings suggesting that palliative home care can reduce resource use and estimated costs.(120,121)

Building a strong evidence base on effective palliative home care interventions in dementia

To further build a strong evidence-base on effective palliative home care interventions in dementia, findings from this dissertation identified a number of crucial aspects that should be taken into account during the development and evaluation of such interventions. ***First***, despite the benefits of palliative home care support in improving quality and reducing total costs of end-of-life care in dementia, it is concerning that three out of four people with dementia who could potentially use palliative home care support did not do so, and of those who did use it, one in three received it for the first time only within 14 days of death (Chapter 6). This finding concurs with widespread reports of suboptimal access to palliative care for people with dementia.(101,116,123) Potentially, GPs in Belgium, who like in many countries are gatekeepers for initiating palliative home care support, are not always aware that palliative care is appropriate for people living with dementia or are reluctant to initiate conversations on palliative care due to its connotation with dying.(124,125) Considering the protracted and unpredictable disease trajectory of dementia,(1,7) it is also difficult, even for GPs, to identify when certain palliative care support measures might be appropriate, further hindering access.(28,126) Interestingly, about one in three of those persons with dementia who received palliative home care support died of cancer. Hence, having cancer might have been an important 'trigger' to initiating such support rather than the fact that the person who do not have dementia, which further highlights the difficulty of accessing such support for those with dementia but has no cancer. It is therefore important to identify strategies and identification tools that could improve the timely access to palliative home care of older people with dementia.

Second, the identified palliative home care interventions in dementia in the systematic review most frequently addressed optimal symptom management, continuity of care and psychosocial support, which reflect clinician priorities and the core values of palliative care, irrespective of diagnosis.(122) However, another priority for people with dementia, such as 'person-centred care, communication and shared-decision-making' was only modestly addressed by the interventions. This is surprising when some of the most influential writing on person-centred care is situated in the dementia literature.(127) The studies failed to map according to 'applicability of palliative care' and 'societal/ethical issues' even though this is a patient population that is increasing but poorly understood by commissioners and policymakers and stigmatised in society.(128) Other palliative care in dementia domains that were under-represented in the evidence reviewed: prognostication and timely recognition of dying, avoidance of overly aggressive, burdensome or futile treatments and setting of care goals and advance care planning are similarly problematic areas in dementia care. For instance, despite the fact that most older people prefer to die at home,(104) there may still be a substantial proportion of older people with dementia dying in hospitals,(117) which is likely to occur if the palliative phase is not promptly recognised. Also, progressive cognitive decline is inherent in advanced dementia, which hinders the communication between healthcare providers and people with dementia.(7) The hospital deaths and suboptimal communication between healthcare professionals and patient have also been observed as a persistent issue in Chapter 4.

Third, it is notable that only one of the identified interventions in the systematic review offered additional support to address the emotional and psychological needs of family carers. The family carers of people with dementia, who are critical part of the equation, often lack emotional support, disease education and care for their own health and medical care needs.(129,130) Of the strong predictors for institutionalisation of older people with dementia, family caregiver burden is the only factor that is modifiable to healthcare interventions.(40,119,131) Promoting well-being of family carers is therefore important not only for themselves but also for enabling older people with dementia to stay at home for as long as possible.(40,132)

Fourth, evidence on cost-effectiveness is also scarce. Whilst some studies reported resource use, it was solely based on estimated costs while disregarding health benefits. ***Fifth***, none of the identified evaluation studies of palliative home care interventions in the systematic review provided a detailed description of how the complex interventions have been developed, and none had embedded a process evaluation. ***Sixth***, most of the identified evaluation studies in the systematic review were also appraised to have weak quality in part due to their inability to measure/report intervention integrity, which has been found as a persistent issue in clinical trials in palliative care.(133) ***Finally***, the systematic review also showed a lack of consensus on the outcomes used, which limited comparisons and meta-analysis; thus, hindering the continuous building of evidence on the effects of palliative home care interventions in dementia. Important end of life care outcomes according to literature, such as patient death at home and quality of life were also not consistently measured.(104,122)

1.4. Implications of this dissertation

RECOMMENDATIONS FOR PRACTICE

1) *Increase the timely access to palliative care for nursing home residents with dementia*

A generalist palliative care approach in the nursing home setting, such as the approach that PACE Steps to Success aimed to implement, is a promising way forward to increase the timely access to palliative care of nursing home residents dying with dementia (Figure 1). This would mean that for all residents, regardless of whether or not they are dying or are in their final months of life, a palliative care approach focusing on residents' quality of life, and their needs and preferences, including a focus on resident's families, is a suitable approach for nursing homes. Such an approach would be innately complementary to a high-quality dementia care approach, which also focuses on person-centred care, optimal symptom management, psychosocial and spiritual support, advance care planning, continuity of care, multidisciplinary collaborations, education and support of healthcare professionals, and support and bereavement counselling for family carers.(1,122)

The involvement of specialist palliative care services might also be important, particularly in times when the care needs of patients or their families become too complex for the general care providers in nursing homes. Such collaborative practice might result in reciprocal sharing of knowledge and skills, and in the long run, this might further improve the capabilities of generalist palliative care providers in delivering complex palliative care services in dementia. Of course, the operationalisation of such a generic model might differ between countries, depending on the care services available and accessible for this setting, but overall, enhancing collaboration between palliative care, nursing home care, and dementia care, and between nursing home, hospitals and/or home care settings seems crucial for the future.

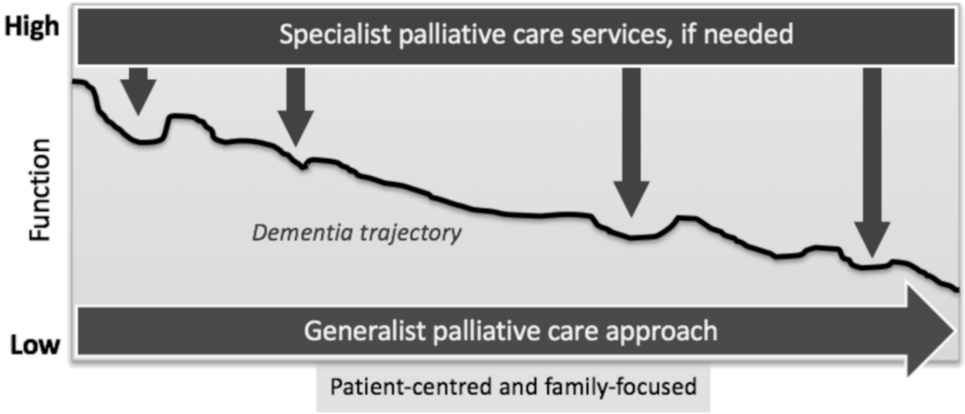

Figure 1. A model for timely integration of palliative care for nursing home residents, including those with dementia (Adapted from Van den Block's plenary presentation - Alzheimer Europe Conference (2017))(134)

2) ***Promote comfort at the end of life of nursing home residents with dementia***

Findings from this dissertation revealed no improvement in total comfort at the end of life in a growing number of residents who died with dementia between 2010 and 2015, and this is a cause for concern. To ultimately improve comfort at the end of life of residents with dementia, this dissertation emphasises the need to continue exerting more efforts to comprehensively assess and manage physical, psychosocial and spiritual care needs that commonly occur in this population by improving their access to medical/nursing care services, psychosocial interventions and spiritual support. (1,84,135,136) Further, while we found an encouraging improvement in pain assessment that needs to be set forth, we must exert more efforts in optimally managing pain. For effective pain management in dementia, earlier studies recommend the importance of multidisciplinary collaboration between healthcare and palliative care professionals, such as nursing home staff, GPs or physicians and specialist palliative care services.(50,137) While non-pharmacological management programmes have been tested predominantly in younger populations without dementia, many of them have been proven to be relatively safe and effective.(50) Literature therefore suggests that they deserve a first place in pain management guidelines.(50)

Second, there is an urgent need for physicians, and especially nursing home staff, to be aware that developing pneumonia likely involves substantial discomfort in all, regardless of the presence and severity of dementia.(138) While this finding may not be surprising,(139) it is remarkable that despite numerous efforts to improve end-of-life care in nursing home, pneumonia still seems to cause considerable suffering. Providing those who are dying with symptom-relieving treatments such as antipyretics, opioids or oxygen may promote comfort and relieve suffering.(67) Nonetheless, it should be considered that there is a myriad of potential causes of pneumonia and there may be no single approach to address related discomfort.(139)

Third, although intake problems may not be associated with comfort in residents with advanced dementia, if such problems are present, it remains essential to consider rigorous clinical assessment to exclude acute conditions (e.g. stroke) and to address easily-reversible causes (e.g. dental problems).(140) High-calorie supplements and other oral feeding options can also be offered to this population as an alternative to tube feeding.(141) Further, while we found that intake problems may be associated with discomfort in residents with non-advanced and no dementia, the evidence base to guide clinicians about artificial nutrition and hydration is still limited.(140,142) Overall, clinicians can address intake problems after careful assessment and consideration of different options as guided by the goals of care that should be discussed where possible with the resident who is dying and those close to them.(140,142)

3) *Improve the access to and quality of palliative care for older people with dementia living at home*

Considering the identified benefits of palliative home care support for older people with dementia living at home, the low and late uptake of this support in this population highlights an urgent need to increase the timely access to palliative home care support for older people with dementia. While we still lack evidence on how to effectively increase their timely access to this kind of support, there are strategies that might contribute to achieving this, such as the active screening or case-finding of people with dementia in primary care using pre-defined criteria based on patient needs and preferences rather than prognosis alone to 'trigger' the initiation of palliative home care support; raising awareness about the benefits of palliative care in dementia among primary care and secondary care professionals involved in dementia care; improving professionals' communication skills to introduce such sensitive topics; and introducing financial or other incentives to increase uptake.(4,7,31).

To improve the quality of palliative care for older people with dementia, this dissertation highlights the importance of enhancing multidisciplinary collaborations to promote collaborative practice and reciprocal sharing of knowledge, expertise and information between GPs, palliative home care teams, community nurses and other healthcare professionals in primary and secondary care (e.g. physiotherapists, geriatricians, psychologists or neurologists). Such multidisciplinary collaboration can also contribute to improving the comprehensiveness of care delivered to older people with dementia living at home.(90) However, compared with the nursing home setting, facilitating multidisciplinary collaboration is more challenging in the home setting. One potential reason is the geographical challenge, in which one partner may need to collaborate with other partners who are not in the same location.(143) It therefore takes more time and effort to collaborate, and it becomes more challenging especially when the financing of care services does not encourage such activity, for instance if care services are being paid per patient/case. Advancements in digital communication technology, such as virtual team meetings that are being used widely during the COVID-19 crisis,(144–146) offer a promising solution to enhance multidisciplinary collaborations between healthcare providers in the home setting in the future. Nevertheless, the standard use of such technology in palliative care in dementia needs further research to determine how to tackle ethical dilemmas related to privacy and security.(147)

In addition, pain assessment has been identified as a room for improvement for older people with dementia living at home.(1,50) Accurate assessment of pain due to inherent issues in dementia is a challenging endeavour.(93) When self-reporting is not possible due to cognitive decline inherent in dementia, direct observation of behavioural cues can be used to assess pain (i.e. vocalisations, facial expressions and body movements).(96) Because pain has been related to behavioural disturbances, such as agitation and aggression, healthcare professionals may misinterpret these symptoms as neuropsychiatric symptoms of dementia. Hence, a differential assessment of dementia, its presenting neuropsychiatric symptoms and the potential presence of pain are crucial to provide the correct treatment. To achieve this, the use of pain assessment tools that are responsive to change and are validated for use in dementia is a prerequisite,(96) such as the Pain Assessment in Advanced Dementia (PAINAD) scale.(148,149) The implementation of standardised pain assessments adapted to the cognitive abilities of patients may foster the pain recognition, warrant optimal pain management, reduce inadequate pain medication to optimally raise the chance of equally effective pain treatment regardless of dementia diagnosis.(58)

The inclusion and communication with family and family carers is important in palliative care in dementia.(1,150) The identified high relative-GP communication in Chapter 4 is thus encouraging. Nevertheless, findings from this dissertation also suggest the critical need to improve communication with older people with non-advanced and advanced dementia. Many patient organisations have overlapping recommendations for successful verbal and non-verbal communication with people with varying stages of dementia, all of which emphasise that it is highly important and possible to communicate with these people, even when their cognitive capacities have diminished.(151–154) It is also imperative to not make assumptions about a person’s ability to communicate based on the mere diagnosis of dementia or old age, as there are individual variations in their symptoms and clinical course. Shared-decision making is crucial in health and care practice and is also recognised as an integral component of person-centred care, which has been found to be valued highly by people with dementia.(155) Advance care planning (ACP) discussions is also an opportunity to establish patients’ values and preferences about their future care and to make this known for their family, family carers and healthcare professionals, in the event that patients are no longer able to express these values and preferences. ACP has been associated with improved outcomes in people with dementia, such as decreased hospitalisations and increased concordance between care received and prior wishes.(156) Finally, reducing potentially-avoidable hospitalisations in dementia is another room for improvement identified in this dissertation. As older people with dementia are encouraged to stay at home for as long as possible, measures should be taken to reduce potentially-avoidable hospitalisations in this setting; though more research is needed to identify effective interventions to do so.(105)

4) *Educate and train existing and future health and social care professionals about palliative care for older people with dementia*

Health and social care professionals working in the nursing home and home settings have a major role to play in identifying and managing the palliative care needs of older people with dementia. If they are to carry out these roles effectively, they need continuous education and training to provide them with a wide range of up-to-date skills and knowledge related to palliative care in dementia.(157–159) This can be done by incorporating crucial topics related to palliative care in dementia either through continuing professional education or trainings for existing professionals or through the educational curriculum of students, aspiring to become healthcare professionals in the future (e.g. nurses, physiotherapist, or physicians). While this recommendation in itself is not unique, this dissertation underscores the need to repeat and further emphasise it in order to better integrate a comprehensive palliative care approach in the knowledge and skills of care professionals. Findings from this dissertation also highlight some aspects where this education and training can focus on, which may include the benefits of palliative care in dementia, the specific symptoms and disease trajectory of dementia, the importance of comprehensive care encompassing physical, psychosocial and spiritual support, multidisciplinary collaboration, optimal symptom assessment and management (including pain and the associated with misconceptions, pneumonia and intake problems), communication with patients, potentially-avoidable hospitalisations, and supporting family carers. Doing this will increase their awareness of the importance of palliative care services in dementia, the basic knowledge and skills on how to deliver palliative care to this population, and the negative impact that poor or late access to these services can have on older people with dementia and their family carers. Dementia-specific trainings for specialist palliative care services working in both the home and nursing home settings can also contribute to improving the quality of and access to optimal palliative care of older people with dementia, especially in times when their care needs become too complex to be managed by other healthcare professionals.

5) *Strengthen support services for family carers of older people with dementia*

Comprehensive management of older people with dementia requires the building of partnership between healthcare professionals and family carers. Family carers of older people with dementia are critical to providing care to maintain or improve the quality of life of care recipients, especially of those living at home.(160) While being a family carer is worthwhile for many people, as it encompasses personal accomplishment and strengthens relationships, family caregiving can also be challenging and could be emotionally and physically burdensome.(160–162) A person with dementia may be a parent or spouse who has been known, loved and respected, and for their family carers, it may be difficult to watch them functionally and cognitively deteriorate. In the advanced stages of dementia, there may be physical problems, such as the inability to perform activities of daily living or incontinence. Due to behavioural disturbances, a person with dementia may also seem ungrateful and might be aggressive, which can be hurtful for the carer. Consequently, family caregiving has been associated with caregiver burden, physical or psychological morbidity, social isolation, and financial hardships.(162) It is therefore important to strengthen support services for family carers of older people with dementia, especially of those living at home.(150,163) It is also crucial to identify family carers who are vulnerable to adverse effects, as well as factors that can ameliorate or exacerbate caregiver burden or strain, so that these factors can also be addressed.(150,163,164)

6) *Facilitate optimal transition of older people with dementia from home to a nursing home*

We also identified that despite growing policy efforts to enable older people with dementia to live at home for as long as possible, the prevalence of dementia in nursing homes remains increasing. These findings imply that for some older people with dementia, a transfer to a nursing home is inevitable, which is a common occurrence among older people. However, transitions from home to a nursing home can be experienced as emotionally burdensome by older people and their family carers.(165) These experiences might be compounded when the transition is poorly coordinated and fragmented.(166,167) For older people, a transfer to a nursing home entails a sudden change in identity associated with changes in autonomy, daily routine, social status and contacts,(168–170) while family carers may be confronted with feelings of grief, loneliness, guilt and failure.(171–173) Facilitating optimal transition from home to a nursing home is therefore crucial for older people with dementia. This can be done by comprehensively addressing the challenges before, during and after transitions, for instance by providing advice in deciding about the nursing home transfer, by offering assistance during the transfer, and through ad hoc and post hoc counselling. However, to date, there remains a lack of high-quality evidence on the what optimal transition from home to a nursing home entails (e.g. best possible timing) for older people with dementia, and on effective interventions that could effectively facilitate such transition in this population.(174,175)

RECOMMENDATIONS FOR FUTURE RESEARCH

1) *Develop and evaluate a generalist palliative care intervention for nursing homes that takes the specific care needs of residents with dementia into account*

Although PACE Steps to Success clearly needs further improvement, its apparent positive effects on quality of care and dying and its medical cost-saving potential showed that this generalist non-disease-specific palliative care programme can be a useful starting point for future improvement in palliative care in nursing homes.(3,81) Despite efforts to enable older people with dementia to stay at home for as long possible, this dissertation also showed that the prevalence of dementia in nursing homes apparently remains increasing. Future developments of such a generalist palliative care intervention in nursing homes should therefore take into account dementia as an important subgroup. As end-of-life symptoms in dementia might be very specific compared with other diseases, a strong collaboration among experts in research and practice in palliative care and dementia seems important.(82,84)

Further, the primary analyses of the PACE cluster-RCT cited several factors that might explain why PACE Steps to Success did not achieve its desired outcome – better comfort at the end of life. These factors include the content of the intervention itself, the quality of its implementation, a possible mismatch between the intervention and the primary outcome, or the combination of these factors.(3) Addressing these factors during future development and evaluation phases of such generalist palliative care programmes might help in improving residents' comfort at the end of life. ***First***, we need to investigate whether we should focus on developing a more targeted intervention to treat dying symptoms, or if we can find the right balance to offer comprehensive care while effectively managing dying symptoms in residents with and without dementia. ***Second***, while the PACE cluster-RCT and another comparable palliative care trial in the US showed that it is feasible to conduct such complex trials in the nursing home setting,(3,176) implementing new palliative care programmes in this setting remains challenging due to barriers, such as those relating to residents (e.g. complex care needs), staff (e.g. high workload or staff turnover and low level of education) or organisations (e.g. funding or resources).(87,177) For optimal implementation of future generalist palliative care programmes in the complex nursing home setting, it might help to find some inspiration from implementation science. For example, the Promoting Action on Research Implementation in Health Services (PARiHS) framework proposes that a balance is crucial between the evidence incorporated within a new intervention, the context in which it is implemented and the degree of facilitation provided.(178–180) Similarly, the Extended Normalisation Process Theory and ecological theory highlight the need to obtain a good understanding of all factors – at the levels of patients, families, nursing home staff, nursing homes up to health systems – that could affect the implementation and outcomes of new interventions, and to identify the role played by the context in which the implementation process is situated, so that these can be taken into account in developing and evaluating such interventions.(181–184) Finally, the process evaluation embedded in the PACE cluster-RCT recommends to allow some flexibility for implementers to tailor both the content and implementation strategy (e.g. timing) of a new intervention, so that it can adapt to the local context.(87) ***Third***, while RCTs remain the gold standard for evaluating complex interventions, it remains important to recognise the substantial potential of other evaluation methods, such as participatory action research that intentionally and equitably engages researchers and stakeholders in all aspects of the research process, including decision-making, capacity building, knowledge generation and dissemination of findings.(185) If a trial has been chosen to evaluate such a generalist palliative care intervention, it is crucial to follow the formal rules for planning and conducting subgroup analysis based on the presence and severity of dementia during the conceptualisation phase of the trial, for instance by calculating power based on the pre-specified subgroups.(186,187)

2) *Develop and evaluate palliative care interventions for older people with dementia living at home*

Developers of palliative home care interventions in dementia should continue addressing the core values of palliative care irrespective of diagnosis (such as optimal symptom management, continuity of care and psychosocial support). They should also incorporate the principles of palliative care that are important in dementia (such as person-centred care and communication and decision-making); and address specific areas that remain problematic for this population (such as applicability of palliative care, societal/ethical issues, prognostication and timely recognition of dying, avoidance of overly aggressive, burdensome or futile treatments and setting of care goals and advance care planning). Further, these interventions should include components that could address the persistent issues in palliative care for older people with dementia living at home identified in Chapters 4 and 5, such as pain assessment and management, communication with patients and reduction of potentially-avoidable hospitalisations, as well as the emotional and psychological needs of family carers. To incorporate these important domains into a palliative home care intervention in dementia, a strong collaboration between experts in palliative care and dementia care in research and practice may also be required.

It is also worthwhile to explore whether and how other innovative interventions beyond palliative care can be useful for improving palliative home care in dementia. A good example is the Care Ecosystem developed in the US, which is a telephone-based collaborative dementia care intervention delivered by a trained care team navigator, who provides education, support and care coordination with a team of dementia specialist, including advanced practice nurse, social worker and pharmacist.(188) It has been recently tested in a single-blind randomised clinical trial and was found effective in improving the quality of life of patients, reducing emergency department visits and decreasing caregiver depression.(189) Its acceptability and potential adaptability is currently being studied in Flanders, Belgium,(190) and it is interesting to investigate whether palliative home care services can be incorporated in this dementia-specific intervention.

In evaluating such palliative home care interventions in dementia, it is also essential to embed a process evaluation and cost-effectiveness analysis – as has been widely recommended by acknowledged research institutes, such as the Medical Research Council (MRC). Process evaluation is an integral part of designing and evaluating complex interventions such as palliative care interventions, and performing it in accordance with the MRC guidance would allow the critical exploration of factors and causal mechanisms that could explain variations in observed outcomes.(191) Performing concurrent cost-effectiveness analysis using existing guidance could provide a better view of interventions that could potentially yield the greatest improvement in dementia care for the least resources.(192)

Finally, it is advisable to transparently provide a detailed description of the rationale, decision-making processes, and methods on how the intervention has been developed.(193) We can enhance the reporting of both the interventions and their evaluation using standard reporting tools, e.g. Template for Intervention Description and Replication (TIDIER) checklist and guide and Consolidated Standards of Reporting Trials (CONSORT) statement.(193–196) With the transparency of providing more information on how an intervention has been developed and of assessing how it has been implemented during an evaluation study, scientific rigour will be improved. Doing this also opens up the ‘black box’ of future intervention studies in palliative home care interventions in dementia, so that developers can learn from each other’s experiences and together, we can build a stronger evidence-base on this important topic, a strategy that we have also used in the PACE cluster-RCT.

3) *Develop a core outcome set for evaluating palliative care interventions for older people with dementia living at home*

Based on existing evidence and consultations with people with dementia and care partners, Harding and colleagues (2020) developed a core set of 13 outcomes for non-pharmacological community-based interventions for people with dementia living at home.(197,198) A core outcome set is defined as “*an agreed standardised set of outcomes that should be measured and reported, as a minimum, in all clinical trials in specific areas of health or healthcare*”.(199) Examples of the 13 outcomes included in the core outcome set are ‘meaningful activities’, ‘personal hygiene and cleanliness’, ‘communication’, ‘falls’, ‘feeling safe or secure’ and ‘feeling valued or respected by others’.(197) However, as this core outcome set is more related to social health, it is important to further explore the extent to which these outcomes would be relevant and applicable in evaluating palliative care interventions for older people with dementia living at home. A guideline on how to develop such core outcome sets exist, such as the handbook developed by the Core Outcome Measures in Effectiveness Trials (COMET) initiative, which has also been used by Harding and colleagues.(197) The COMET initiative aims to guide the development of core outcome sets by using existing evidence and bringing together relevant key stakeholders, including patients and healthcare professionals.(199,200)

RECOMMENDATIONS FOR POLICY

1) *Make palliative care for older people with dementia a public health priority*

The lack of preventive or curative treatment for dementia now and in the foreseeable future implies that a fast-growing number of older people with dementia will live and die with complex care needs that would require palliative care. Promoting timely access to palliative care in dementia is important, as about half of the people with dementia die before they reach the advanced stage. Hence, in line with the strong advocacy of the World Health Organisation to make dementia a global health priority and its recognition that palliative care is a global health issue,(201,202) evidence from this dissertation also recommends to make palliative care in dementia a public health priority and to integrate palliative care in dementia policies. Such explicit expression of commitment by national or regional governments for better palliative care in dementia can provide the structure and resources that could stimulate and facilitate initiatives and research efforts to contribute to improving palliative care for older people with dementia.

2) *Support initiatives that aim to improve the quality of and access to palliative care services of older people with dementia*

Evidence from this dissertation points that the quality of palliative care in dementia is progressing, albeit slowly, towards the right direction. There is therefore an urgent need to keep this momentum and to exert more intensive efforts, so that we can move forward in a faster pace. Providing care to a fast-growing number of older people with dementia is a highly demanding and complex work for both the family carers and health and social care professionals. To promote comfort at the end of life in a growing number of residents with dementia and to improve the quality of palliative care for older people with dementia living at home, continued and stronger public health investments are vital to deliver a more comprehensive palliative care in dementia approach in this sector.(1,203) Long-term, continuous and consistent implementation of a comprehensive palliative care in dementia approach requires a strong national and regional policy commitment.(201) Besides structural and financial support, it is also crucial to continue in explicitly showing appreciation for the hard work invested by family carers, healthcare and social care professionals and organisations in delivering comprehensive palliative care to older people with dementia.(150,204)

3) *Allocate research funding to stimulate the development and evaluation of high-quality, cost-effective and accessible palliative care interventions in dementia*

In the last seven years, there have been an increasing policy commitment with a concomitant increase in research funding to improve palliative care for people with dementia living in nursing homes and at home.(16,85,205–208) Such studies and trials aiming to improve palliative care for people with dementia would not have been possible without the engagement of international and national policymakers and funding agencies. As the need to improve palliative care in dementia persists as a growing public health issue, there is a critical need to continue allocating research funding to stimulate further development and evaluation of high-quality, cost-effective and accessible palliative care interventions for older people with dementia.

4) ***Boost national public awareness campaigns regarding the applicability and benefits of palliative care for older people with dementia***

To ultimately improve the quality of life of older people with dementia, it is imperative to instil a mind shift among patients and their families, healthcare professionals, policymakers and the general public from "*recognizing palliative care as an alternative to life-prolonging treatments*" to "*promoting palliative care as a complementary approach that can be offered alongside life-prolonging treatments*" through national public awareness campaigns.(1,123,209,210) We also need to spread the word that palliative care is not only about dying but also in living well until death, as well as to highlight the benefits of palliative care for older people with dementia.(211) National public awareness campaigns on palliative care in dementia should be located within the framework of wider public health promotion campaigns, and there should be a synergy between short national mass media campaigns and longer term, more sustained local community action initiatives.(212) Campaign messaging and modalities should also be designed specifically for people with dementia, ideally by involving them and other relevant stakeholders in the process.(201,213) By boosting this kind of national public awareness campaigns, we can provide correct knowledge on palliative care in dementia and promote a mind shift aiming to address the associated misconceptions and stigma, which can stimulate the timely access to existing palliative care services of older people with dementia and their family.(212,214–216)

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English Summary

INTRODUCTION

The world's populations continue to age. Because old age is the strongest known risk factor for dementia, the prevalence of dementia has also been projected to increase to about 131.5 million worldwide and to about 18.8 million in Europe by 2050. Dementia is recognised as a progressive, incurable condition, and the fast-growing number of older people affected by this condition experience multi-faceted physical, psychosocial and spiritual care needs that persist for months or years until death. Living and dying with dementia therefore significantly and primarily affects older people with dementia and their families, including those people close to them. Further, because providing care to older people with dementia is a highly demanding and complex work, dementia also affects family carers, healthcare professionals, communities, healthcare systems and societies worldwide. Dementia also has far-reaching ramifications to economies in terms of direct medical, social and informal care costs. In 2015, the global cost of dementia was estimated at about US$818 billion, and the highest economic burden was incurred in high-income countries, such as the countries in Europe, North America and Australia.

To date, there were consistent reports that the care needs of older people with dementia often remain unmet, and thus many of them still live with distressing symptoms and problems and die with discomfort. Due to the incurable nature of dementia combined with the associated multi-faceted care needs, a palliative care approach has been advocated widely for older people with dementia. 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, whether physical, psychosocial or spiritual*". A growing body of evidence consistently showed that palliative care could improve the symptom burden and quality of life in adults with incurable conditions. Yet, there remains a paucity of high-quality evidence on palliative care for older people with dementia, especially in the nursing home and home settings where they often live, receive care and die.

Over the past decade, there have been important policy developments related to dementia and palliative care in the nursing home sector in many countries, which might have influenced which people die in nursing homes and how they die, and can impact the provision of palliative care for nursing home residents with dementia. However, there is a lack of high-quality data on the number of residents dying in nursing homes with varying stages of dementia, the extent to which they use palliative care services, and their comfort at the end of life, and how these are changing over time. Furthermore, while discomfort at the end of life of residents with dementia has been associated with the occurrence of clinical events, such as pneumonia or intake problems, little is known on how such clinical events are associated with comfort at the end of life of residents with varying stages of dementia, and if such associations are different from those without dementia. Moreover, to contribute high-quality evidence to improve palliative care for nursing home residents, of whom a large proportion have dementia, we developed 'PACE Steps to Success' and evaluated it using a cluster-randomised controlled trial (RCT). PACE Steps to Success is a multicomponent programme aiming to integrate generalist and non-disease-specific palliative care into nursing homes in six steps using a train-the-trainer approach. This programme did not improve residents' comfort in the last week of life, but it appeared to improve quality of care and dying in their last month of life. Nevertheless, because this programme was designed for all residents and included only three dementia-specific elements, we hypothesised a priori that its effects might differ between those with and without dementia in favour of those with mild/moderate or no dementia compared with advanced dementia. Hence, at the outset of the PACE cluster-RCT, we planned to investigate whether the effects of PACE Steps to Success on comfort at the end of life and quality and care dying differ between residents with advanced, non-advanced and without dementia.

With regard to palliative care for older people with dementia living at home, there were earlier reports suggesting poor quality and access to palliative care for this population. However, no study has yet systematically measured the quality of primary palliative care for older people with mild and severe dementia living at home. Finally, existing evidences underscore the very limited evidence on the effects of palliative care interventions for older people with dementia living at home.

RESEARCH AIMS

To address these research gaps, the aim of this dissertation was two-fold. First, focusing on nursing home residents with dementia, we aimed to describe how many people with dementia die in nursing homes, how these residents die in relation to their palliative care service use and comfort in the last week of life, and if there were changes over time, as well as to evaluate whether a generalist palliative care programme for nursing homes affects comfort at the end of life and quality of care and dying of residents with dementia differently than those without dementia. Second, focused on older people with dementia living at home, we aimed to describe the current quality of primary palliative care and the current evidence on palliative home care interventions, as well as to evaluate the effects of palliative home care support on quality and costs of end of life care in Belgium.

METHODS

Multiple study designs and research methods were used. Research aim 1 was addressed using three studies in nursing homes, which include two comparable retrospective epidemiological studies (namely the Dying Well with Dementia study conducted in 2010 in Flanders, Belgium and the PACE study conducted in 2015 in six European countries, including Flanders, Belgium) and the PACE cluster-RCT in seven European countries (Part I of this dissertation). Research aim 2 was addressed using a mortality follow-back study using existing epidemiological surveillance system (i.e. the Sentinel Networks of General Practitioners in Belgium, Italy and Spain), a systematic review of interventions and a nationwide propensity score-matched decedent cohort study using routinely-collected nationwide administrative databases (Part II of this dissertation).

MAIN FINDINGS

The first three Chapters focused on palliative care for nursing home residents with dementia (**Research Aim 1 – PART I**) In **Chapter 1**, we examined the differences between 2010 and 2015 in the prevalence and characteristics of residents with dementia in nursing homes in Flanders and their palliative care service use and comfort in the last week of life. We found a 15%-point increase in dementia prevalence, with almost no change in residents' clinical and demographic characteristics. At the end of life, there was an increase in the use of pain assessment, but in both years, between 37% and 52% of residents neither received psychosocial intervention nor spiritual care. We found no change in residents' total comfort at the end of life. In **Chapter 2**, we investigated the occurrence rates of clinical events in the last month of life and their associations with comfort in the last week of life of nursing home residents with advanced, non-advanced and no dementia in six EU countries. We found that about a quarter of nursing home residents developed pneumonia across the three resident groups. Overall, developing pneumonia and intake problems was associated with less comfort, but this varied according to the presence and severity of dementia. Less comfort was observed in residents with advanced, non-advanced and no dementia who developed pneumonia. Among residents who developed intake problems, less comfort was observed only in residents with non-advanced dementia and no dementia. In **Chapter 3**, we assessed whether the effects of PACE Steps to Success palliative care programme on comfort in the last week of life and quality of care and dying in the last month of life differ between residents with advanced, non-advanced, and no dementia in seven European countries. We found that the effects of PACE Steps to Success on both outcomes did not differ between the three subgroups.

The following Chapters focused on palliative care for older people with dementia living at home (**Research Aim 2 – PART II**). In **Chapter 4**, we systematically investigated the overall quality of primary palliative care for older people with dementia in Belgium, Italy and Spain using a validated core set of quality indicators. Quality indicator scores in Belgium were higher than Italy, but not appreciably higher than Spain. Nevertheless, they have similar opportunities for improvement, such as pain assessment, communication with GPs and reduction of potentially-avoidable hospitalisations. In **Chapter 5**, we systematically reviewed the international evidence on specialist and non-specialist palliative home care interventions in dementia. The evidence, albeit of generally weak quality, showed the potential benefits of the interventions in improving end of life care outcomes, e.g. behavioural disturbances. The interventions most commonly focused on optimal symptom management, continuity of care and psychosocial support. Other palliative care domains that were previously identified as important for people with dementia, such as prognostication of dying or avoidance of burdensome interventions, were under-reported. No direct evidence on facilitators and barriers to implementation was found. In **Chapter 6**, we aimed to fill some of the gaps related to the lack of evidence on the effects of palliative care in dementia. In this study, we found that palliative home care use by home-dwelling older people with dementia is associated with improved quality and reduced costs of end-of-life care.

DISCUSSION OF MAIN FINDINGS

PART I: Palliative care for nursing home residents with dementia

Three main findings from this dissertation suggest the increasing demand for palliative care to promote comfort at the end of life of nursing home residents with dementia, and this is in spite of the growing number of policies that support older people with dementia to stay at home for as long as possible. First, between 2010 and 2015, there was a substantially higher prevalence of dementia in nursing homes. Second, their demographic and clinical characteristics of residents with dementia remained almost similar, which implies that their complex care needs seem to persist over the years. Third, the total comfort in the last week of life of residents with dementia did not change between 2010 and 2015. To promote comfort at the end of life of residents with dementia, this dissertation suggests the need for a more comprehensive palliative care approach encompassing physical, psychosocial and spiritual support and the need to address the major clinical events that were found to be associated with discomfort at the end of their life, such as pneumonia and intake problems. Finally, contrary to our hypothesis for the subgroup analysis of the PACE cluster-RCT, we found that the stepwise training of nursing home staff through the PACE Steps to Success palliative care programme was not sufficient to improve comfort in the final days of life in residents without dementia, nor in those with different stages of dementia. This study confirmed the negative results of the primary trial analyses on comfort at the end of life. Nevertheless, for the secondary outcome, our analyses showed that this programme improved quality of care and dying in the last month of life equally for those with dementia (regardless of the stage) and those without dementia. Although this finding needs to be interpreted cautiously as this is a secondary outcome and the effect is only medium-sized, they are remarkable, as this palliative care programme only had a limited number of dementia-specific elements as part of the training. The primary analyses combined with the process evaluation of the PACE cluster-RCT discussed a number of potential factors that can explain why PACE Steps to Success did not affect the primary outcome – comfort at the end of life. These factors include 1) the content of the intervention itself, 2) the quality of its implementation in several nursing homes, 3) a possible mismatch between the intervention and the primary outcome, or 4) a combination of these factors. In order to improve palliative care for residents with dementia, future development and evaluation of such palliative care interventions in nursing homes should target these factors while taking the specific care needs of people with dementia into account.

PART II: Palliative care for older people with dementia living at home

Findings from this dissertation also bring light to aspects of palliative care where improvements can be made for older people with dementia living at home. First, we argue that incorporating palliative care in national or regional policies with a concomitant increase in resources, especially for older people with dementia, and enhancing multidisciplinary collaboration among GPs, palliative home care teams and other healthcare networks seem imperative in improving the quality of palliative care for older people with varying stages of dementia who live at home. Second, we identified similar opportunities for improvement in primary palliative care in dementia, including pain assessment, communication with patients, and prevention of avoidable hospitalisations. Findings from the systematic review suggest the potential benefits of palliative home care interventions in improving behavioural symptoms and enhancing pain assessment in older people with dementia living at home. However, the identified evidence base is insufficient and generally too weak to robustly assess their effects. Hence, we evaluated palliative home care support for older people with dementia living at home. We found that while it improves quality and reduces total direct medical costs of end-of-life care, the uptake is low and late. To further build a strong evidence base on palliative home care interventions in dementia, seven crucial points have been discussed, which for example include the need for timely access to this kind of interventions and for a comprehensive approach to address the specific care needs of older people with dementia and their family.

IMPLICATIONS OF THIS DISSERTATION

This dissertation offers ***six recommendations for practice***, which include: 1) Increase the timely access to palliative care for nursing home residents with dementia; 2) Promote comfort at the end of life of nursing home residents with dementia; 3) Improve the access to and quality of palliative care for older people with dementia living at home; 4) Educate and train existing and future health and social care professionals about palliative care for older people with dementia; 5) Strengthen support services for family carers of older people with dementia; 6) Facilitate optimal transition of older people with dementia from home to a nursing home. It also offers ***three recommendations for future research***, which include: 1) Develop and evaluate a generalist palliative care intervention for nursing homes that takes the specific care needs of residents with dementia into account; 2) Develop and evaluate palliative care interventions for older people with dementia living at home; and 3) Develop a core outcome set for evaluating palliative care interventions for older people with dementia living at home. Finally, ***four recommendations for policy*** have been provided, including: 1) Make palliative care for older people with dementia a public health priority; 2) Support initiatives that aim to improve the quality of and access to palliative care services of older people with dementia; 3) Allocate research funding to stimulate the development and evaluation of high-quality, cost-effective and accessible palliative care interventions in dementia; 4) Boost national public awareness campaigns regarding the applicability and benefits of palliative care for older people with dementia.

Nederlandse Samenvatting

INLEIDING

De wereldbevolking is aan het vergrijzen. Omdat ouderdom, voor zover bekend, de sterkste risicofactor voor dementie is, zal de prevalentie van dementie naar verwachting ook toenemen en tegen 2050 stijgen tot ongeveer 131,5 miljoen wereldwijd en tot ongeveer 18,8 miljoen in Europa. Dementie wordt erkend als een progressieve, ongeneeslijke aandoening. Het snelgroeiende aantal ouderen dat aan deze aandoening lijdt, krijgt te maken met veelzijdige lichamelijke, psychosociale en spirituele zorgbehoeften die maanden of jaren aanhouden tot aan het overlijden. Leven en sterven met dementie treft daarom in belangrijke mate vooral ouderen met dementie en hun familieleden, met inbegrip van de mensen uit hun naaste omgeving. Omdat de zorg voor ouderen met dementie zeer veeleisend en complex is, heeft dementie ook gevolgen voor mantelzorgers, gezondheidswerkers, gemeenschappen, gezondheidszorgsystemen en samenlevingen over de hele wereld. Dementie heeft ook verstrekkende gevolgen voor de economie in termen van directe medische, sociale en informele zorgkosten. In 2015 werden de wereldwijde kosten van dementie geschat op ongeveer 818 miljard US$, en de grootste economische last werd geleden in hoge inkomenslanden, zoals de landen in Europa, Noord-Amerika en Australië.

Tot op heden was er consistent bewijs dat de zorgnoden van ouderen met dementie vaak onvervuld blijven, waardoor velen van hen nog steeds met schrijnende symptomen en problemen leven en met ongemak overlijden. Vanwege de ongeneeslijke aard van dementie en de veelzijdige zorgbehoeften van personen die aan de aandoening lijden, is op grote schaal gepleit voor een palliatieve zorgbenadering voor ouderen met dementie. Volgens de definitie van de Wereld Gezondheidsorganisatie is palliatieve zorg "*een benadering die de levenskwaliteit verbetert van patiënten en hun familie die geconfronteerd worden met het probleem van een levensbedreigende ziekte, door het voorkomen en verlichten van het lijden door middel van vroegtijdige identificatie en onberispelijke beoordeling en behandeling van pijn en andere problemen, zowel lichamelijke, psychosociale als spirituele*". Er is steeds meer bewijs dat aantoont dat palliatieve zorg de last van symptomen en de levenskwaliteit van volwassenen met ongeneeslijke ziekten kan verbeteren. Toch is er nog steeds een gebrek aan kwalitatief hoogstaande gegevens over palliatieve zorg voor ouderen met dementie, met name in de woonzorgcentra en in de thuissituatie waar zij vaak wonen, zorg ontvangen en sterven.

In het afgelopen decennium zijn er in veel landen belangrijke beleidsontwikkelingen geweest met betrekking tot dementie en palliatieve zorg in de sector van de woonzorgcentra, die mogelijk van invloed kunnen zijn geweest op wie in woonzorgcentra sterven en hoe zij sterven en die van invloed kunnen zijn op het verlenen van palliatieve zorg aan bewoners met dementie. Er is echter een gebrek aan gegevens van hoge kwaliteit over het aantal bewoners met verschillende stadia van dementie die sterven in woonzorgcentra, de mate waarin zij gebruik maken van palliatieve zorg, hun comfort aan het levenseinde, en de evolutie hierin overheen de tijd. Terwijl comfort aan het levenseinde van bewoners met dementie in verband is gebracht met het optreden van klinische gebeurtenissen, zoals longontsteking of problemen met opname van vocht en voeding, is er weinig bekend over hoe dergelijke klinische gebeurtenissen geassocieerd zijn met comfort aan het levenseinde van bewoners met verschillende stadia van dementie en of dergelijke associaties verschillend zijn voor bewoners met of zonder dementie.

Om bij te dragen aan de verbetering van palliatieve zorg voor bewoners van woonzorgcentra, van wie een groot deel dementie heeft, hebben wij de 'PACE Steps to Success' interventie ontwikkeld en geëvalueerd met behulp van een cluster-gerandomiseerde gecontroleerde trial (cluster RCT). PACE Steps to Success is een programma bestaande uit verschillende componenten, dat gericht is op het integreren van generalistische palliatieve zorg in woonzorgcentra in zes stappen met behulp van een train-de-trainer aanpak. De cluster RCT heeft aangetoond dat dit programma het comfort van de bewoners in de laatste week van hun leven niet verbetert, maar het leek de kwaliteit van zorg en sterven wel te verbeteren. Omdat dit programma voor alle bewoners was ontworpen en slechts drie dementie-specifieke elementen bevatte, veronderstelden wij van tevoren dat de effecten ervan zouden kunnen verschillen voor bewoners met en zonder dementie, in het voordeel van bewoners met milde/matige of geen dementie in vergelijking met gevorderde dementie. Daarom waren wij bij aanvang van de PACE cluster-RCT van plan te onderzoeken of de effecten van PACE Steps to Success op het comfort aan het levenseinde, de kwaliteit van zorg en sterven verschillen voor bewoners met gevorderde, niet-gevorderde en zonder dementie.

Wat betreft palliatieve zorg voor thuiswonende ouderen met dementie waren er eerdere rapporten die duiden op een slechte kwaliteit en toegang tot palliatieve zorg voor deze populatie. Desalniettemin is er nog geen enkele studie die systematisch de kwaliteit van de eerstelijns palliatieve zorg voor thuiswonende ouderen met milde en ernstige dementie heeft gemeten. Ten slotte onderstrepen de bestaande gegevens het zeer beperkte bewijs van de effecten van palliatieve zorginterventies voor thuiswonende ouderen met dementie.

ONDERZOEKSDOELEN

Om deze hiaten in de kennis op te vullen, was het doel van dit proefschrift tweeledig. Ten eerste, waarin we ons richten op bewoners van woonzorgcentra met dementie, wilden we beschrijven hoeveel mensen met dementie sterven in woonzorgcentra, hoe deze bewoners sterven in relatie tot hun gebruik van palliatieve zorg en comfort in de laatste week van het leven, en of er veranderingen waren in de loop van de tijd, alsmede te evalueren of een generalistisch palliatief zorgprogramma voor woonzorgcentra het comfort aan het levenseinde en de kwaliteit van zorg en overlijden van bewoners met dementie anders beïnvloedt dan bij bewoners zonder dementie. Ten tweede, waarin we ons richten op thuiswonende ouderen met dementie, wilden we de huidige kwaliteit van de eerstelijns palliatieve zorg en het huidige bewijsmateriaal over palliatieve thuiszorginterventies voor personen met dementie beschrijven, alsmede de effecten van palliatieve thuiszorgondersteuning op de kwaliteit en de kosten van de zorg rond het levenseinde in België beoordelen.

METHODEN

Er werden meerdere studieopzetten en onderzoeksmethoden gebruikt. Onderzoeksdoel 1 werd aangepakt met behulp van drie studies in woonzorgcentra, waaronder twee vergelijkbare retrospectieve epidemiologische studies (namelijk de Dying Well with Dementia-studie uitgevoerd in 2010 in Vlaanderen en de PACE-studie uitgevoerd in 2015 in zes Europese landen, waaronder België (Vlaanderen)) en de PACE cluster-RCT in zeven

Europese landen (Deel I van dit proefschrift). Onderzoeksdoel 2 werd aangepakt met behulp van een mortaliteitsopvolgingsstudie gebruikmakend van bestaande epidemiologische surveillancesystemen (d.w.z. de Sentinel Netwerken van huisartsen in België, Italië en Spanje), een systematische review van interventies en een landelijke propensity score-matched cohortstudie van overledenen gebruikmakend van routinematig verzamelde landelijke administratieve databanken (Deel II van dit proefschrift).

BELANGRIJKSTE BEVINDINGEN

De eerste drie hoofdstukken focusten op palliatieve zorg voor bewoners van woonzorgcentra met dementie (**Onderzoeksdoel 1 - DEEL I**). In **Hoofdstuk 1** onderzochten we de verschillen tussen 2010 en 2015 in de prevalentie en kenmerken van bewoners met dementie in woonzorgcentra in Vlaanderen en hun gebruik van palliatieve zorgdiensten en comfort in de laatste week van het leven. We vonden een toename van 15%-punt in de prevalentie van dementie, met bijna geen verandering in de klinische en demografische kenmerken van de bewoners. Aan het einde van het leven was er een toename in het gebruik van pijnbeoordeling, maar in beide jaren kreeg tussen 37% en 52% van de bewoners geen enkele psychosociale interventie, noch spirituele zorg. We vonden geen verandering in het totale comfort van de bewoners aan het einde van het leven. In **Hoofdstuk 2** onderzochten we het voorkomen van klinische gebeurtenissen in de laatste maand van het leven en de associaties met comfort in de laatste week van het leven van bewoners van woonzorgcentra met gevorderde, niet-gevorderde en geen dementie in zes EU landen. We ontdekten dat ongeveer een kwart van de bewoners (in de drie groepen) een longontsteking had ontwikkeld. In het algemeen ging de ontwikkeling van een longontsteking en problemen met de opname van vocht en voeding gepaard met minder comfort, maar dit varieerde naargelang de aanwezigheid en de ernst van de dementie. Er werd minder comfort waargenomen bij bewoners met gevorderde, niet-gevorderde en zonder dementie die een longontsteking ontwikkelden. Bij bewoners die problemen hadden met de opname van vocht en voeding werd alleen minder comfort waargenomen bij bewoners met niet-gevorderde dementie en zonder dementie. In **Hoofdstuk 3** onderzochten we of de effecten van het PACE Steps to Success palliatieve zorgprogramma op comfort in de laatste levensweek en kwaliteit van zorg en sterven in de laatste levensmaand verschillen tussen bewoners met gevorderde, niet-gevorderde, en geen dementie. De effecten van het PACE Steps to Success programma op beide uitkomsten verschilden niet tussen de drie subgroepen.

De volgende hoofdstukken richtten zich op palliatieve zorg voor thuiswonende ouderen met dementie (**Onderzoeksdoel 2 - DEEL II**). In **Hoofdstuk 4** onderzochten we systematisch de algemene kwaliteit van palliatieve zorg in de eerste lijn voor ouderen met dementie in België, Italië en Spanje met behulp van een gevalideerde kernset van kwaliteitsindicatoren. De scores op de kwaliteitsindicatoren waren in België hoger dan in Italië, maar niet significant hoger dan in Spanje. Desondanks hebben de drie landen vergelijkbare mogelijkheden voor verbetering, zoals pijnbeoordeling, communicatie met huisartsen en vermindering van potentieel vermijdbare ziekenhuisopnames. In **Hoofdstuk 5** hebben we systematisch het internationale bewijsmateriaal over gespecialiseerde en niet-gespecialiseerde palliatieve thuiszorginterventies bij dementie beoordeeld. Het bewijs, hoewel over het algemeen van zwakke kwaliteit, toonde de potentiële voordelen van de interventies voor het verbeteren van de levenseinde uitkomsten, bijvoorbeeld gedragsstoornissen. De interventies waren het meest gericht op optimale symptoombestrijding, continuïteit van zorg en psychosociale ondersteuning. Andere domeinen van palliatieve zorg die eerder als belangrijk werden beschouwd voor mensen met dementie, zoals prognosticatie van het sterven of het vermijden van belastende interventies, waren ondervertegenwoordigd. Er werd geen direct bewijs gevonden wat betreft facilitatoren en barrières voor implementatie van de interventies. In **Hoofdstuk 6** hebben we getracht enkele van de hiaten op te vullen die samenhangen met het gebrek aan bewijs over de effecten van palliatieve zorg bij dementie. In deze studie vonden we dat palliatieve thuiszorg voor thuiswonende ouderen met dementie geassocieerd is met een verbeterde kwaliteit en lagere kosten van zorg aan het einde van het leven.

BESPREKING VAN DE BELANGRIJKSTE BEVINDINGEN

DEEL I: Palliatieve zorg voor ouderen met dementie in woonzorgcentra

Drie belangrijke bevindingen uit dit proefschrift wijzen op de toenemende vraag naar palliatieve zorg om het comfort aan het einde van het leven van ouderen met dementie die in woonzorgcentra wonen te bevorderen, ondanks het groeiende aantal beleidsmaatregelen die ouderen met dementie ondersteunen om zo lang mogelijk thuis te blijven wonen. Ten eerste was er een aanzienlijk hogere prevalantie van dementie in woonzorgcentra in 2015 in vergelijking met 2010. Ten tweede bleven de demografische en klinische kenmerken van bewoners met dementie vrijwel gelijk, wat impliceert dat hun complexe zorgbehoeften in de loop der jaren lijken te blijven bestaan. Ten derde veranderde het totale comfort in de laatste week van het leven van bewoners met dementie niet significant tussen 2010 en 2015. Om het comfort aan het einde van het leven van bewoners met dementie te bevorderen, suggereert dit proefschrift de behoefte aan een meer omvattende palliatieve zorgbenadering die fysieke, psychosociale en spirituele ondersteuning omvat en de behoefte om de belangrijkste klinische gebeurtenissen aan te pakken die geassocieerd bleken te zijn met ongemak aan het einde van hun leven, zoals longontstekingen en problemen met opname van vocht en voeding. Ten slotte vonden wij, in tegenstelling tot onze hypothese voor de subgroep analyse van de PACE cluster-RCT, dat de stapsgewijze training van personeel van woonzorgcentra via het PACE Steps to Success palliatieve zorgprogramma niet voldoende was om het comfort in de laatste levensdagen te verbeteren bij bewoners met- of zonder dementie. Deze studie bevestigde de negatieve resultaten van de analyses op de primaire uitkomst van de trial, namelijk comfort aan het einde van het leven. Voor de secundaire uitkomst van de trial toonden onze analyses niettemin aan dat dit programma de kwaliteit van de zorg en het sterven in de laatste levensmaand in gelijke mate verbeterde bij bewoners met dementie (ongeacht het stadium) en bij bewoners zonder dementie. Hoewel deze bevinding voorzichtig geïnterpreteerd moet worden aangezien dit een secundaire uitkomst is en het effect slechts middelgroot is, is het toch opmerkelijk aangezien dit palliatieve zorgprogramma slechts een beperkt aantal dementie-specifieke elementen bevatte als onderdeel van de opleiding. De primaire analyses in combinatie met de procesevaluatie van de PACE cluster-RCT wezen op een aantal potentiële factoren die kunnen verklaren waarom PACE Steps to Success geen effect had op de primaire uitkomst - comfort aan het einde van het leven. Deze factoren zijn onder andere 1) de inhoud van de interventie zelf, 2) de kwaliteit van de implementatie van de interventie in verschillende woonzorgcentra, 3) een mogelijke mismatch tussen de interventie en de primaire uitkomst, of 4) een combinatie van deze factoren. Om de palliatieve zorg voor bewoners met dementie te verbeteren, moet de ontwikkeling en evaluatie van dergelijke palliatieve zorginterventies in woonzorgcentra in de toekomst gericht zijn op deze factoren, terwijl rekening moet worden gehouden met de specifieke zorgbehoeften van mensen met dementie.

DEEL II: Palliatieve zorg voor thuiswonende ouderen met dementie

De bevindingen uit dit proefschrift werpen ook licht op aspecten van palliatieve zorg waar verbeteringen kunnen worden aangebracht voor thuiswonende ouderen met dementie. Ten eerste stellen wij dat het opnemen van palliatieve zorg in nationaal of regionaal beleid met een gelijktijdige toename van middelen, vooral voor ouderen met dementie, en het verbeteren van multidisciplinaire samenwerking tussen huisartsen, palliatieve thuiszorgteams en andere zorgnetwerken noodzakelijk lijkt om de kwaliteit van palliatieve zorg te verbeteren voor deze populatie. Ten tweede identificeerden we vergelijkbare mogelijkheden voor verbetering in de eerstelijns palliatieve zorg bij dementie, waaronder pijnbeoordeling, communicatie met patiënten en voorkomen van vermijdbare ziekenhuisopnames. De bevindingen van de systematische review suggereren de potentiële voordelen van palliatieve thuiszorginterventies voor het verbeteren van gedragssymptomen en het verbeteren van de pijnbeoordeling bij thuiswonende ouderen met dementie. Echter, het gevonden bewijs is onvoldoende en over het algemeen te zwak om de effecten ervan robuust te beoordelen. Daarom hebben wij vervolgens in een retrospectieve cohortstudie de palliatieve thuiszorgondersteuning voor thuiswonende ouderen met dementie geëvalueerd. We ontdekten dat deze ondersteuning weliswaar de kwaliteit van de zorg verbetert en de totale directe medische kosten van de zorg aan het levenseinde verlaagt, maar dat het gebruik ervan laag is en de inzet te laat komt. Om verder te bouwen aan een sterke empirische basis voor palliatieve thuiszorginterventies bij dementie zijn zeven cruciale punten besproken, waaronder bijvoorbeeld de noodzaak van tijdige toegang tot dit soort interventies en van een alomvattende aanpak om tegemoet te komen aan de specifieke zorgbehoeften van oudere mensen met dementie en hun familie.

IMPLICATIES VAN DIT PROEFSCHRIFT

Dit proefschrift biedt ***zes aanbevelingen voor de praktijk***, waaronder: 1) Verhoog de tijdige toegang tot palliatieve zorg voor bewoners in woonzorgcentra met dementie; 2) Bevorder comfort aan het levenseinde van bewoners met dementie; 3) Verbeter de toegang tot en de kwaliteit van palliatieve zorg voor thuiswonende ouderen met dementie; 4) Train bestaande en toekomstige gezondheids- en sociale zorgverleners, op het gebied van palliatieve zorg voor ouderen met dementie; 5) Versterk de ondersteunende diensten voor mantelzorgers van ouderen met dementie; 6) Zorg voor optimale transitie van ouderen met dementie van thuis naar een woonzorgcentrum.

Dit proefschrift biedt ook ***drie aanbevelingen voor toekomstig onderzoek***, waaronder: 1) Ontwikkel en evalueer een generalistische palliatieve zorginterventie voor woonzorgcentra die rekening houdt met de specifieke zorgbehoeften van bewoners met dementie; 2) Ontwikkel en evalueer palliatieve zorginterventies voor thuiswonende ouderen met dementie; en 3) Ontwikkel een kernset van uitkomstmaten voor het evalueren van palliatieve zorginterventies voor thuiswonende ouderen met dementie.

Tenslotte zijn er ***vier aanbevelingen voor beleid***, waaronder: 1) Maak van palliatieve zorg voor ouderen met dementie een prioriteit op het gebied van volksgezondheid; 2) Ondersteun initiatieven die gericht zijn op het verbeteren van de kwaliteit van en toegang tot palliatieve zorgdiensten voor ouderen met dementie; 3) Wijs onderzoeksfinanciering toe om de ontwikkeling en evaluatie van kwalitatief hoogwaardige, kosteneffectieve en toegankelijke palliatieve zorginterventies bij dementie te stimuleren; 4) Stimuleer nationale bewustwordingscampagnes met betrekking tot de toepasbaarheid en voordelen van palliatieve zorg voor ouderen met dementie.

Curriculum vitae

Rose Miranda (°1986) has a Bachelor's degree in Nursing from the Philippines. She also has an Honour's Bachelor in Health Science and a Research Master in Global Health degrees from VU University Amsterdam, the Netherlands. While studying in Amsterdam, she also worked as a nursing aid for older people, including older people with dementia, who were living in the community. After completing her Research Master's degree, she started as an Early Stage Researcher within the Interdisciplinary Network for Dementia Using Current Technology (INDUCT), a prestigious and highly-competitive European Union-funded Marie-Skłodowska Curie Actions Innovative Training Network. As a part of INDUCT, Rose joined the End-of-Life Care Research Group (VUB-UGhent) in 2016 as a PhD researcher, working on several national and international research projects that include older people with dementia. During her PhD, Rose also completed a six-month research secondment at the University of Hertfordshire in the United Kingdom. Rose was supervised by Prof. Dr. Tinne Smets, Prof. Dr. Nele Van Den Noortgate, and Prof. Dr. Lieve Van den Block. All findings reported and discussed in her dissertation were published in international high-impact journals and presented in renowned national and international conferences, primarily in the domains of palliative care and dementia.

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