Introduction
INTRODUCTION

The study presented in this thesis is about reducing discomfort and distressing symptoms in nursing home residents with dementia and pneumonia. This general introduction outlines the context of an intervention study in the Netherlands and provides background on the setting, dementia and pneumonia, care and treatment, and the study’s methods and outcome measures, after which the objectives and an outline of the thesis are provided.

The impact of dementia

Dementia is a progressive disease characterized by a gradual impairment of mental functions which may include loss of memory, disorientation, personality change, difficulties with activities of daily living, and neuropsychiatric symptoms. Dementia is not a part of normal ageing, but a disease caused by different underlying etiologies. The most common subtypes of dementia are Alzheimer dementia (50-75%), vascular dementia (20-30%), frontotemporal dementia (5-10%) and dementia with Lewy bodies (<5%). However, mixed pathologies, mostly Alzheimer dementia in combination with vascular dementia may occur even more frequently than pure forms, especially at older ages.

Dementia mainly affects older people. Only in a minority of cases the dementia onset is before the age of 65. As the disease progresses, people with dementia become more and more susceptible to infections, which often induce distressing symptoms. Moreover, problems with intake of food and drinks and swallowing difficulties often occur, posing patients at an increased risk of aspiration pneumonia. Dementia is associated with a reduced life expectancy. The disease presents a burden, not only for patients but also for their family and caregivers, who are forced to participate as proxy decision makers in complex (medical) decisions for their loved ones who are no longer capable of doing so for themselves.

The number of people with dementia in the Netherlands was estimated to be over 260.000 in 2014. The latest estimations of worldwide dementia prevalence indicate that 46.8 million of people were living with dementia in 2015, which is expected to almost double every 20 years to 74.7 million in 2030 and 131.5 million in 2050, with the largest increase in developing countries. Estimations of these numbers are based on extrapolations of current incidence rates. Recent cohort studies in western countries have suggested declining trends in dementia frequency, although findings are inconsistent even within Europe. Considering the serious impact on disability, the high prevalence of the disease, and the burden for all involved, dementia has significant consequences. For that reason it has been described as a public health priority.
Nursing homes in the Netherlands

In the first stages of dementia many people live at home, but most people are admitted to a nursing home at some point in their disease course. A nursing home is a place of residence for people requiring continuous care and help with activities of daily living. Of the approximately 65,000 people currently residing in Dutch nursing homes, 43% has dementia. In nursing homes, patients with dementia often stay at so called psychogeriatric units, and the large majority of patients on these units have dementia. The Dutch nursing home setting is distinct from other countries with regard to the presence of elderly care physicians, who are on the staff and are the ones responsible for treatments and care provided to the nursing home residents, after having followed a three-year specialist training. Elderly care medicine is a distinct medical specialty in the Netherlands which has emerged from nursing home medicine and community geriatric medicine. In most other countries, people who reside in nursing homes receive care provided by the general practitioner, or by hospital specialists, e.g. geriatricians.

Dementia, palliative care and comfort

Estimations of median survival times from the onset of dementia symptoms range from 3.3 to 11.7 years. Large variations between studies may be explained by differences in age, and by variable definitions of dementia onset. Anyhow, excess mortality was present for patients with dementia compared with matched controls without dementia. Dementia is a life-limiting disease, as there is no curative treatment for dementia foreseen in the near future. Palliative care is regarded appropriate, but there is still little evidence on the efficacy of palliative care approaches.

The WHO defines 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, physical, psycho-social and spiritual.” Considering life-expectation, palliative care certainly applies to patients in the more advanced stages of dementia, but may be relevant as well in earlier stages. Nonetheless, opinions regarding the time point of starting palliative care for a patient with dementia vary among health care professionals.

More than a decade ago, a novel model for palliative care in older people was presented by Lynn and Adamson, displaying that disease modifying, “curative care” and symptom management “palliative care” may co-exist, while the proportion between the two shifts over time as patients are nearing death (Figure 1a). However, in contrast to other life-limiting diseases such as cancer, the disease trajectory of dementia is characterized by a slow and gradual decline, and disabilities as a result of the
dementia may persist for years. Lynn and Adamson’s model may fit a trajectory of steady progression, but for dementia patients there is need for a more specific model providing alternatives for curative or palliative care only. A white paper on palliative care in dementia published on behalf of the European Association for Palliative Care (EAPC), identified eleven domains, with 57 recommendations for palliative care and a model of changing care goals and priorities throughout the course of dementia (Figure 1b). This model shows that a focus on quality of life, and the initiation of treatment of intercurrent illnesses that may prolong life are not mutually exclusive.

Maximization of comfort is one of the main possible care goals for patients with dementia in this model. The concept of comfort has been defined by Kolcaba as the immediate state of being strengthened through having the human needs for relief, ease, and transcendence addressed in four contexts of experience (physical, psychospiritual, sociocultural, and environmental). In the most advanced stages of dementia, a treatment goal primarily aimed at comfort is appropriate, while for patients with moderate dementia prolongation of life may still be at issue, although maximizing comfort and maintaining of function often dominate.

Figure 1: a. “trajectory” model of palliative care (Lynn et al. 2003) and b. model of changing care goals (van der Steen et al. 2014).
In the Netherlands, the Dutch association of elderly care physicians and social geriatricians “Verenso” formulated four distinct care goals for patients with dementia: 1) a curative goal, 2) a rehabilitative goal, 3) a palliative goal and 4) a symptomatic goal. A palliative care goal and a symptomatic care goal are both aimed primarily at safeguarding optimal wellbeing and an acceptable quality of life of the patient with dementia. These goals are achieved by: treatment of other complaints, co-morbidity, symptoms and complications resulting from the dementia. However, for a palliative care goal, extending life as a potential side effect of this treatment is not contraindicated – or is even part of the care goal. In contrast, for a symptomatic care goal, a life-extending side-effect as a result of medical treatment aimed at this goal is undesirable. 33

Dementia and pneumonia

Care goals provide guidance when patients with dementia develop burdensome complications such as a (suspected) pneumonia. 4, 34 In a general nursing home population, reported pneumonia incidence rates range from 0.3 to 2.5 per 1000 patient days. 35-37 The large range in pneumonia incidence may be explained by differences in the study design, setting, and population. For example, patients with more severe dementia have a higher probability of developing a pneumonia, which may have an immediate impact on incidence-rates. Also, diagnostic criteria for pneumonia differ, and in clinical practice, X-ray or laboratory examination for biomarkers are rarely performed so that estimations are often based on pneumonia as most probable clinical diagnosis. Along with cardiovascular disorders, and dehydration/cachexia, pneumonia is an important cause of death in (Dutch) patients with dementia. 38-40 Death certificate studies and autopsy reports indicate that from patients dying with dementia up to 66% had a pneumonia reported. 40-42

While addressing the subject of pneumonia in older people, sir William Osler’s view on pneumonia in older people – “The old man’s best friend” – is often cited. 43 Remarkably, only a few years before this statement, Osler argued that pneumonia should be regarded “the special enemy of old age”. 44 At Osler’s time, at the end of the 19th century, there was no cure for infections, and Osler thoughtful reasoned that although death from pneumonia affects many, it also offers a rather swift and seemingly painless end of a life that is often already of poor quality. From this point of view, the pneumonia was a welcome way out of suffering. Some still think that pneumonia is to be welcomed as a friend in older people, as it may result in a peaceful and painless death. However, times have changed, and nowadays, we know much more about the assessment of discomfort and symptoms, and about treatment options; and even more important, there is the option of antibiotic treatment.
Treatment with antibiotics

For the treatment of an infection, antibiotics are the default option. However, prevalence of antibiotic use in dementia patients varies across countries and settings, and the decision whether or not antibiotics should be prescribed is complicated. Namely, treatment is strongly related to the degree of diagnostic (un)certain. and to the patient’s care goal, and cultural and ethical issues apply.[45] Moreover, from a public health point of view, the emergence of antibiotic resistance may be considered when deciding about antibiotic treatment.[46,47]

The majority of patients with dementia and pneumonia, in both Dutch and US studies (77-91%) receive antibiotics.[48,49] Nonetheless, there are many questions to be answered about the role of antibiotics in the treatment of pneumonia in patients with dementia. For example, it has been suggested that in patients with advanced dementia, antibiotics prolong the dying process, rather than extend life.[50,51] Furthermore, there is still ambiguity about whether antibiotics may relieve symptoms of pneumonia. Although antibiotics are in some cases prescribed with a palliative intent, the actual effects on improving comfort are unknown.[52,53] Altogether, deciding about treatments for patients with dementia and pneumonia, whether aimed at curing the infection, or at symptom relief, is not as straightforward as we may wish.

Pneumonia and symptom burden

Pneumonia in patients with dementia has been associated with severe symptom burden especially before death. For example, among a sample of Dutch dementia patients who died from respiratory infections (81% had pneumonia) shortness of breath was present in 78% of patients, and 50% were agitated compared to respectively 23% and 31% in patients for whom dehydration/cachexia was the cause of death.[54] Also, pain may be an issue, whether or not directly caused by the infection i.e. pleuritic chest pain, or pain as a result of coughing. It presented in 50% of patients dying from respiratory infection, compared to 52% for patients with dehydration/cachexia and 40% for cardiovascular disease. Moreover, it is suggested that patients with dementia (irrespective of the pneumonia) are of high risk of underestimation of pain.[55] Symptom burden for patients with pneumonia may be affected by various internal or external factors. For example, suffering may be reduced while patients are asleep or unconscious.

Observing discomfort in dementia and pneumonia

Pain and pneumonia symptoms likely involve discomfort, which may be defined as a negative emotional and/or physical state, subject to variation in magnitude in re-
ponse to internal or environmental conditions. Hurley et al. developed a tool to systematically assess discomfort on a nine-item scale (range 0-27) during five minutes of observation: the Discomfort Scale – Dementia of Alzheimer Type (DS-DAT). This instrument enables researchers and clinicians to assess discomfort in patients with dementia with various conditions and under multiple circumstances. Subsequently, the DS-DAT has been used to compare discomfort in patients with dementia during a fever episode after a palliative or aggressive treatment approach.

The Dutch Pneumonia Study, conducted in 61 Dutch nursing homes in the late 1990’s, applied the DS-DAT to examine to what extent patients with dementia experienced discomfort when they had developed a pneumonia. In that study, patients were observed by the attending physicians, who knew the patients well. Observations were performed at the moment of the treatment decision, after three and ten days, and after one and three months. Although no cut-off value for discomfort has been established on the DS-DAT, levels at above eight are suggested to indicate discomfort. With this threshold in mind, patients with dementia and pneumonia experienced discomfort, which peaked at the moment of the treatment decision and dropped until the level before the onset of the pneumonia in about ten days. Discomfort was also high for patients who died from the pneumonia, and this was even higher than for patients dying from other causes.

Relieving discomfort and symptoms

The treatment of pneumonia in populations other than patients with dementia mainly focuses on cure of the infection and may include aggressive approaches such as intravenous antibiotics, artificial rehydration and hospitalization. In literature focusing on symptom relief as part of palliative care, recommendations on treatment of symptoms associated with intercurrent illnesses such as pneumonia are mostly lacking. Last years, there seems to have been a trend towards an increased focus on symptom relief, and palliative care. For example, a comparison between the Dutch Pneumonia study and a smaller sample study also conducted in the Netherlands, showed that more treatments to relieve symptoms were provided for patients with dementia and pneumonia in 2006-2007 compared to 1996-1998. Nevertheless, the effect on comfort remains unknown. Evidence on effectiveness of interventions to relieve symptoms specifically for patients with dementia and pneumonia is still lacking. Furthermore, no studies yet used evidence based guidelines to intervene in discomfort for these patients. Intervening into usual care may result in even more adequate symptom relief and thereby improve patient outcomes.
Objectives of the study

The primary objective of this study is to assess the effectiveness of an intervention for optimal symptom relief, and of antibiotics on discomfort, (lack of) comfort, pain, and shortness of breath – referred to in this thesis as ‘discomfort and symptoms’, or ‘suffering’ – and to assess effects on the level of sleepiness and survival in patients with dementia and pneumonia. To provide more context, we investigate the prevalence of antibiotic use in dementia patients and the factors that are associated with antibiotic use in literature.

Design and main features of the methods

To address the primary objective, a multicenter single-blinded cluster randomized controlled trial was conducted on psychogeriatric wards of 32 Dutch nursing homes. The trial assessed the effects of an intervention for optimal symptom relief that was developed using a Delphi study with a multidisciplinary and international expert panel.

The trial design covered a pre-intervention phase, and an intervention phase to allow for adjustment for possible time-related changes in the outcomes (Figure 2). In the pre-intervention phase, physicians included patients with dementia and pneumonia, and provided care as usual while observations of discomfort and symptoms were performed. After assignment of a nursing home to either the control or the intervention group, the intervention phase started. Control homes continued to provide care as usual, and the intervention to relieve pneumonia symptoms was implemented in the intervention homes. It was also planned to intervene with antibiotics for patients with a palliative care goal in the intervention group during the last period of the intervention phase (Figure 2), only if data collected in the pre-intervention phase would confirm greater comfort for patients treated with antibiotics than for those treated without antibiotics as found previously in the observational pneumonia study.59

Figure 2: Design of the study.
Throughout the two phases of the 3.5-year data collection of the study, physicians included patients with a clinical diagnosis of pneumonia. Subsequently, physicians provided details on antibiotic treatment, and treatments to relieve pneumonia symptoms, on the patients’ health condition, and on survival. Starting directly after pneumonia diagnosis until 14 days later, almost daily observations of discomfort and symptoms, and sleepiness were performed by observers who were unaware of the patients’ condition, treatments and the intervention. Four validated observational instruments were applied to assess discomfort, (lack of) comfort, pain and shortness of breath, which were developed specifically for patients unable to communicate themselves.

The characteristics and quality of the implementation, as well as barriers for using the intervention were addressed in a mixed methods process evaluation, using data collected in qualitative interviews and closed-ended questionnaires.

Outline of the thesis

Chapter 2 presents a systematic literature review about the use of antibiotics in patients with dementia, describing the prevalence of antibiotic use, and factors associated with prescribing or withholding antibiotics in patients with dementia, in various care settings and countries.

Chapter 3 provides a description of the course of discomfort, (lack of) comfort, pain and shortness of breath from the diagnosis of pneumonia, until death or cure within 14 days, using data collected in the first, pre-intervention phase of the study. Furthermore, this chapter describes differences between patients who were, and who were not treated with antibiotics, and between patients who were observed awake or asleep.

The intervention to enhance comfort in this study was a practice guideline for optimal symptom relief. Chapter 4 provides a detailed description of the development of this practice guideline using a Delphi study, and describes conceptual issues encountered during the developmental process.

Chapter 5 concerns the effects of the practice guideline for optimal symptom relief on reducing the level of discomfort, (lack of) comfort, and the symptoms pain and shortness of breath in the fourteen days following the diagnosis of pneumonia, and also addresses differences in the level of the outcomes that occurred over time (during the study period).

Chapter 6 provides the results of a process evaluation that was conducted in parallel to the trial, to examine the implementation of the practice guideline, intervention quality, and barriers the physicians encountered using the guideline in the intervention nursing homes.
Chapter 7 is a general discussion of the results described in this thesis, in which overall strengths and limitations of the study are discussed. Further, the discussion reflects upon the results of the study, and describes implications of the study for both research and clinical practice.
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