Pharmacological treatment and assessment of symptoms at the end of life in European nursing homes

Marc Tanghe

UNIVERSITEIT GENT

VUB VRIJE UNIVERSITEIT BRUSSEL

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Marc Tanghe

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Supervisors:

Ruth Piers, MD, PhD; Lieve Van den Block, PhD;

Nele Van Den Noortgate, MD, PhD; Luc Deliens PhD

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Supervisors

Prof. dr. Ruth Piers

Faculty of Medicine and Health Sciences, Ghent University

Department of Geriatric Medicine, Ghent University Hospital

Prof. dr. Lieve Van den Block

End-of-Life Care Research Group,

Department of Family Medicine and Chronic Care, Vrije Universiteit Brussel

Prof. dr. Nele Van Den Noortgate

Faculty of Medicine and Health Sciences, Ghent University

Department of Geriatric Medicine, Ghent University Hospital

Prof. dr. Luc Deliens

End-of-Life Care Research Group

Department of Family Medicine and Chronic care, Vrije Universiteit Brussel

Department of Public Health and Primary Care, Universiteit Gent

Examination committee

Chair

Prof. Dr. Ernst Rietzschel

Faculty of Medicine and Health Sciences, Ghent University

Members of the jury

Prof. dr. Yvonne Engels

Department of Anesthesiology, Pain, Palliative Medicine, Radboud UMC, Nijmegen

Prof. dr. Tinne Dilles

Department of Nursing and Midwifery Sciences, Universiteit Antwerpen

Prof. dr. Dirk Devroey

Dean of the Faculty of Medicine and Pharmacy, Vrije Universiteit Brussel (VUB)

Prof. dr. Anja Velghe

Faculty of Medicine and Health Sciences, Ghent University

Prof. dr. Peter Pype

Faculty of Medicine and Health Sciences, Ghent University

Prof dr. Thierry Christiaens

Department of Clinical Pharmacology, Ghent University

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«Il nous faut des sages-femmes pour mettre les gens au monde,

et des hommes-encore-plus-sages pour les aider à le quitter.»

«phrase-cadeau» van dr C Torck, naar Michel de Montaigne

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List of abbreviations

BANS S	**B**edford **A**lzheimer **N**ursing **S**everity **s**cale
CI	confidence interval
EOLD-CAD	**E**nd-**O**f-**L**ife in **D**ementia - **C**omfort **A**ssessment in **D**ying
EU	**E**uropean **U**nion
EMA	**E**uropean **M**edicines **A**gency
ICC	**I**ntraclass **c**orrelation **c**oefficient
MMSE	**M**ini **M**ental **S**tate **E**xamination
NH	nursing home
PACE	**PA**lliative **C**are for the **E**lderly
PC	Palliative care
SATISFIE	**S**ymptom **A**ssessment **T**o **I**mprove **S**ymptom control **F**or **I**nstitutionalized **E**lderly
WHO	**W**orld **H**ealth **O**rganisation

Chapter 1: General introduction

1.1 Palliative care in nursing homes

The global population is growing older [1]. In Europe[2], the population aged 80 and above will be the fastest growing cohort by 2030. A significant proportion of older people will spent the last years of their live in residential care[3]: an institution where they reside for an undefined period of time, receiving personal assistance for daily living and nursing care 24 hours a day, 7 days a week, and medical attention. Many expressions refer to these institutions: care homes, residential care, residential aged care and long-term care facilities. In this dissertation, we prefer the term "nursing home". Most of the people, living in nursing homes, will eventually die there [4, 5]. In Flanders, the proportion of people dying in a nursing home grew from 22% of all deaths in 2007 to 26% in 2012 and to 31% in 2017[6].

Given this evolution, nursing homes will continue to be major providers of palliative care for the frail aged and for people whose complex care needs exceed available community resources and capacity of family caregivers[7]. It has been advocated that palliative care should be integrated early into chronic disease management[8]; and that a palliative approach should be implemented from the moment a person enters a nursing home[9], as older people frequently have palliative care needs at any point in the illness trajectory, and not exclusively in the terminal phase (WHO definition of palliative care, Table 1).

Table 1: WHO DEFINITION OF PALLIATIVE CARE[10]

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

Palliative care:

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

Nursing home residents are a highly dependent, frail population with multiple incurable, complex chronic diseases[15-17], various disease-trajectories towards end of life[18] and may be suffering of a variety of symptoms. Palliative care needs at the end of life have been established to have a direct relationship with symptoms experienced during that time[19]. In relation to many specific diseases at the end of life[20, 21], symptom management is also generally acknowledged as an important need, among many palliative care needs[22]. Consequently, palliative care in nursing homes requires that the residents' symptoms be assessed in a systematic and appropriate manner[23].

In the terminal phase of life, which is defined as a period of irreversible decline in functional status prior to death[11] and is often estimated as the last 72 hours of life, palliative care switches from the alleviation of suffering and optimization of quality of life to the provision of comfort in death [12, 13]. In this perspective, terminal care is an integral part and even the capstone of palliative care because, in terminal care, all the aspects of palliative care should fit as pieces of a jigsaw puzzle. Goals of care, commonly shared by patient/ representatives, and caregivers (physician and nurses) can help determine priorities and thus give direction to daily practice, based on the patients and family's concerns. Even unexpected clinical events (stroke; Covid-19) can than be situated in the residents' general medical situation and personal preferences and give direction to the ongoing care project.

1.2 Challenges of palliative care in European nursing homes

Palliative care provision in European nursing homes is known to be suboptimal. Literature reveals room for improvement in various aspects of palliative care; such as symptom management[14], collaboration and information transfer[15], infection management in palliative care[16], and general palliative care knowledge[17, 18]. Several reasons might have contributed to this situation. Firstly, the governments' efforts to support and develop qualitative nursing care and palliative care are not keeping pace with the increasing number of older nursing home residents nor the increased complexity of their palliative care needs. The European Commission estimated that public long-term care expenditures will increase from 1.6% of gross domestic product in 2013 to 2.7% by 2060[36], which makes long-term

care one of the most pressing issues to spend public funds for the European Union Member States.

Secondly, in several European countries like Germany[19], Switzerland[20] and the United Kingdom, a shortage of professional staff has been identified as a potential problem. In 2014, the Care Quality Commission of the United Kingdom warned of a shortage of nurses in care homes in England; in some places one in three vacancies was unfilled and 20% of the care homes inspected had too few staff on duty to ensure patient safety and good quality care[19, 20]. Thirdly, the lack of skills among available nursing personnel is identified as an important barrier in providing palliative care[15(21-24)]. Residents' palliative care needs might be overlooked or neglected, and poor knowledge of palliative care, pain and symptom management has been described(25, 26).

1.3 Symptom management in nursing homes

In daily clinical practice, symptom management is an ongoing cycle of symptom assessment and symptom treatment. Although symptoms are inherently subjective, symptom assessment aims to shed light on the measurable aspects of symptoms, such as frequency and duration, severity and distress, the impact on general functioning and on psychological, social, spiritual and existential resources and concerns of the patient[27].

Symptom treatment originates from these assessments and aims to alleviate the earlier defined symptoms or to decrease their impact. Symptom treatment can be non-

pharmacological, for example exercise therapy by a physiotherapist or frequent repositioning of the patient as a nursing intervention. This dissertation, however, is confined to pharmacological treatment: the use of medication to alleviate the symptoms.

Once pharmacological treatment is initiated, re-assessment of the symptoms is needed to evaluate the treatment's effectiveness and to check for undesired side-effects that might result in additional symptom burden for the resident. Re-assessment of the symptoms can lead to continuation, readjustment or suspension of the pharmacological treatment.

In palliative care, more specifically, symptom treatment is even more important, since treatment of the underlying diseases is no longer possible or preferable.

Unsurprisingly, the challenges mentioned in the previous paragraph, can impact the quality of symptom management for nursing homes' residents.

Families have expressed concerns that dying residents' needs weren't sufficiently addressed because of difficulties accessing medical care and the limited palliative care capabilities of aged care personnel[7, 28]. Nursing home staff need to recognize symptom burden and ought to know the effects and possible side-effects of the drugs they administer. Despite significant advances in palliative care treatments and interventions, research suggest that unmet symptom-related health-care needs, amenable to palliative care, persist at the very end of life[29]. In nursing homes, there is still room for improvement in symptom management. Research in nursing homes from several EU countries indicated prevalence of pain in 32 to 68 % of residents[14, 30]. In nearly half of the cases, pain was present daily and in over 50%, pain was moderate-to-severe[14, 30]. Among other symptoms, agitation (57%)[14] anxiety (44.0%), shortness of breath (14.1%) and nausea (10.2%)[31] were the most common.

In the last days of life, symptoms evolve rapidly[32]. Sleep disturbance, agitation and neuropsychiatric symptoms decrease; while pain, feeding problems, breathing abnormalities, apathy and anxiety increase[33]. Pain prevalence up to 78% of cases[14] has been reported.

1.3.1 Pharmacological treatment of symptoms

At the World Health Organisations' request, the International Association for Hospice and Palliative Care (IAHPC) developed the List of Essential Medicines in Palliative Care to improve the worldwide availability[34] of these essential medicines and to increase awareness and knowledge about the use of these medications in palliative care. The list focused on medications to treat symptoms and was completed in 2006[35]. In accordance with this list, guidelines concerning terminal care recommend the use of opioids, hypnotics and antipsychotics to control pain, dyspnoea, agitation, anxiety and delirium[10, 36-38] in the dying phase. These medications - opioids, hypnotics, and antipsychotics - define the scope for pharmacological treatment of symptoms in this dissertation.

For several reasons, data on pharmacological treatment of symptoms in the last days of life in nursing homes are scarce to date.

Firstly, the oldest old are less often involved in research of medication use; and when medication use in nursing homes is studied, dying residents are often excluded[30, 39].

Secondly, existing studies regarding medication prescription at the end-of-life often overlook the complexity of caring for patients with severe frailty and multiple comorbidities, since they are focused on specific populations such as patients with dementia or cancer patients.

In contrast with cancer patients, where analgesic use of opioids is well-established, the use of opioids to treat non-cancer pain is less known or more controversial[40].

Pharmacotherapeutic guidelines warn for opioid use in chronic non-cancer pain and recommend time-limited use below 90 days or reserve opioid use for the terminal phase[41].

Pharmacotherapeutic guidelines recommend opioids in acute pulmonary oedema, and off label use is recognised to alleviate dyspnoea in terminal chronic obstructive pulmonary disease[42]. Palliative care guidelines[43, 44] recommend opioids to treat pain and dyspnea in the dying phase. Underuse is defined as "the absence of initiation of an effective treatment in subjects with a medical condition or symptom for which one or several drug classes have demonstrated their efficacy[45]". To operationalize potential opioid underuse in this dissertation, we defined opioid underuse as the "absence of an opioid prescription in the last three days of life of residents suffering from pain and/or dyspnea", since palliative care guidelines[43, 44] recommend opioids to treat pain and dyspnea in the dying phase.

Also, international comparison of medication use during the last days of life in nursing homes is lacking. Nevertheless, from a public-health perspective, it is important to develop benchmarks within health services and/or specific, carefully described populations to assess outcomes and quality of care[29] and to find out if common practice is, or is not, in accordance to the guidelines.

This dissertation aims to contribute to improving knowledge concerning the prescription of opioids, antipsychotics, and hypnotics in the last three days of life in nursing home residents in six European countries and the associated factors of medication prescription. For opioids, more specifically, we will explore its possible underuse and the associated factors.

1.3.2. Symptom assessment in nursing homes

Older residents with non-malignant diseases and those with cognitive impairment are most at risk of inadequate assessment and management of pain in all settings, including nursing homes[7]. Cognitive impairment, most often due to dementia syndrome and/or delirium, impedes communication about pain and pain behavior [46-50]. Studies indicate that self-assessment is valid and even preferable for patients with moderate dementia[51), (50]. As a result of their multimorbidity, old people may suffer from multiple, various[32, 52], and sometimes unexpected symptoms[53]. Whenever possible, it is important to question the residents about other symptoms, besides pain.

Therefore, effective symptom treatment should be based on regular assessment of multiple symptoms, for which valid and feasible instruments are needed.

Currently, several symptom assessment scales are available, however, the development and validation of symptom scales for palliative care have predominantly taken place in cancer patients[54-56] and may therefore lack validation in populations other than those with cancer[27]. With the exception of selected pain measures, symptom questionnaires have frequently not been tested for validity in patients with cognitive impairment or multiple symptoms[27]. To our knowledge, only two multiple symptom instruments have been specifically tested in and adapted for an older population: the Symptom Assessment Scale for Elders (SAS-E)[57] and the MIDOS tool (Minimal Documentation System for palliative care)[58], a German version of the Edmonton System Assessment Scale.

Nonetheless, it is crucial that aged care providers have access to validated tools that are both sensitive to the needs of older people with multiple comorbidities and high levels of cognitive impairment and easily administered by a diverse and largely unskilled workforce[27]. Therefore, in this PhD project, we developed an instrument for regular,

multiple symptom assessment in institutionalized frail older persons. The tool is designed for regular symptom assessment in nursing home residents in the palliative phase, during their stay in the facility, and not exclusively in the terminal phase.

Nevertheless, the gold standard of self-report[27, 59, 60] for symptom assessment is not always applicable when nursing home residents are severely cognitively impaired or when they lose their communication ability in the dying process. A transition from verbal rating scales to observational scales, and sometimes to proxy assessments may be necessary to provide information throughout the terminal phase[27]. When asked for possible strategies to improve care, 75% of nursing home physicians suggest to introduce protocols for pain and symptom assessment and to involve family carers[39] Moreover, as the complexity of the resident's symptoms increases, it requires more input than solely the assessment made by staff during caregiving activities. In that case, physicians also have to rely on observations and on information from third parties.

Family carers often know the resident's reactions, behaviour and personality and spend larger timespans with the resident during various activities and situations. As such, we could hypothesize that family carers can meaningfully contribute to the residents' symptoms assessment. Moreover, family carer's perception of the comfort of dying of their loved one is essential for their own well-being and the quality of their own grieving process[61]. The validity of this approach, however, remains to be determined[27].

Therefore, we aimed to study the extent to which professional staff and family caregivers have a similar or different view on the resident's symptom burden. Differences in symptom assessment between patients and professional staff[62], [53, 59] and between patients and family caregivers[63] have been described in earlier studies. However, direct multiple-

symptom rating comparisons between family carers and staff in nursing homes is scarce. To our knowledge, only one study, based on 48 patients, has been published[64].

1.4 Study objectives of this PhD dissertation

In this PhD project, we focus on the symptom management at the end of life in nursing homes in 6 European countries. As discussed, symptom management encompasses a continuous interaction of both symptom treatment and symptom assessment.

1.4.1 Pharmacological treatment of symptoms

As mentioned earlier, the non-pharmacological treatment of symptoms is left aside in this PhD project. With regards to the pharmacological treatment, we studied the use of opioids, hypnotics and antipsychotics at the end of life in nursing homes. We compared the prevalence of the prescription of opioids, antipsychotics, and hypnotics in the last three days of life in nursing home residents between six European countries and investigated possible associated factors for opioids. In particular, we explored possible underuse and searched for associated factors related to the resident, the nursing home and the organization of care.

1.4.2 Assessment of symptoms

With regards to assessment of symptoms, we described the symptom distress at the end of life in a nursing home population. Second, we explored similarities and differences in the perception of symptoms between professional staff and family carers both at group and

individual resident level. At group level, we compared the mean scores per symptom of residents dying in their nursing homes, as rated by professional staff and by family carers. At an individual level, we explored to what extent professional staff and family carers agreed or disagreed in symptom ratings and which characteristics were associated with possible symptom score discrepancies.

We developed an instrument for regular, multiple symptom assessment in institutionalized frail older persons and validated it by exploring the difference in symptom burden in residents with a palliative status, compared to residents without a palliative status.

1.5 Methods

For the study objectives concerning pharmacological treatment and symptom assessment, we conducted a retrospective, cross-sectional post-mortem survey of deceased residents of nursing homes in 6 European countries, as part of the PACE 1 project.

For the development of a symptom assessment tool in frail older persons, we performed a literature search for most prevalent symptoms in old people or geriatric patients, we developed a multiple-symptom assessment tool by Delphi procedure and validated the assessment tool.

1.5.1 PACE 1 project: Retrospective cross-sectional study of deceased nursing home residents in six European countries.

The research in chapters 2 to 4 is part of the PACE 1 research project, is funded by the PAlliative Care for older people in nursing homes in Europe (PACE) project of the EU

(Framework Programme7 Grant Agreement 603111, and partially co-financed by the Polish Ministry of Science and Higher Education in the years 2014-2019.

PACE aimed to compare the effectiveness of palliative care for older people in nursing homes in Europe and to advise policy-makers on optimal palliative care practices. PACE 1 is the retrospective cross-sectional study of deceased nursing home residents.

1.5.1.1 Purpose of the PACE 1 study project

One of the Taskforces of the European Association for Palliative care (EAPC) mapped the extent to which different EU countries have palliative care policies or regulations for palliative care in nursing homes, and the extent to which palliative care initiatives are present on a meso or micro level [(3)]. However, there was a large knowledge gap regarding the actual care residents are receiving at the end of life[(65)].

The overarching aim of one of the EU funded PACE 1 project was to describe and compare how nursing home residents are currently dying and what care they are receiving at the end of life in different EU countries, and evaluate current knowledge and attitudes towards palliative care. Therefore, PACE conducted nationally representative, comparative research on palliative care practice in nursing homes across 6 European countries, Belgium, the Netherlands, England, Finland, Italy and Poland.

1.5.1.2 Study design

PACE 1 included a retrospective, cross-sectional post-mortem survey of deceased residents of nation-wide representative samples of nursing homes in 6 European countries: Belgium, Finland, Italy, the Netherlands, Poland and the United Kingdom. The participating countries

were selected in order to obtain a good geographical spread, countries with varying economic growth, health care systems and levels of palliative care, as described in previous research[3].

1.5.1.3 Sampling

In each country, nursing homes, which we defined as "a collective institutional setting where care, on-site provision of personal assistance of daily living, and on-site or off-site provision of nursing and medical care, is provided for older people who live there, 24 hours a day, 7 days a week, for an undefined period of time[66]", were selected through proportional stratified random sampling to obtain representative samples in terms of region within country, nursing home type and bed capacity. For each country, with the exception of Italy, we used publicly available lists of nursing homes. In Italy, no public list of nursing homes is available; therefore a convenience sample was used, based on a previously constructed cluster of nursing homes, covering the three macro regional areas. The selected nursing homes reported all deaths of residents that occurred over the period of 3 months prior to the distribution of questionnaires. For each case, structured after-death questionnaires concerning the deceased resident's care were sent to (1) the nursing homes administrator or manager, (2) the nurse most involved in care of the deceased resident, (3) the treating physician, and (4) a closely involved family member.

1.5.1.4 Measurements

At resident level, the nursing home management provided socio-demographic data. Clinical characteristics about the resident's health and quality of dying were registered by the nurse and the family member. Based on the resident's medical file, the nurse provided information on the resident's medication use in the last 3 days of life. Quality of dying was assessed with End-Of-Life in Dementia-Comfort At Dying (EOLD-CAD)[67]; a validated questionnaire which assesses quality of dying by measuring symptom burden in the last week of life on four subscales: physical distress, dying symptoms, emotional distress, well-being. Previous reviews have recommended this scale as the most appropriate post-mortem instrument for measuring quality of dying in mixed nursing home populations with various levels of cognitive and physical functioning[68, 69]. The EOLD-CAD was completed by staff and family caregivers. The underlying cause of death was based on the clinical judgment of the treating physician, or the staff member. Dementia was determined as present if either the treating physician or the staff member most involved in care indicated so. Medication use was assessed by a questionnaire, developed by the PACE research consortium, completed by the staff, based on the resident's nursing and medical record.

At nursing home level, palliative care structures and policies were assessed by a questionnaire, based on a Belgian survey[70] and EU FP7 IMPACT Structural Quality Indicators for palliative care[71] completed by the nursing home's management. The complete study methods are published in detail[65].

1.5.1.5 Inclusion criteria, covariates and statistics

For study objectives concerning pharmacological treatment, we included the residents who died in the nursing home and measured the prevalence of opioid, antipsychotic and hypnotic prescription, based on the nurses' questionnaire.

Multivariable logistic regression was performed to adjust for resident's demographic characteristics, dementia status, dependency score, length of stay, cause of death and the nursing home type.

For studying opioid underuse, we included residents who died in the nursing home, with pain/dyspnea in CAD-EOLD and without opioid prescription. All resident's demographic and clinical factors, and nursing homes characteristics which could hypothetically be associated with opioid prescription, were taken into account as covariates. We estimated opioid underuse per country and per symptom. We calculated associations of clinically relevant resident, nursing home and palliative care provision characteristics by multilevel, multivariable analysis.

For comparing symptom assessment between staff and family caregivers, we included residents who died in the facility, with family caregivers present in the last week of life and with > 50 % response-rate per country in family caregivers and staff. Family caregivers' age, relationship, the hours spent in the resident's presence in the last week, whether or not the resident's death was expected and staffs age, years of experience and palliative care education were taken into account as covariates, together with the resident's age, length of stay, dependency of care, dementia status and sentinel events. We calculated mean paired differences in symptom, subscale score and total scores at a group level and inter-rater agreement and percentage of perfect agreement at a resident level. We assessed factors

associated with mean paired score differences between staff and carers by multilevel multinomial logistic regression.

1.5.1.6 Ethics

The research teams in all participating countries obtained ethical approval from their respective ethics committees. All respondents remained anonymous and participated voluntarily. Returning the questionnaire was considered as consent to participate.

1.5.2. Symptom Assessment to Improve Symptom control for Institutionalized Elderly (SATISFIE): validation-study

We performed a literature search for most prevalent symptoms in old people or geriatric patients. We developed a multiple-symptom assessment by Delphi procedure and validated the assessment tool.

1.5.2.1 Literature search

We searched for “symptom control, measuring symptoms, measuring tool, symptom scale”, combined with “end-of-life, palliative patient, palliative care, palliative elderly or geriatric patient” and developed a list of 30 symptoms, prevalent in an older population.

1.5.2.2 Delphi procedure

In a first round, we presented this list in alphabetical order to an expert panel, consisting of 7 physicians and 6 nurses working in geriatric and palliative care settings, and familiar with the use of assessment instruments. The experts scored these 30 symptoms for frequency (1=rarely 2=sometimes 3=often 4=very often) and distress (1=light 2=average 3=serious). The frequency and distress scores per symptom were multiplied, resulting in a total score, ranging from 1 to 12. Symptoms were ranked by median and in case of equality, also by mean score from high to low, and selected the top 10 of most relevant symptoms.
In a second round, experts were asked any additions or comments. Only 3 of the 12 participants in the second round had an addition and no comments were made.
Since each additional symptom was mentioned by only one expert, no changes were made in the existing scale.

1.5.2.3 Development of new instrument.

After comparison of these ten items with assessment instruments found in literature none of the existing instruments contained all ten items. Therefore, it was decided to develop a new scale containing the top 10 symptoms, with the possibility to add three symptoms which patients might experience. A horizontal numerical scale was chosen, with 0 being “not at all” and 10 being “worst possible”.

1.5.2.4 Validation study sample

For validation, we hypothesized that overall symptom burden in a palliative population would exceed the symptom burden of a non-palliative population. Sample sizes of 96 and 48 were needed to achieve 80 % power to detect a clinically relevant difference between the two groups with a significance level of 0.05, using a two sided two-sample t-test. Participants were recruited from 7 nursing homes and 3 acute geriatric wards and were included when aged 70 years or more, able to sign informed consent and having a Mini Mental State Examination score of 18/30 or more). Participants were classified as palliative when the medical record mentioned a palliative care oriented nursing plan or a formal palliative status. Other participants were considered as a non-palliative group.

1.5.2.5 Statistics

Participants performed symptom self-assessment with the SATISFIE-instrument on two consecutive days. After scoring of the 10 listed symptoms, participants were asked if they suffered from other symptoms, which were also scored on a level from 0 to 10. Nurses only completed the assessment on day 1.

Descriptive statistics describe the characteristics of the study population and symptom scores. To evaluate the concurrent validity of the SATISIFIE-instrument, we analyzed the symptom scores differences between the palliative and non-palliative group participants with the help of the non-parametric Mann-Whitney U test. Test-retest or intra-rater reliability was calculated by means of an intraclass correlation coefficient (variability between the participants' score on the first and the second day), as was the inter-rater reliability (difference between participants' and nurses' rating on the first day). In order to

verify if reduction of the number of symptoms in the scale is needed, possible symptom clusters were detected by means of factor analysis. Feasibility was evaluated with the help of the assessment time and a questionnaire for the nurses.

1.5.2.6 Ethics

The ethical committee of Ghent University Hospital (Belgium) approved the study protocol. Informed consent was obtained from all participants.

1.6 Outline of this dissertation

1.6.1 Pharmacological treatment

In the first part of this dissertation, we aimed to explore the use of pharmacological treatment during the last days of life in nursing home residents in the European context. In chapter 2, we especially focussed on the use of opioids, antipsychotics and hypnotics addressing following research questions:

1) what is the prevalence of the prescription of opioids, antipsychotics, and hypnotics in the last three days of life in nursing home residents in six European countries;

and

2) what factors are associated with this medication prescription?

In Chapter 3, we explored the opioid underuse in end of life in nursing home residents. We defined opioid underuse as the absence of an opioid prescription in the last three days of life of residents suffering from pain and/or dyspnea. We addressed following research questions:

3) What is the prevalence of long-term care facility residents with underuse of opioids in 6 European countries?
4) What is the prevalence of long-term care facility residents with underuse of opioids for pain, dyspnea and both symptoms?
5) Which characteristics, regardless of country, but related to the resident, the long-term care facility and the organization of care, are associated with opioid underuse?

1.6.2 Symptom assessment

The second part of this dissertation is focussed on symptom assessment.

In chapter 4 we compared symptom ratings between family carers and nursing staff in nursing home residents in the last days of life. Following research questions are addressed:

6) At a group level, what are the mean symptom scores of residents dying in long-term care facilities, scored by professional staff and by family carers? And is there any difference in mean symptom scores between staff and family carers?
7) Which resident, staff and family carer characteristics are associated with symptom score discrepancies?
8) At an individual level, what is the interrater agreement in symptom ratings between staff and family carers and what is the extent of the perfect match?

In chapter 5, we described the development of an instrument (the SATISFIE scale) for regular, multiple symptom assessment in institutionalized frail older persons. To validate the instrument, we compared the symptom scores between patients with and without a palliative status. We addressed following research questions:

9) What is the prevalence of symptom distress in a nursing home population?
10) Is there any difference in symptom burden in residents with a palliative status, compared to residents without a palliative status?
11) Is the SATISFIE self-rated symptom assessment tool a valid instrument in an old palliative population?

1.7 Published papers, incorporated in this dissertation

Chapters 2 to 5 of the dissertation are based on papers, **published** in academic peer-reviewed journals.

Title	Authors	Journal	Impact factor
CHAPTER 2 **Opioid, antipsychotic and hypnotic use in end of life in nursing homes in 6 European countries. Results of PACE**	**Tanghe M**, Van Den Noortgate N, Pivodic L, Deliens L, Onwuteaka-Philipsen B, Szczerbińska K, Finne-Soveri H, Collingridge-Moore D, Gambassi G, Van den Block L, Piers R.	Eur J pub Health; 2018; 10.1093/eurpub/cky196	2018 SCI impact factor 2.234; Ranking Q2; ranking n° 80 of 186 in PUBLIC, ENVIRONM and OCCUPATIONAL HEALTH
CHAPTER 3 **Opioid underuse in terminal care of long-term care facility residents with pain and/or dyspnoea. A cross-sectional PACE-survey in 6 European countries**	**Tanghe M**., Van Den Noortgate N., Deliens L., Smets T ., Onwuteaka-Philipsen B, Szczerbińska K., Finne-Soveri H., Payne S, Gambassi G., Van den Block L., Piers R.	Palliat Med.; 2020; 34(6):784-794. doi:10.1177/0269216320910332	2018 SCI impact factor 4.956; Ranking D1; ranking n° 6 of 98 in HEALTH CARE SCIENCES & SERVICES
CHAPTER 4 **Comparing symptom ratings by staff and family carers in residents dying in long-term care facilities in three European countries, results from a PACE-survey**	**Tanghe M**, Van Den Noortgate N, Deliens L, Smets T, Onwuteaka-Philipsen B, Finne-Soveri H, Van den Block L, Piers R.	J Pain Symptom Manage.; 2020; S0885-3924(20)30128-7. doi:10.1016/j.jpainsymman.2020.03.002	2018 SCI impact factor 3.378; Ranking Q1; ranking n° 19 of 98 in HEALTH CARE SCIENCES & SERVICES
CHAPTER 5 **Development and Validation of the Symptom Assessment to Improve Symptom Control for Institutionalized Elderly Scale**	De Roo M, **Tanghe M**, Van Den Noortgate N, Piers R.	JAMDA; 2017; t9(7),148-153 e5	2017 SCI impact factor4.899, Ranking Q1; ranking n°6 of 53 in GERIATRICS & GERONTOLOGY

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Part 1

Pharmacological treatment of symptoms

Chapter 2: Opioid, antipsychotic and hypnotic use in end of life in long-term care facilities in 6 European countries. Results of PACE

Marc Tanghe[1], Nele Van Den Noortgate[2], Lara Pivodic[3], Luc Deliens[3], Bregje Onwuteaka-Philipsen[4], Katarzyna Szczerbińska[5], Harriet Finne-Soveri[6], Danni Collingridge-Moore[7], Giovanni Gambassi[8], Lieve Van den Block[3], Ruth Piers[2], On behalf of PACE.

1 End-of-Life Care Research Group, Ghent University, Ghent, Belgium.

2 Ghent University Hospital, Department of Geriatrics, Ghent, Belgium.

3 End-of-Life Care Research Group, Vrije Universiteit Brussel, Brussels, Belgium.

4 Vrije Universiteit, Medisch Centrum, Amsterdam, The Netherlands.

5 Jagiellonian University Medical College, Kraków, Poland.

6 National Institute for Health, Helsinki, Finland.

7 Lancaster University, Lancaster, United Kingdom.

8 Università Cattolica del Sacre Cuore, Roma, Italy.

Tanghe M, Van Den Noortgate N, Pivodic L, Deliens L, Onwuteaka-Philipsen B, Szczerbińska K, Finne-Soveri H, Collingridge-Moore D, Gambassi G, Van den Block L, Piers R. Opioid, antipsychotic and hypnotic use in end of life in nursing homes in 6 European countries. Results of PACE. Eur J pub Health, 2018, 10.1093/eurpub/cky196

Abstract

Background

Opioids, antipsychotics and hypnotics are recommended for comfort care in dying. We studied their prescription during the last three days in residents deceased in the long-term care facility (LTCF).

Methods

In a retrospective, cross-sectional survey in Belgium, England, Finland, Italy, the Netherlands and Poland, LTCFs, selected by proportional stratified random sampling, reported all deaths over the previous three months. The nurse most involved in the residents' care reviewed the chart for opioid, antipsychotic and hypnotic prescription, cause of death and comorbidities. Multivariable logistic regression was performed to adjust for resident characteristics.

Results

Response rate was 81.6 %. We included 1079 deceased residents in 322 LCTFs. Opioid prescription ranged from 18.5 % (95 % confidence interval [95%CI]: 13.0-25.8) of residents in Poland to 77.9 % (95%CI: 69.5-84.5) in the Netherlands, antipsychotic prescription from 4.8 % (95%CI: 2.4-9.1) in Finland to 22.4 % (95%CI: 14.7-32.4) in Italy, hypnotic prescription from 7.8 % (95%CI: 4.6-12.8) in Finland to 47.9% (95%CI: 38.5-57.3) in the Netherlands. Differences in opioid, antipsychotic and hypnotic prescription between countries remained significant ($p < 0.001$) when controlling for age, gender, length of stay, cognitive status, cause of death in multilevel, multivariable analyses. Dying from cancer showed higher odds for receiving opioids (OR 3.51; $P < 0.001$) and hypnotics (OR 2.10; $p = 0.010$).

Conclusions

Opioid, antipsychotic and hypnotic prescription in the dying phase differed significantly between six European countries. Further research should determine the appropriateness of their prescription and refine guidelines, especially for LTCF residents dying of non-cancer diseases.

Key words

End-of-life, nursing home, opioids, antipsychotics, hypnotics.

2.1 Introduction

Long term care facility (LTCF) residents in Europe evolve to a highly dependent population with complex, often incurable multi-morbidity[1]. Consequently, palliative and terminal care should be key components in LTCF care, with adequate pain- and symptom-management as a priority.

Previous research documented a high prevalence of pain in LTCF residents. In a cross-sectional study in three European countries, the presence of pain varied between 32% and 57%. In nearly half of the cases, pain was present every day and in over 50%, pain was rated moderate-to-severe[2]. A longitudinal study in the Netherlands revealed pain prevalence up to 68%, with 41 % of residents in persistent pain[3]. With regard to other symptoms, this study indicated that agitation is the most common symptom, with prevalence ranging from 57% to71%[3].

Pain treatment in a LTCFs is evolving, illustrated by an increase in opioid prescription in LTCFs[,4]. Nevertheless, recent research established undertreatment in residents with persistent pain[,5]. Especially the group of residents with cognitive impairment, received less opioid analgesics[6],. In contrast, residents with dementia received more psychotropic medication [7], although their use is recently decreasing in the long term care[4],[8]. Besides these studies about central nervous agents in

general, specific data about antipsychotic and hypnotic prescription in LTCF residents near to death are rare as some studies on medication use in LTCFs exclude dying patients[7],[4],[6],[2],[5],,.

In the last days of life, symptoms evolve rapidly. Sleep disturbance, agitation and neuropsychiatric symptoms decrease; while pain, feeding problems, breathing abnormalities, apathy and anxiety increase[9]. Pain prevalence up to 78%[3] has been reported.

Recent guidelines concerning terminal care recommend the use of opioids, hypnotics and antipsychotics to control pain, dyspnoea, agitation, anxiety and delirium[10] in the dying phase.

Existing studies examining the impact of the guidelines regarding medication prescription at the end-of-life often focused on specific populations such as cancer patients and patients with dementia or are performed in acute care hospitals and palliative care settings. Consequently, to date, little is known about the prescription of opioids, hypnotics and antipsychotics in the last days of life in a general LTCF population. The PACE study (**PA**lliative **C**are for the **E**lderly), a EU funded research project to assess quality of palliative care delivery in the European community's LTCFs, created the opportunity to conduct research in a larger, European population sample and allowed epidemiological comparison of the factual practice between participating countries. In this study, following research questions were addressed: (1) what is the prevalence of the prescription of opioids, antipsychotics, and hypnotics in the last three days of life in LTCFs' residents in six European countries and (2) what factors are associated with this medication prescription?

2.2 Methods

2.2.1 Study design, setting and participants

In six participating countries, Belgium, England, Finland, Italy, the Netherlands, and Poland a cross-sectional survey collected data on deceased LTCF residents. Countries were selected in order to obtain a good spread in geography, history of economic growth, health care system, and level of palliative care development, The study methods are described in the published study protocol[11]. In this paper, 'LTCF' refers to a 'collective institutional settings where care, on-site provision of personal assistance of daily living, and on-site or off-site provision of nursing and medical care, is provided for older people who live there, 24 hours a day, 7 days a week, for an undefined period of time',. LTCFs were identified using proportional stratified random sampling, to guarantee nation-wide representativeness. Participating LTCFs reported all residents who died in a retrospective three month period, prior to the researchers visit to the LTCF. For this survey, we included residents who died in their LTCF and of whom the nurses' questionnaire was completed.

2.2.2 Data collection

Through an anonymized procedure, structured after-death questionnaires, regarding each deceased resident were sent to the treating physician, the nurse or care assistant most involved in the resident's care and the LTCF management.

2.2.3 Measurements

Demographic data and length of stay were extracted from the LTCF managements questionnaire regarding the deceased resident; LTCF characteristics from the LTCF managements questionnaire regarding their LTCF. In this study, "LTCF type" refers to the staffing structure, depending on whether physicians and nurses are on-site or off-site. In every participating country, we found LTCFs with nurses on site 24/7, and physicians off-site. In Italy, the Netherlands and Poland, some LTCFs reported physicians and nurses on-site. LTCFs with on-site care assistants and off-site nurses and physicians only participated in the study in England[11].

Based on the nursing records, the nurses provided information on the residents prescriptions, functional and cognitive status, dementia status and cause of death. Based on a list of available medications per country, the nurses executed a chart review to check whether or not opioids (e.g. morphine, oxycodone, hydromorphone, fentanyl, buprenorphine, tramadol), antipsychotics (e.g. haloperidol, risperdone, olanzapine, clotiapine) and hypnotics (e.g. midazolam, oxazepam, lorazepam, lormetazepam, zopiclone, zolpidem, zaleplon) had been prescribed to the resident in the last 72 hours of life. Functional and cognitive status was estimated by the Bedford Alzheimer Nursing Severity scale (BANS S), a rating scale, comprising cognitive and functional items, developed for grading severity of dementia[12]. Higher scores indicate higher functional disability and dependency. In the database, a resident "with dementia" was defined as a resident to whom the nurse and/or the physician referred to as a resident with dementia. Cause of death was determined by means of a predefined checklist.

2.2.4 Statistical analysis

Descriptive statistics were provided per country as percentages (for categorical outcomes) and mean and standard deviation (for continuous outcomes). Differences in residents' and LTCFs' characteristics between countries were explored by means of normal, multinomial and logistic regression, depending if the dependent variable was continuous, categorical or binary. Secondly, the estimated percentage and corresponding 95% CI of opioid, antipsychotic and hypnotic prescription was estimated using a mixed logistic regression model with LTCF as random factor and country as fixed factor. Lastly, to assess factors associated with medication prescription, a multilevel binary logistic regression model was built. All residents' and LTCFs' characteristics, showing a difference in opioid use prevalence with P value < 0.100 in univariable multilevel analysis were included in a stepwise backward model building procedure, with P-value < 0.01 as boundary for statistical significance. Country was included as fixed effect to compare data between countries, LTCF was defined as a random effect. Other fixed effects were age category, gender, length of stay, BANS-S score, dementia status and cause of death on resident level and staffing structure on LTCF level. The resulting model was applied to explore associations with prevalence of antipsychotic and hypnotic use. Associated factors were calculated for the entire survey population and per country. The estimated variance between LTCFs was used to calculate the adjusted intraclass correlation coefficients on the LTCF level to explore variation between LTCFs[13]. Statistical analyses were performed in SPSS 23.

2.3 Results

The PACE database contains data from 1707 deceased residents in 322 LTCFs. The nurses response rate was 81,6 % (ranging from 54.2 % in England to 95.1 % in Finland). For this survey, we excluded

323 residents of whom we didn't receive the nurses' questionnaire and 305 residents who died outside their LTCF, resulting in a study sample of 1079 residents, deceased in their LTCF.

2.3.1 Residents' and LTCFs' characteristics

As shown in **Table 1**, significant differences in LTCF type were identified. The deceased residents differed between countries by age, length of stay, BANS-S score, prevalence of dementia status and cancer versus non-cancer cause of death. Compared to other countries, LTCF residents were younger and had a shorter stay in Poland, where the cause of death was predominantly cardiovascular and cerebrovascular disease. Polish residents also had the highest BANS-S score, reflecting a higher dependency rate in daily life activities. Finnish LTCF residents had the highest percentage of dementia.

Table 1. Comparison of resident characteristics between countries

Country		POLAND	ITALY	FINLAND	ENGLAND	BELGIUM	NETHERLANDS	p-value
n		234	144	196	72	237	196	
LTCF TYPE								
Type of LTCF where residents died	Physicians & nurses offsite	0 %	0 %	0 %	43.1 %	0 %	0 %	< 0.001 [a]
	Physicians offsite, nurses on site	32.5 %	75.2 %	100 %	56.9 %	100 %	38.9 %	
	Physicians & nurses on site	67.5 %	24.8 %	0 %	0 %	0 %	61.1 %	
RESIDENT CHARACTERISTICS								
Residents' gender (% Female)		65.5	66.7	68.6	74.6	63.8	67.0	0.668 [b]
Residents' age in years	≥ 90	22.4 %	27.8 %	36.4 %	46.0 %	43.9 %	40.9 %	0.036 [a]
	80 – 89	46.1 %	55.5 %	52.3 %	38.1 %	45.7 %	42.6 %	
	< 80	31.5 %	16.7 %	11.3 %	15.9 %	10.4 %	16.5 %	
Residents' mean age (SD)		81.3 (11.0)	85.6 (7.5)	86.6 (8.2)	88.3 (7.3)	87.5 (7.5)	86.9 (8.1)	< 0.001 [c]
Length of stay in years (SD)		1.8 (3.0)	2.3 (3.2)	2.7 (2.9)	2.5 (3.0)	3.4 (3.6)	2.9 (3.2)	0.002 [c]
Mean Total BANS-S score[d] (SD)		22.4 (4.3)	21.9 (3.9)	20.0 (3.8)	17.7 (3.9)	19.1 (4.8)	18.2 (4.6)	< 0.001 [c]
Resident with dementia[e]		67.7 %	79.1 %	87.2 %	60.3 %	66.4 %	65.9 %	< 0.001 [b]
Cause of death	Non-cancer	95.2 %	89.8 %	91.9 %	80.0 %	89.7 %	91.1 %	0.050 [b]
	cancer	4.8 %	10.2 %	8.1 %	20.0 %	10.3 %	8.9 %	

LTCF = long term care facility

[a] Calculated with multinomial logistic regression. [b] Calculated with binary logistic regression. [c] Calculated with linear regression.

[d] Bedford Alzheimer Nursing Severity Scale (BANS-S). 7 items scale, scores range 7 -24, Higher scores indicate higher functional disability and dependency.

[e] in this survey, a resident "with dementia" is a resident which is designated as "suffering from dementia" by the nurse and/or the physician.

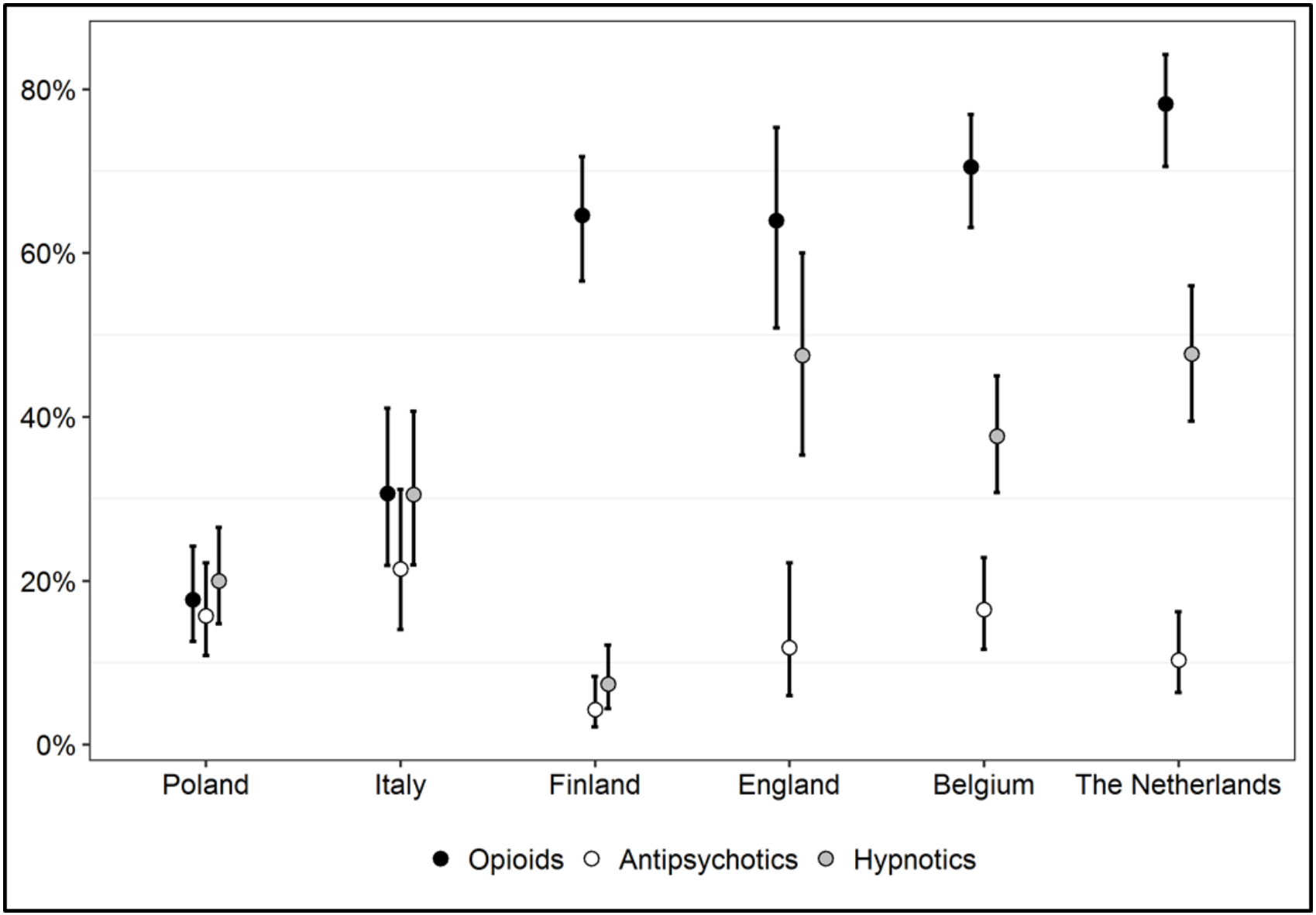

Figure 1: estimated prevalence of opioid, antipsychotic and hypnotic prescription in the last three days of life per country

2.3.2 Medication prescription prevalence

The estimated prevalence of opioid, antipsychotic and hypnotic prescription in the last three days of life (**Figure 1**) differed ($p < 0.001$) between countries. Opioid prescription varied from 18.5 % in Poland to 77.9 % in the Netherlands. Antipsychotic prescription varied from 4.8 % in Finland to 22.4 % in Italy. Hypnotic prescription ranged from 7.8 % in Finland to 47.9% in The Netherlands.

2.3.3 Factors associated with medication prescription

After statistical adjustment for LTCF type and resident's characteristics, odds of opioid prescription in the last three days of life were significantly higher in all countries compared to Poland, with exception of Italy (**Table 2**). Odds ratios ranged from 9.46 in Finland (95%CI: 4.58 – 19.52) to 23.11 in England (95%CI: 7.12 – 75.4 Opioid prescription was associated with the BANS-S score (OR 1.07; 95%CI: 1.03 -1.11), reflecting an increase in opioid prescription for residents with more severe physical disability. Odds of opioid prescription was 3.5 times higher for residents dying of cancer (OR 3.51; 95%CI: 1.83 – 6.72) compared to residents dying of non-cancer causes.

Odds of antipsychotics were about a fourth in Finland (OR 0.23; 95%CI: 0.09 -0.56) in comparison to Poland.

Odds of hypnotic prescription were about a fourth in Finland (OR 0.24; 95%CI: 0.11 – 0.53) though were higher in the Netherlands (OR 3.80; 95%CI: 1.98 – 7.30) compared to Poland. Odds of hypnotic prescription were higher (OR 2.10; 95%CI: 1.20 – 3.67) for residents dying of cancer, compared to residents dying of other causes. In this study, the dementia status did not show any significant association with opioid, antipsychotic and hypnotic prescription.

The intra-class correlation coefficient within the level of LTCFs was 14.7 for opioid prescription, meaning that about 15 % of the variation was due to factors of the LTCF. The intra-class correlation coefficient within the level of the LTCF was 9 % for antipsychotic and 13% for hypnotic prescription.

Table 2. Resident and LTCF characteristics associated with medication prescription in the last three days of life

		OPIOIDS OR [95 % CI]	ANTIPSYCHOTICS OR [95 % CI]	HYPNOTICS OR [95 % CI]
Country				
	the Netherlands	21.22 [10.37 – 43.39]	0.56 [0.27 – 1.19]	3.80 [1.98 – 7.30]
	Belgium	14.68 [6.92 – 31.11]	0.79 [0.38 – 1.64]	1.71 [0.86 – 3.39]
	England	23.11 [7.12 – 75.04]	0.78 [0.24 – 2.58]	3.42 [1.23 – 9.48]
	Finland	9.46 [4.58 – 19.52]	0.23 [0.09 – 0.56]	0.24 [0.11 – 0.53]
	Italy	1.76 [0.83 – 3.73]	1.22 [0.59 – 2.50]	1.14 [0.55 – 2.36]
	Poland	Ref.	Ref.	Ref.
Type of LTCF				
	Physicians & Nurses off site	0.37 [0.08 – 1.65]	1.40 [0.26 – 7.47]	1.10 [0.27 – 4.47]
	Physicians off site, nurses on site	0.99 [0.54 – 1.82]	1.24 [0.66 – 2.32]	1.87 [1.05 – 3.32]
	Physicians & nurses on site	Ref.	Ref.	Ref.
Resident's gender	Female	1.10 [0.78 – 1.57]	0.85 [0.55 – 1.30]	0.93 [0.65 – 1.32]
	Male	Ref.	Ref.	Ref.
Resident's age in years	≥ 90	1.00 [0.59 – 1.68]	0.76 [0.40 – 1.42]	0.56 [0.33 – 0.93]
	80 - 89	1.12 [0.69 – 1.80]	1.20 [0.68 – 1.09]	0.93 [0.58 – 1.48]
	< 80	Ref.	Ref.	Ref.
Length of stay in years		0.94 [0.89 – 0.99]	1.000 [0.99 – 1.01]	0.94 [0.89 – 1.00]
Total BANS-S score[a]		1.07 [1.03 – 1.11]	0.98 [0.93 – 1.02]	0.99 [0.95 – 1.02]
Resident with dementia[b]	Yes	0.96 [0.65 – 1.40]	0.96 [0.60 – 1.54]	0.84 [0.57 – 1.24]
	No	Ref.	Ref.	Ref.
Cause of death	Cancer	3.51 [1.83 – 6.72]	1.65 [0.86 – 3.13]	2.10 [1.20 – 3.67]
	Non-cancer	Ref.	Ref.	Ref.

Multilevel multivariable logistic regression

Opioids: 917 included, 162 missing. Antipsychotics: 917 included, 162 missing. Hypnotics: 908 included, 171 missing.

[a] Bedford Alzheimer Nursing Severity Scale (BANS-S). 7 items scale, scores range 7 -24, Higher scores indicate higher functional disability and dependency

[b] in this survey, a resident "with dementia" is a resident which is designated as "suffering from dementia" by the nurse, the physician or both.

2.3.4 Factors associated with medication prescription within a country

We found associations between opioid prescription and dying of cancer within some countries. Compared to residents, deceased of non-cancer diseases, odds for receiving opioids among residents dying of cancer were 14.28 in Italy (95%CI: 2.26 – 90.3) 8.96 in Poland (95%CI: 1.6 – 49.40; P=0.012). We found no other significant associations for cancer. Other variables did not show significant associations with medication prescription in any of the countries studied, which could be explained by small sample sizes per country.

2.4 Discussion

2.4.1 Principal findings

In our study, we found significant differences between six European countries in opioid, psychotic and hypnotic prescriptions in the last three days of life of LTCF residents. The most striking differences were found in opioid prescription estimated percentages, ranging from 18.5 % in Poland to 77.9 % in the Netherlands. Low prevalence of antipsychotic (4.8 %) and hypnotic (7.8 %) prescription in Finland was also noteworthy. Differences in medication prescription between countries stood firm after multiple statistical adjustment, meaning that LTCF type or residents characteristics alone do not explain these differences. Country appears as the most important determinant for the prevalence of opioid, antipsychotic and hypnotic prescription in the last three days-of life in LTCFs. Dying of cancer triples the odds of opioid prescription and doubles the odds of hypnotic prescription in LTCFs' residents end-of-life.

2.4.2 Relation to other studies and possible explanations

Opioid prescription prevalence in the last days of life of 60 %[14], and 70 %[15],[16] is regularly documented. Klapwijk[17] even described opioid prescription prevalence up to 100 % of LTCF residents of whom death was expected. Also in our study, the Netherlands had the highest opioid prescription prevalence. The low prevalence of opioid prescription in Italy (31.7 %) and Poland (19.6 %) is remarkable, but consistent with other research. In both countries, opioid prescription per capita was found to be lower than in other West-European countries[18]. Opioid prescription in LTCFs may reflect the low prevalence in both countries[7],[19] in general. Although death is not often easily predictable in LTCF residents, prevalence of pain increases to 78 % and shortness of breath to 52 % in the last week of life[16]. Taken into account the high prevalence of pain in LTCF residents, low opioid prescription prevalence in Italy and Poland could be questioned, since guidelines consider opioids as a as an effective treatment for pain symptoms during the last days of life and also recommend opioids to treat dyspnoea in the last days of life[10],[20].

Low opioid availability and prescription in Poland was described in a EU report[21, 22]. The ATOME group identified legislative barriers to opioid consumption in Poland: palliative care support initiatives are almost exclusively consulted for cancer patients to whom every cancer treatment is declined due to the feeble prognostic. Moreover, complete reimbursement of opioids was exclusively entitled to cancer patients, whereas other patients receive only 30 % reimbursement in Poland. The low frequency of medical consultations could be an additional factor. Visits of the treating physician are planned every fortnight or even once monthly. As symptom burden[17], and hence, the need for treatment[15] quickly evolves in the last days of life, this frequency is too low to provide effective response. Popular convictions and attitudes are another barrier to effective opioid use. The ATOME report[22] already defined fear of opioids as an important factor. This fear and negative image of opioids is wide spread in the Polish society, even amongst health care

professionals. In Italy, the reluctance to communicate openly[23] about end-of-life and dying could explain the low opioid prescription, since opioids, by mistake, still might be seen as life-shortening[23] or causing respiratory depression[24]. For the same reason, family members often oppose opioid use[23], although cancer seemed to be a potent driver of opioid prescription, as opposed to non-malignant conditions.

Antipsychotic prescription prevalence in LTCF end-of-life care is, in our findings, lower than published in other research[15], and was remarkably low in Finland, which is consistent with another study. In Finland, there is a trend to decrease central nervous agents in patients, especially with dementia, as described by Pitkala[4].

The wide variation in hypnotic prescription prevalence between participating countries might reflect different clinical practices regarding hypnotic prescription.

In our study, we found no association between dementia and medication prescription. Poorer analgesic treatment for persons with dementia has been documented [25], but for opioid treatment, a shift in awareness has been noticed in the last decade[26],[27]. Our findings might be considered confirmatory of this trend, suggesting that residents with dementia are as likely as those without to receive opioids. Moreover, in Finland, the increase in opioid prescription is established concomitantly with the decrease in psychotropic medication[4].

Residents dying of cancer are 3.5 times more likely to receive opioids, compared to residents who died of other diseases. Opioid treatment for non-malignant pain remains a controversial issue[28]. Guidelines advise caregivers to remain vigilant about long-term side effects and opioid dependence[29]. As a consequence, physicians and their patients feel insecure about misuse and addiction[30] and tend to have a wait-and-see approach towards opioids. Physicians often doubt the objectivity of non-malignant pain complaints, the appropriateness of opioid therapy and feel less confident and more concerned to prescribe opioids for non-malignant pain, compared to cancer-

related pain. They attribute their reluctance to a lack of knowledge and training[31]. This may explain why the discrepancy in opioid prescription between cancer pain and non-malignant pain is more explicit in countries with lower palliative care knowledge.

2.4.3 Strengths and limitations

To our knowledge, this is the first European cross-country study concerning opioid, antipsychotic and hypnotic prescription in the dying phase in LTCF residents. The large population sample, the cross-country survey design, the focus on all LTCF deaths, regardless of cause of death and the high response rate are the main strengths of this study. Nevertheless, some limitations have to be acknowledged. We excluded 305 residents who died outside the LTCF. Some of them were transferred to the hospital for further diagnosing, for symptom control, because an exacerbation of their general condition or because a life-threatening situation occurred. This exclusion may lead to a bias and underestimate the medication use in the dying phase. Secondly, the study only provided dichotomous data on medication prescription: whether or not, an opioid, antipsychotic or hypnotic was prescribed in the last three days of life. We had no information about the indication, the prescribed dosage nor the prescription date. Higher dose of opioid prescription is not an unambiguous proof of improved treatment since overuse or misuse of opioids cannot be excluded based on the data we ‘ve got available. The link between the residents’ symptom burden and drug prescription needs further consideration. Whether or not death was expected, is not taken into account in our study. Since this information was provided by the physicians’ questionnaire, with a lower response rate (68,3 %), we did not take it into consideration to avoid drop-out. Finally, although the response rate differs between countries, it was only the low response rate in England which hampers the generalisation in England. Furthermore, The non-respondents analysis for care

staff showed no significant differences in the residents demographic and clinical characteristics and the stay in the nursing home between residents with and without participating nursing staff.

2.4.4 Implications for clinicians and policymakers

Our study pointed to the existence of important differences in medication prescription in the last three days of life of LTCF residents between participating European countries. Further research is needed to explain these differences. Disseminating correct information on the indication of use to the broad public and developing palliative care knowledge amongst health care professionals remain important points of action.

The existing difference in medication prescription between cancer and non-cancer patients is a concern both for clinical practice and research. In palliative care, clinicians should focus on the symptoms as such, and aim to improve the patients comfort, regardless of the underlying cause. Symptom relieve is not justified because a patient has cancer, but because he or she is suffering. In any case, palliative guidelines need to be developed or refined for older patients and those dying from non-cancer diseases, taking the multi-morbidity, the specific responsiveness and vulnerability for side effects of older patients into account.

Key points

- We found large differences between European countries in opioid, antipsychotic and hypnotic prescription in end-of-life in LTCFs.

- These differences remained significant after statistical adjustment for LTCF type and resident characteristics.
- Further research is needed to refine palliative care for European older citizens, dying in LTCFs, especially for those, dying from non-cancer diseases.

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Chapter 3: Opioid underuse in terminal care of long-term care facility residents with pain and/or dyspnoea. A cross-sectional PACE-survey in 6 European countries

Marc Tanghe[1], Nele Van Den Noortgate[2], Luc Deliens[3], Tinne Smets[3], Bregje Onwuteaka-Philipsen[4], Katarzyna Szczerbińska[5], Harriet Finne-Soveri[6], Sheila Payne[7], Giovanni Gambassi[8], Lieve Van den Block[3], Ruth Piers[2]; on behalf of PACE

1 End-of-life care research group, Vrije Universiteit Brussel & Ghent University, Ghent, Belgium.
2 Ghent University and Ghent University Hospital, Department of geriatric medicine, Ghent, Belgium
3 End-of-life care research group, Vrije Universiteit Brussel & Ghent University, Brussels, Belgium.
4 Amsterdam UMC, Vrije Universiteit Amsterdam, department of public and occupational health, Amsterdam Public Health Research Institute, Expertise Center for Palliative Care, Amsterdam, The Netherlands
5 Jagiellonian University Medical College, Kraków, Poland
6 National Institute for Health and welfare, Helsinki, Finland
7 International Observatory on End of Life Care, Division of Health Research, Lancaster University, Lancaster, United Kingdom
8 Fondazione Policlinico Universitario A. Gemelli, IRCCS and Università Cattolica del Sacro Cuore, Roma, Italy

Opioid underuse in terminal care of long-term care facility residents with pain and/or dyspnoea. A cross-sectional PACE-survey in 6 European countries. Tanghe M., Van Den Noortgate N., Deliens L., Smets T ., Onwuteaka-Philipsen Szczerbińska K., Finne-Soveri H., Payne S, Gambassi G., Van den Block L., Piers R. Palliat Med. 2020;34(6):784-794. doi:10.1177/0269216320910332

Abstract

Background/objectives

Opioids relieve symptoms in terminal care. We studied opioid underuse in long-term care facilities, defined as residents without opioid prescription despite pain and/or dyspnoea, three days prior to death.

Design and setting

In a proportionally stratified randomly selected sample of long-term care facilities in six EU countries, nurses and long-term care facility management completed structured after-death questionnaires within three months of residents' death.

Measurements

Nurses assessed pain/dyspnoea with CAD-EOLD and checked opioid prescription by chart review. We estimated opioid underuse per country and per symptom and calculated associations of opioid underuse by multilevel, multivariable analysis.

Results

Nurses' response rate was 81.6%, 95.7% for managers.

Of 901 deceased residents with pain/dyspnoea reported in the last week, 10.6 % had dyspnoea, 34.4 % had pain, 55.0 % had both symptoms.

Opioid underuse per country was 19.2 % [95 % CI: 12.9 - 27.2] in the Netherlands, 25.2 % (18.3 - 33.6) in Belgium, 29.3 % (16.9 -45.8) in England, 33.7 % (26.2 – 42.2) in Finland, 64.6 % (52.0 – 75.4) in Italy, 79.1 % [71.2 – 85.3] in Poland ($P < 0.001$).

Opioid underuse was 57.2 % (33.0 – 78.4) for dyspnoea, 41.2 % (95 % CI: 21.9 – 63.8) for pain and 37.4 % (19.4 – 59.6) for both symptoms ($P = 0.013$).

Odds of opioid underuse were lower (OR 0.33; 95 % CI: 0.20 – 0.54) when pain was assessed.

Conclusion

Opioid underuse differs between countries. Pain and dyspnoea should be formally assessed at the end of life and taken into account in physicians orders.

Key words

opioids, opioid underuse, older adults, nursing home, end-of-life.

Key statements

What is already known

- Palliative care guidelines recommend opioids to relieve pain or dyspnoea in the dying phase
- Symptom management in end-of life in long-term care facility residents is often suboptimal

What this paper adds

- A cross sectional survey of residents who died in their long-term care facility shows that 86,2% had symptoms which can be treated with opioids in the dying phase, of which 34.4% with pain, 10.6% had dyspnoea, 55.0% had both symptoms;
- Opioid underuse is more frequent in patients with dyspnoea in the dying phase and is associated with the lack of symptom assessment
- Opioid underuse in the dying phase of long-term care facility residents greatly differs between participating countries

Implications for practice

- Systematic symptom assessment is warranted in long-term care facility residents for optimising symptom relief in the dying phase
- The use of opioids for treating dyspnoea in the terminal phase should be considered more often

- The large variation of opioid underuse between countries suggests that each country may require its own policy to inform the public and health care professionals about appropriate use of opioids in the dying phase

3.1 Introduction

Symptom management in end-of-life care of long-term care facility residents is challenging, as symptoms evolve rapidly in the dying phase. Studies report pain prevalence up to 68-78 %[1]and prevalence of dyspnoea up to 52%[1] in the last week of life. Opioids should always be considered in the care of dying people[2] to manage pain[3] and dyspnoea[4, 5].

Recently, we reported a significant difference across six European countries in opioid prescription in the last three days of life in long-term care facilities, ranging between 18.5 % and 77.9 %[6]. The coexistence of high pain prevalence in the dying phase in long-term care facility residents and low opioid use in some countries is deplorable, while pain is mentioned as the symptom which can, with 46.3% to 84.7%[7] of residents, most often been totally relieved.

We aimed to identify residents' and long-term care facilities' characteristics associated with opioid underuse. Underuse is defined as the absence of initiation of an effective treatment in subjects with a medical condition or symptom for which one or several drug classes have demonstrated their efficacy[8]. Since palliative care guidelines[3],[9] recommend opioids to treat pain and dyspnoea in the dying phase, we defined opioid underuse as the absence of an opioid prescription in the last three days of life of residents suffering from pain and/or dyspnoea. The following research questions were addressed:

1) What is the prevalence of long-term care facility residents with underuse of opioids in 6 European countries?
2) What is the prevalence of long-term care facility residents with underuse of opioids for pain, dyspnoea and both symptoms?
3) Which characteristics, regardless of country, but related to the resident, the long-term care facility and the organisation of care, are associated with opioid underuse?

3.2 Methods

3.2.1 Study design, setting and participants

As part of the PACE project (**PA**lliative **C**are for the **E**lderly), we performed a cross-sectional survey describing the dying phase in long-term care facility residents in six European countries; the Netherlands, Belgium, England, Finland, Italy and Poland, in 2015. In this paper, 'long-term care facility' refers to 'collective institutional settings where care, on-site provision of personal assistance of daily living, and on-site or off-site provision of nursing and medical care is provided for older people who live there, 24 hours a day, 7 days a week, for an undefined period of time[10],[11]. National lists of certified care homes were stratified by region, facility type and bed capacity. Then long-term care facilities were sampled randomly within each of the strata, to guarantee nation-wide representativeness. These facilities reported all residents deceased in and outside of the facility in the previous three month period. The study methods are described in detail in the published study protocol[12].

Through an anonymised procedure, structured after-death questionnaires, regarding each deceased resident were sent to the nurse or care assistant most involved in the residents' daily care. In this paper, this questionnaire is referred to as the nurses questionnaire. The long-term care facility management completed a questionnaire concerning the deceased resident and a questionnaire concerning the long-term care facility and the provision of palliative care. For this paper, we selected residents who died in their long-term care facility and of whom the nurses questionnaire retrospectively reported pain or dyspnoea in the last week of life. The researchers, all experienced nurses and physicians with backgrounds in geriatric medicine, nursing home care and palliative care, scrutinised these questionnaires for variables which could hypothetically be associated with opioid prescription. On resident level we examined medical and nursing

treatments, factors related to advance care planning and communication with staff and family. On facility level we looked for factors related to the organisation of palliative care delivery and the availability of opioids.

3.2.2 Data collection and measurements

Opioid underuse was calculated as the estimated prevalence of deceased residents with pain and/or dyspnoea in the last week of life and without an opioid prescription. Pain and/or dyspnoea were evaluated on the nurses questionnaire by the score on the pain and dyspnoea items of the Comfort Assessment in Dying with Dementia (CAD-EOLD) scale, a list of 14 symptoms to be scored as “not at all”, “somewhat” or “a lot”. The nurses conducted a chart review to check whether or not opioids (e.g. Morphine, Oxycodone, Hydromorphone, Fentanyl, Buprenorphine, Tramadol) had been prescribed to the resident in the last 72 hours of life.

Resident characteristics such as gender, age and length of stay, were available in the long-term care facility managements questionnaire. From the nurses questionnaire, we extracted data on functional and cognitive status, whether or not the resident’s pain was assessed in the last week of life, the cause of death and the existence of any advance care planning.

Functional and cognitive status one month before death was estimated by the Bedford Alzheimer Nursing Severity scale (BANS S), a rating scale, developed for grading the severity of dementia[13]. A resident was classified as a person with dementia if the nurse and/or the physician identified the resident as having symptoms of dementia. Medical or nursing procedures, including pain assessment, received in the last week of life and cause of death were determined by means of checklists, mentioned in the questionnaires.

With regard to advance care planning, the nurses indicated on their questionnaire, whether or not the resident had ever expressed his/her specific preferences about a medical treatment he/she did (not) want during the last phase of life; if the nurse ever spoke with the resident about medical treatments or about the preferred course of care; if she -prior to a decision- spoke with a resident's relative about medical treatments; if the resident, in a prior living will, gave a power to a third party to take decisions for him/her in case he/she would be no longer competent to do so; whether a contact person was mentioned in the resident's records. Nurses also indicated the degree of consensus on care and treatment in the last month of the resident's life: between the long-term care facility staff themselves, the relatives amongst themselves or amongst caregivers and relatives. Based on the long-term care facility managements' questionnaire, we investigated the Long-term care facilities' staffing type and the existence of palliative care provisions: whether the facility had specific written guidelines with regard to providing palliative care; whether a specialist palliative care team was present in the facility (employed in the facility); whether an external specialist palliative care team was available for advice, and if opioids were available 24/7.

3.2.3 Statistical analysis

Descriptive statistics are used to study country, Long-term care facilities and resident characteristics. Differences between residents with opioid prescription versus residents with opioid underuse were explored by means of binomial regression.

Multilevel binary logistic regression analyses were applied to investigate opioid underuse and corresponding 95% confidence interval (CI). The prevalence per country was estimated by a first regression model with country as fixed effect and long-term care facility as random effect. To estimate the underuse prevalence per symptom, a second model in which symptom category (pain,

dyspnoea or both) was defined as a fixed effect and country and long-term care facility (nested in country) as random effect. A third regression model was built to explore associations between underuse and clinical factors, regardless of country. We included all variables, which could hypothetically be associated with opioid prescription, showing a P value < 0.100 in univariable multilevel analysis and subsequently followed a backward stepwise procedure. As we were interested in associations with resident's, long-term care facility and advance care planning -related factors, we did not include country as a fixed effect but as a random effect to account for the data structure.

In a post-mortem study, the terminal phase is obvious. In daily practice, however, death is only predictable in about 61 % of cases[13]. To overcome this problem, we repeated the multilevel regression model building procedure in the 500 cases of residents where the physician had recognised the terminal phase in the last week of life. Statistical analyses were performed in SPSS 24.

3.2.4 Ethics

The research teams in all participating countries obtained ethical approval from their respective ethics committees. All respondents remained anonymous and participated voluntarily. Returning the questionnaire was considered as consent to participate.

3.3 Results

3.3.1 Response rate and study populations characteristics

Response rate was 81.6 % for nurses' and 95.7% for facility managers' questionnaires. Of all 1045 deceased residents with completed symptom scores in the last week of life, 144 had neither pain nor dyspnoea recorded and were consequently left out of this study (**Figure 1**).

Of the remaining 901 residents, 308 residents (34.4) suffered from pain, 93 residents (10.6) had dyspnoea and 500 residents (55.0%) had both symptoms. The residents' and Long-term care facilities' characteristics are shown in **Table 1** and **2**. Two thirds of the study population was female, mean age was 85.5 years and 71.9 % had dementia. Cerebrovascular or cardiovascular disease was the cause of death in 32.2 %, respiratory disease in 10.9 %, cancer in 8.3 %. In 20.3 %, dementia was designated as cause of death.

In 77.0 % of cases, there was no evidence of either wishes or preferences about medical treatment in end-of-life. An official representative was appointed in 35.9 %, although in 88.9 %, a contact person was recorded to consult, prior to medical decisions. In 27.3 % of cases, the nurses talked with the resident about medical treatments or the preferred course of care, in 18.7 % even on several occasions. They spoke with the residents' relatives about medical treatments the resident would (not) want in 62.8 % of cases. Full consensus on care and treatment in the last month of life existed amongst long-term care facility staff in 83.9 % of cases, amongst family/representatives in 69.9 %, and amongst family and staff in 72.8 % of cases.

The Long-term care facilities had written palliative care guidelines in 54.4 % of the residents and a palliative care team within the care home in 24.3 %. In 59.4 % of cases, the LTFC teams could seek external palliative care advice. Opioids were available to all residents in 74.4 %, to some residents in 16.7 % while 8.9 % of residents lived in a LTFC were opioids were never available.

Figure 1: Study population selection process

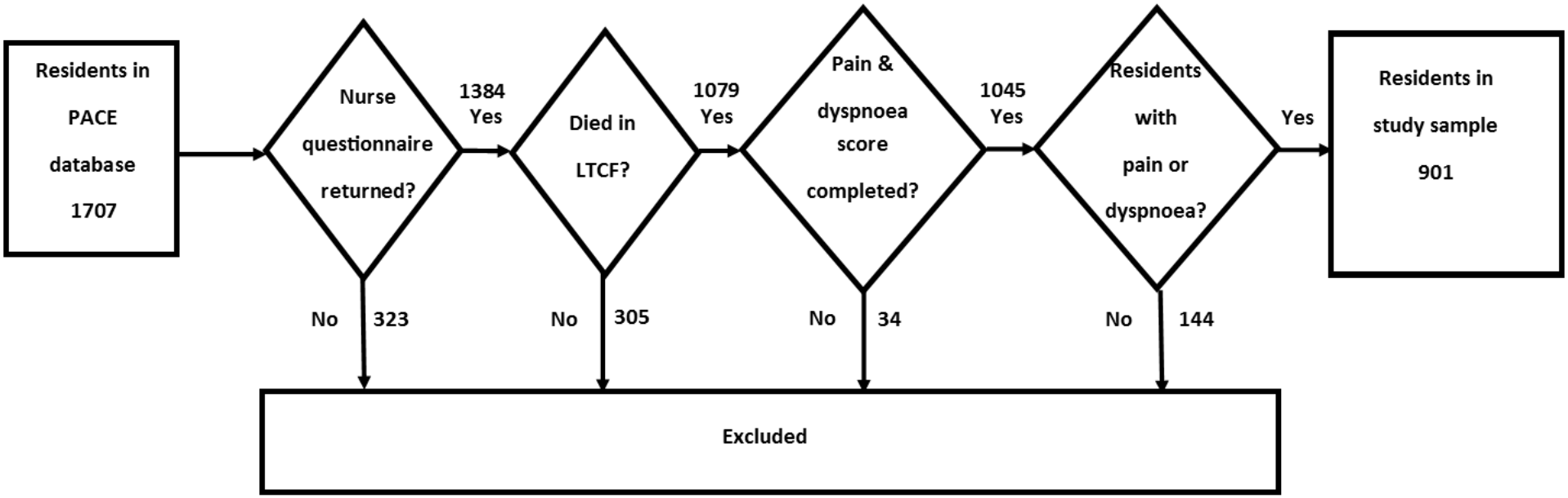


Table 1. Resident characteristics and comparison between subgroups with opioid prescription versus opioid underuse

		% (n = 901)	Opioid Prescription % (n=498)	Opioid UNDERuse % (n=373)	P value
RESIDENTS' CHARACTERISTICS AND SYMPTOM BURDEN					
Gender:	Female	66.9	67.9	65.6	0.373 [a]
(missing n = 61)	Male	33.1	32.1	34.4	
Age resident in years	≥ 90	34.6	36.0	32.8	0.477 [a]
	80 - 89	47.9	48.7	46.9	
(missing n = 62)	< 80	17.5	15.3	20.3	
Length of stay in days: mean [SD] (missing n =30)		908 [1124]	904 [999]	912 [1273]	0.067[a]
What was the residents total BANS-S[b] score? Mean [SD] (missing n = 42)		20.25 (4.48)	19.88 (4.31)	20.74 (4.66)	0.874[a]
Was the resident suffering from dementia [c]?	Yes	71.9	71.4	72.6	0.797 [a]
(missing n = 36)	No	28.1	28.6	27.4	
Did the resident receive a pain assessment in the last week of life? Yes		57.7	61.6	52.4	0.001 [a]
(missing n = 43)	No/unknown[f]	42.3	38.4	47.6	
Pain burden	Not at all[d]	10.6	8.8	12.9	< 0.001 [a]
	Somewhat	68.9	65.3	73.7	
(missing n = 30)	A lot	20.5	25.9	13.4	
Dyspnoea burden	Not at all[e]	34.4	36.3	31.9	0.608 [a]
	Somewhat	45.7	43.8	48.3	
(missing n = 30)	A lot	19.9	19.9	19.8	
Cause of death	Cancer	8.3	11.7	3.8	< 0.001 [a]
	Cerebro- / Cardiovascular	32.2	21.9	46.0	
	Respiratory disease	10.9	12.3	9.0	
	Dementia	20.3	23.7	15.6	
(missing n = 47)	Other	28.3	30.5	25.5	
RESIDENTS' ADVANCE CARE PLANNING-RELATED ITEMS					
Did the resident ever express specific preferences about a medical treatment he/she did (not) want during the last phase of life?					
	No/unknown[f]	77.0	72.2	83.3	0.258 [a]
(missing n = 37)	Yes	23.0	27.8	16.7	
Did you ever speak with the resident about medical treatments or about the preferred course of care?	Yes, Only once	8.6	8.8	8.3	0.116 [a]
	Yes, several times	18.7	22.8	13.0	
(missing n=50)	No	72.7	68.4	78.7	
Did you - prior to a decision - speak with a relative of the resident about medical treatments he or she would or would not want in the last phase of life or about the preferred course of care in the last phase of life?	No	37.2	27.5	50.4	< 0.001 [a]
(missing n = 49)	Yes	62.8	72.5	49.6	
Did the resident, in a prior living will, give a power to a third party to take decisions for him or her in case he or she would be no longer competent to do so?	No	64.1	62.8	65.4	0.631 [a]
(missing n =236)	Yes	35.9	37.2	34.6	
Was a contact person mentioned in the resident's records, which you were able to consult when taking decisions about the end of life in case the resident would be unable to do so?	No	11.1	8.2	15.1	0.007 [a]
(missing n =63)	Yes	88.9	91.8	84.9	

Consensus on care and treatment amongst LTCF staff (missing n = 70)	Full consensus	83.9	83.7	84.2	0.385 [a]
	No full consensus	16.1	16.3	15.8	
Consensus on care and treatment amongst family (missing n = 83)	Full consensus	69.9	72.4	66.6	0.068 [a]
	No full consensus	30.1	27.6	33.4	
Consensus on care and treatment amongst all (missing n = 78)	Full consensus	72.8	72.0	73.8	0.631 [a]
	No full consensus	27.2	28.0	27.2	

[a] Calculated with binary logistic regression.
[b] Bedford Alzheimer Nursing Severity Scale (BANS-S). 7 items scale, scores range 7 -24, Higher scores indicate higher functional disability and dependency
[c] in this survey, a resident "with dementia" is a resident which is designated as "suffering from dementia" by the nurse, the physician or both.
[d] These residents were included because they had dyspnoea
[e] These residents were included because they had pain

[f]: If the respondent did not know the answer to the question, it was categorised as a negative answer (≠ missing value)

Table 2. Long term care facility characteristics and comparison between subgroups with opioid prescription versus opioid underuse

		% (n = 901)	Opioid Prescription % (n=498)	Opioid UNDERuse % (n=373)	P value
LONG-TERM CARE FACILITIES' CHARACTERISTICS					
Staffing type of long term care facility	Physicians and nurses on site	30.5	24.8	37.7	0.027 [a]
	Physicians offsite, nurses on site	67.0	72.6	59.9	
(missing n = 30)	Nurses and physicians offsite	2.5	2.5	2.4	
Does the facility have specific written guidelines with regard to providing palliative care?	No/unknown[f]	45.6	34.8	59.6	< 0.001 [a]
(missing n = 83)	Yes	54.4	65.2	40.4	
Is there a specialist palliative care team present in your facility (employed in your facility)?	No	75.7	69.4	83.8	0.002 [a]
(missing n = 85)	Yes	24.3	30.6	16.2	
Is specialist palliative care advice available to professionals delivering palliative care in your facility?	No	40.6	36.5	46.1	0.095 [a]
(missing n = 90)	Yes	59.4	63.5	53.9	
Are opioids available 24/7 for residents in need of palliative care in your facility?	No, never	8.9	2.8	16.8	< 0.001 [a]
	For some / most residents	16.7	15.6	18.2	
(missing n = 70)	Yes, for all residents	74.4	81.6	65.0	
COUNTRY					
	The Netherlands	19.1	26.7	8.8	< 0.001 [a]
	Belgium	20.8	27.3	12.1	
	England	5.1	6.2	2.5	
	Finland	19.9	22.9	15.8	
	Italy	13.0	8.2	19.3	
(missing n = 30)	Poland	22.3	8.6	40.5	

[a] Calculated with binary logistic regression.

[f]: If the respondent did not know the answer to the question, it was categorised as a negative answer (≠ missing value)

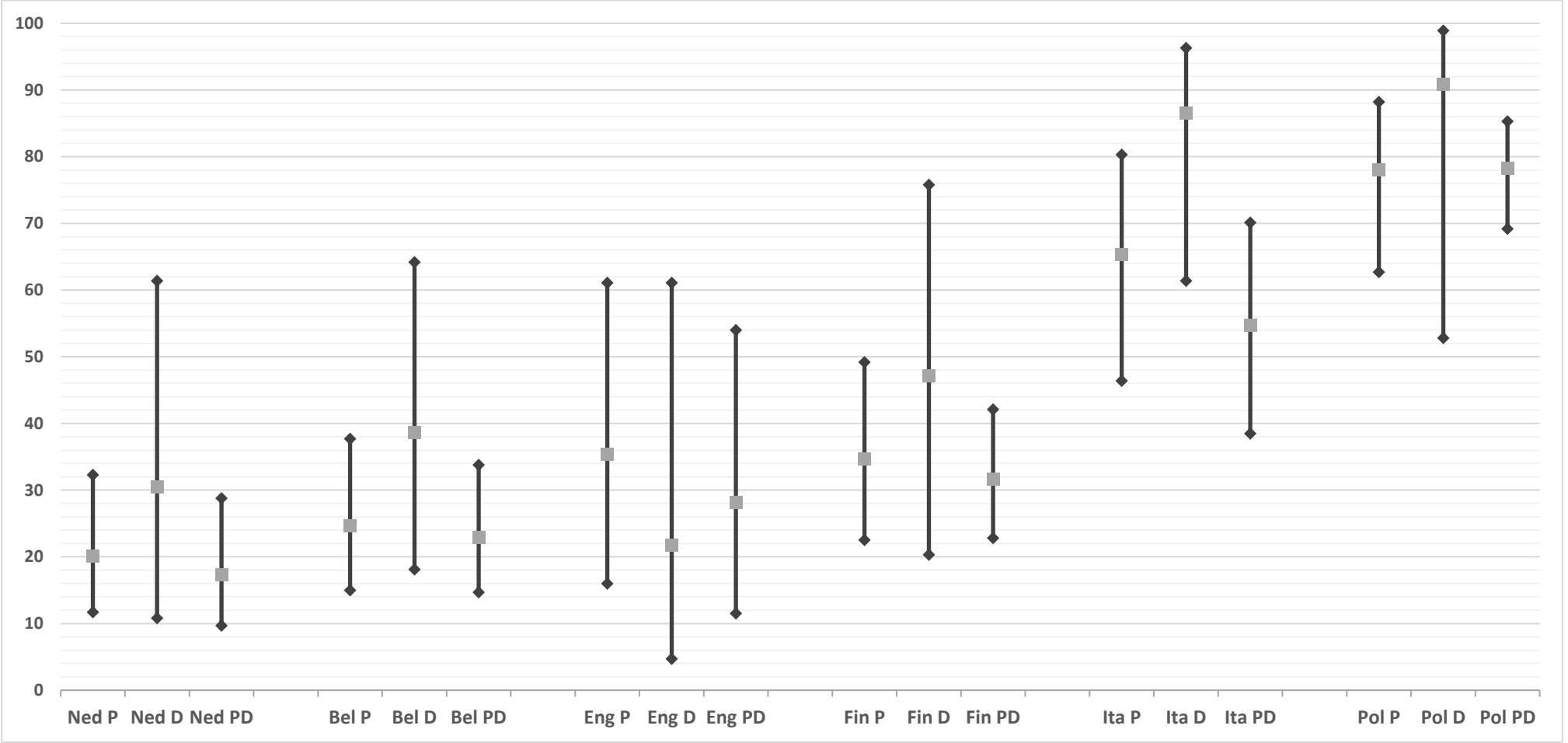
3.3.2 Prevalence of opioid underuse per country and per symptom

The estimated percentage of overall opioid underuse differed significantly between countries (P < 0.001). Estimated percentages ranged from 19.2 % (95 % CI: 12.9 - 27.7) in the Netherlands, 25.2 % (95 % CI: 18.3 - 33.6) in Belgium, 29.3 % (95 % CI: 16.9 -45.8) in England, 33.7 % (95 % CI: 26.2 – 42.2) in Finland, 64.6 % (95 % CI: 52.0 – 75.4) in Italy to 79.1 % (95 % CI: 71.2 – 85.3) in Poland.

The estimated percentage of overall opioid underuse also differed significantly per symptom (P = 0.013) with 57.2 % (95 % CI: 33.0 – 78.4) in residents with dyspnoea, 41.2 % (95 % CI: 21.9 – 63.8) in residents with pain, and 37.4 % (95 % CI: 19.4 – 59.6) in residents with both pain and dyspnoea.

The estimated percentage of opioid underuse per country and per symptom burden is shown in **Figure 2**. In every country, except England, estimated opioid underuse was the highest in residents with dyspnoea without pain.

Figure 2. Estimated percentage and 95% CI of opioid underuse per country and per symptom



Ned: the Netherlands Bel: Belgium Eng: England Fin: Finland Ita: Italy Pol: Poland

P: Pain, no dyspnoea (n =300, P value < 0.001) D: Dyspnoea, no pain (n= 92, P value = 0.011) PD: Pain & dyspnoea (n = 479, P value < 0.001)

Calculated with multilevel binary logistic regression. Opioid underuse = resident with pain/dyspnoea and without opioid prescription.

3.3.3 Residents' and long-term care facilities' characteristics associated with opioid underuse

The residents' and Long-term care facilities' characteristics associated with opioid underuse at the univariable multilevel analysis are also shown in Table 1 and 2. In the building procedure the long-term care facilities' staffing type, the residents' length of stay, the opioid availability in the long-term care facility, the cause of death and the residents' pain score dropped out. The final model, which optimally combined best model fit and case inclusion is presented in **Table 3**.

Odds for opioid underuse were three times lower in cases where pain was assessed during the last week of life (OR 0.33; 95 % CI: 0.20 – 0.54). No other variables showed significant associations.

Table 3: Clinical factors associated with opioid underuse in end of life of LTCF residents

		Opioid underuse	
		OR [95 % CI]	**P-value**
RESIDENTS' CHARACTERISTICS AND SYMPTOM BURDEN			
Did the resident receive a pain assessment during the last week of life?	*Yes*	0.33 [0.20 – 0.54]	< 0.001
(missing n =43)	*No/Unknown* [f]	Ref.	.
RESIDENTS' ADVANCE CARE PLANNING-RELATED ITEMS			
Did you - prior to a decision - speak with a relative of the resident about medical treatments he or she would (not)	*Yes*	0.82 [0.52 – 1.30]	0.400
want in the last phase of life or about the preferred course of care in the last phase of life? (missing n = 49)	*No*	Ref.	.
Was a contact person mentioned in the resident's records, which you were able to consult when taking decisions	Yes	0.89 [0.46 – 1.76]	0.746
about the end of life in case the resident would be unable to do so? (missing n = 63)	No	Ref.	.
Consensus representative or family amongst themselves (= family consensus)	*No full consensus*	1.28 [0.83 – 1.97]	0.257
(missing n = 83)	*Full consensus*	Ref.	.
LONG-TERM CARE FACILITIES' CHARACTERISTICS			
Does the facility have specific written guidelines with regard to providing palliative care?	*Yes*	1.02 [0.59 – 1.77]	0.943
(missing n = 83)	*No, Unknown* [f]	Ref.	.
Is there a specialist palliative care team present in your facility (employed in your facility)?	*Yes*	0.61 [0.31 – 1.15]	0.126
(missing n = 85)	*No*	Ref.	.
Is specialist palliative care advice available to professionals delivering palliative care in your facility?	Yes	1.13 [0.65 – 1.96]	0.666
(missing n = 90)	No	Ref.	.

Multilevel binary logistic regression with country and country*LTCF as random effect
model: n=691 Missing=210 P value of corrected model = 0.001.

[f]: If the respondent did not know the answer to the question, it was categorised as a negative answer (≠ missing value)

Table 4: Clinical factors associated with opioid underuse in cases where the physician recognised the terminal phase in last week of residents life

		Opioid underuse	
		OR [95 % CI]	**P-value**
RESIDENTS' CHARACTERISTICS AND SYMPTOM BURDEN			
Did the resident receive a pain assessment during the last week of life?	*Yes*	0.42 [0.22 – 1.00	0.051
(missing n = 24)	*No/Unknown*	Ref.	.
Pain burden (%)	Not at all[a]	3.90 [1.18 – 12.88]	0.026
	somewhat	2.65 [1.29 – 5.45]	0.008
(missing n = 19)	A lot	Ref.	.
Cause of death (%)	Dementia	5.90 [1.29 – 27.02]	0.059
	Respiratory disease	5.22 [0.96 – 28.46]	0.022
	Cerebro- / Cardiovascular	11.40 [2.59 - 50.16]	0.056
	Other	4.22 [0.95 – 18.78]	0.001
(missing n = 20)	Cancer	Ref	.
RESIDENTS' ADVANCE CARE PLANNING-RELATED ITEMS			
Was a contact person mentioned in the resident's records, which you were able to consult when taking decisions	Yes	0.76 [0.27 – 2.14]	0.608
about the end of life in case the resident would be unable to do so? (missing n = 39)	No	Ref	.
Consensus representative or family amongst themselves (= family consensus)	*No full consensus*	0.90 [0.47 – 1.74]	0.758
(missing n = 46)	*Full consensus*	Ref	.
LONG-TERM CARE FACILITIES' CHARACTERISTICS			
Does the facility have specific written guidelines with regard to providing palliative care?	*Yes*	1.36 [0.59 – 3.18]	0.468
(missing n = 45)	*No, Unknown*	Ref	.
Is there a specialist palliative care team present in your facility (employed in your facility)?	*Yes*	0.45 [0.16 – 1.25]	0.125
(missing n = 46)	*No*	Ref	.
Is specialist palliative care advice available to professionals delivering palliative care in your facility?(%)	Yes	1.27 [0.56 – 2.89]	0.567
(missing n = 29)	No	Ref	.

Multilevel multivariable logistic regression
Model: n=390 Missing=110 P value of corrected model = 0.015.

[a] These residents were included because they had dyspnoea

3.3.4 Residents' and Long-term care facilities' characteristics associated with opioid underuse in case the physician recognised the terminal phase

The final model in the subsample where the physician recognised the terminal phase, is presented in Table 4. Because of the high number of missing values on this variable and the reduced population sample, we did not use this as our main result. When the terminal phase was recognised, the odds of opioid underuse were significantly higher in residents with dyspnoea but without pain (OR 3.90; 95 % CI: 1.18 – 12.88) compared to those with pain. Odds of opioid underuse were also higher for residents dying of dementia (OR 5.90; 95 % CI: 1.29 – 27.02) and cerebro- and cardio-vascular disease (OR 11.40; 95 % CI: 2.59 – 50.16), compared to residents dying of cancer. The association between lack of pain assessment and opioid underuse remained.

3.4 Discussion

3.4.1 Principal findings

The estimated prevalence of opioid underuse in long-term care facility residents in the last 3 days of life strongly differs between countries, ranging from 19.2 % in the Netherlands to 79.1 % in Poland. The estimated prevalence of opioid underuse in the last three days of life was higher in residents with dyspnoea than in residents with pain and it was negatively associated with the receipt of a pain assessment in the last week of life.

3.4.2 Strengths and limitations

The cross-country survey design, the large population sample and the high response rate are the main strengths of this study. The inclusion of all residents who died in the long-term care facility, regardless of the cause of death, makes our results generalizable to all long-term care facility residents. The combination of data about symptom prevalence and medication prescription in the last week of life, created the possibility to identify cases of opioid underuse. These are situations in which the appropriateness of opioid prescription, regardless of the underlying disease, is well established.

The symptom burden is measured by proxy data, consequently we report on pain and dyspnoea as observed by the (assistant) nurses. Dyspnoea is observable, but pain is a purely subjective experience. Since formal pain assessment was often lacking, it is possible that symptom burden, and certainly pain, was underestimated.

As in any retrospective survey, some shortcomings have to be acknowledged.

In a post-mortem study, the terminal phase is obvious, while this is not always clear in daily practice. In order to minimize this problem, we applied the multilevel regression model building procedure to the subsample of residents where the physician had recognised that the resident was dying. This analysis, however, was hampered by the low number of included residents with returned physician's questionnaire. Moreover, due to the low response rate of physicians In this research project, we were obliged to disregard any data from the physicians questionnaire.

The risk of recollection bias, inherent to any retrospective survey was reduced by limiting the inclusion criteria to events occurred in the prior three months. The mean time between the residents death and the completion of the nurses questionnaire was 69 (SD ± 36) days. Moreover, we explicitly requested that the questionnaire was completed by the nurse or assistant nurse most

closely involved in the care of the deceased resident and based on the residents' nursing files and medication charts.

Since we excluded residents without a returned nurse questionnaire, selection bias cannot be excluded. We performed a non-response bias analysis for all available variables. Of the residents without a response to the nurse questionnaire, 66.7 % lived in a long-term care facility with palliative care guidelines, compared to 54.1 % of the residents with a response on the nurse questionnaire (P=0.028). No other significant differences were found.

3.4.3 Relation to other studies and possible explanations

The large difference in opioid underuse between countries in the last week of life is in accordance with earlier research, where we already established differences in opioid prescription prevalence in end-of-life care in long-term care facility residents between countries[6]. These discrepancies are explained by different reimbursement policies, variable attitudes towards opioids and by reluctance to communicate openly with patients and family members about end-of-life situations. Recently, Oosterveld-Vlug et al. identified the physicians' reluctance to recognize the terminal phase and the low prevalence of palliation as treatment goal in Poland and Italy[14]. The low opioid use in Italy and Poland was confirmed by other research[15],[16]. The opioid underuse we found in residents with pain, is in line with other research, since opioid use in the last days of life varied widely, from 44 %[1] up to 100 %, in long-term care facility residents where death was expected[17]. The opioid underuse in patients with dyspnoea, was higher than in the study of Hendriks et al., where morphine was found to be used in 69 % of cases [1].

Opioid underuse was the highest in residents with dyspnoea and without pain. This might be explained by the lack of knowledge and experience in the treatment of shortness of breath in the

last days of life, in particular when not related to cancer. Symptom burden of breathless patients with severe COPD is as high as among patients with advanced lung cancer, irrespective of their survival. But especially in chronic lung disease physicians fear the use of opioids[18]. Qualitative research has even established explicit discrepancies between the positive experiences of patients and family caregivers with opioid treatment for dyspnoea and the reluctance of their physicians to prescribe opioids for refractory dyspnoea, thus causing an important gap in care[19],[20]. Research established nevertheless the effectiveness and safety[21],[22] of opioids and existing palliative care guidelines explicitly mention their use in the treatment of dyspnoea at the end of life. In a disease course with possible exacerbations, however, end-of-life is often unpredictable[23], which might partially explain the low opioid prescription. Lack of transparency and disclosure about end-of life to patients and families is another possible explanation. A survey amongst pulmonologists[24] revealed that 48.5 % of them rarely introduced end-of-life discussions with their COPD patients, 89.5 % perceived these discussions as difficult or very difficult. Only 37.5 % used opioids to treat dyspnoea in the terminal phase.

Consistent with other research [25], [26-28], we found a negative association between opioid underuse and formal pain assessment in the last week of life. Pain assessment occurs more frequently in residents who receive opioids, but the causality remains unclear. Opioids might be prescribed because the pain is recognised, while systematic pain assessment improves the recognition of pain, even in people with impaired cognition[29, 30]. Or, on the contrary, systematic pain assessment can be routinely organised after the prescription of opioids, to evaluate their effect.

3.4.4 Implications for practice

Physicians involved in long-term care facility residents' care, and certainly in end-of-life care, should aim to relieve symptom burden. In end-of-life care, they should overcome their reluctances[31] to discuss end-of-life treatment options with patients and families and to prescribe opioids and consider opioids more often as a possibility to relieve pain and dyspnea. National authorities should, with support of the European Medicines Agency, inform healthcare professionals and patients about the correct indications of opioids.

Nurses and assistant nurses can[32] and should play a vital role as symptom assessors. Nurses can also initiate protocols for pain and symptom management [33] and take the lead in working with anticipatory medication prescriptions[34], thus optimising and accelerating comfort treatment[35] if the necessary measures are foreseen[36]. To achieve this, caregivers have to be provided with validated symptom assessment instruments and sufficiently trained in their use to enhance their confidence in symptom assessment and treatment. This will strengthen them[34] in dealing with family members' fears and physicians' reluctance to appropriate opioid use.

3.5 Conclusion

Opioid underuse for pain and/or dyspnoea in long-term care facility residents' last three days of life differs greatly between EU countries. Opioid underuse is strongly associated with the absence of symptom assessment. Implementation of palliative care in the long-term care facility, including systematic symptom assessment and clearer indications for the use of opioids can contribute to improving symptom management in the dying phase in Long-term care facilities through Europe.

Authors' contribution

Study concept and design:	Marc Tanghe, Nele Van Den Noortgate, Luc Deliens, Lieve Van den Block, Ruth Piers
Acquisition of data:	Marc Tanghe, Tinne Smets, Bregje Onwuteaka-Philipsen, Katarzyna Szczerbińska, Harriet Finne-Soveri, Sheila Payne, Giovanni Gambassi, Lieve Van den Block
Analysis and interpretation of data:	Marc Tanghe, Nele Van Den Noortgate, Ruth Piers
Drafting of the manuscript:	Marc Tanghe
Critical revision of the manuscript for important intellectual content:	Nele Van Den Noortgate, Luc Deliens, Lieve Van den Block, Ruth Piers, Tinne Smets, Bregje Onwuteaka-Philipsen, Katarzyna Szczerbińska, Harriet Finne-Soveri, Sheila Payne, Giovanni Gambassi
Steering committee:	Marc Tanghe, Nele Van Den Noortgate, Luc Deliens, Lieve Van den Block, Ruth Piers

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Part 2

Assessment of symptoms

Chapter 4: Comparing symptom ratings by staff and family carers in residents dying in long-term care facilities in three European countries, results from a PACE-survey

Marc Tanghe[1] RN Msc, Nele Van Den Noortgate[2] MD PhD, Luc Deliens[3] PhD, Tinne Smets[3] PhD, Bregje Onwuteaka-Philipsen[4] PhD, Harriet Finne-Soveri[5] PhD, Lieve Van den Block[3] PhD, Ruth Piers[2] MD PhD; on behalf of PACE

1 End-of-life care research group, Vrije Universiteit Brussel (VUB) & Ghent University, Ghent University, Ghent, Belgium.

2 Ghent University and Ghent University Hospital, department of Geriatrics, Ghent, Belgium

3 End-of-life care research group, Vrije Universiteit Brussel (VUB) & Ghent University, Vrije Universiteit Brussel (VUB), Brussels, Belgium.

4 Amsterdam UMC, Vrije Universiteit Amsterdam, department of public and occupational health, Amsterdam Public Health Research Institute, Expertise Center for Palliative Care, Amsterdam, The Netherlands

5 National Institute for Health and welfare, Helsinki, Finland

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Abstract

Context. Symptom management is essential in the end of life care of long-term care facility residents.

Objectives. To study discrepancies and possible associated factors in staff and family carers' symptom assessment scores for residents in the last week of life.

Methods. A post mortem survey in Belgium, the Netherlands and Finland: staff and family carers completed the "End-Of-Life in Dementia - Comfort Assessment in Dying" scale (EOLD-CAD), rating 14 symptoms on a 1 to 3-point scale. Higher scores reflect better comfort. We calculated mean paired differences in symptom, subscale and total scores at a group level and interrater agreement and percentage of perfect agreement at a resident level.

Results. Mean staff scores significantly reflected better comfort than those of family carers for the total EOLD-CAD (31.61 versus 29.81; P-value < 0.001) and for the physical distress (8.64 vs 7.62; P-value < 0.001) and dying symptoms (8.95 vs 8.25; P-value < 0.001) subscales. No significant differences were found for emotional distress and well-being The largest discrepancies were found for "gurgling", "discomfort", "restlessness" and "choking" for which staff answered "not at all" whereas the family carer answered "a lot", in respectively 9.5, 7.3, 6.7 and 6.1% of cases. Interrater agreement κ ranged from 0.106 to 0.204, the extent of perfect agreement from 40.8 for lack of serenity to 68.7 % for crying.

Conclusion. .

There is a need for improved communication between staff andfamily and discussion about symptom burden in the dying phase in long-term care facilities.

Key message

This article compares “End-Of-Life in Dementia - Comfort Assessment in Dying” (EOLD-CAD) symptom scores of long-term care facility residents in the last week of life by staff and family carers. Comfort, hetero-evaluated by staff, is higher than hetero-evaluated by family carers in total EOLD-CAD score, physical distress and dying symptom subscale scores.

Key words

Nursing home, end-of-life, symptom burden, palliative care, older people, pain.

4.1 Introduction

Long-term care facility residents suffer from multiple, complex symptoms[1, 2], making symptom management essential to maintain their comfort and quality of life, particularly in the dying phase. Systematic symptom assessment is essential to attain good symptom treatment[3].

The gold standard[4] of self-report for symptom assessment is not always applicable as long-term care facility residents are often cognitively impaired or lose their communication skills in the dying process. In these situations, staff have to rely on their own observations and on information from third parties.

Direct, multiple-symptom rating comparisons between family carers and staff in long-term care facilities is scarce. To our knowledge, only one study, based on 48 patients, has been published[5], showing small differences in mean scores with poor to moderate interrater agreement. The importance of this comparison extends beyond the question of validity: the complexity of daily care in long-term care facility residents with various degrees of comorbidity and cognitive impairment , makes efficient symptom assessment require more input than solely the assessment made by staff

during caregiving activities. Family carers often know the resident's reactions, behaviour and personality and spend larger timespans with the resident during various activities and situations. As such, family carers can meaningfully contribute to the residents' symptoms assessment. Moreover, family carer's perception of the comfort of dying of their loved one is essential for their own well-being and the quality of their own grieving process[6]. It is the staff's duty to guide family caregivers in the dying process, and to educate them about the expected symptoms and the way symptom management is performed.

The question remains as to what extent family carers' and staff's symptom ratings reflect a parallel estimation of the resident's comfort levelThis study aims to compare the symptom burden of long-term care facility residents in their last week of life, as rated by professional staff and family carers,. The following research questions are addressed:

> At a group level, what are the mean symptom scores of residents dying in long-term care facilities, scored by staff and by family carers? And is there any difference in mean symptom scores between staff and family carers?
>
> Also, which resident, staff and family carer characteristics are associated with symptom score discrepancies?
>
> At an individual level, what is the interrater agreement in symptom ratings between staff and family carers and what is the extent of the perfect match?

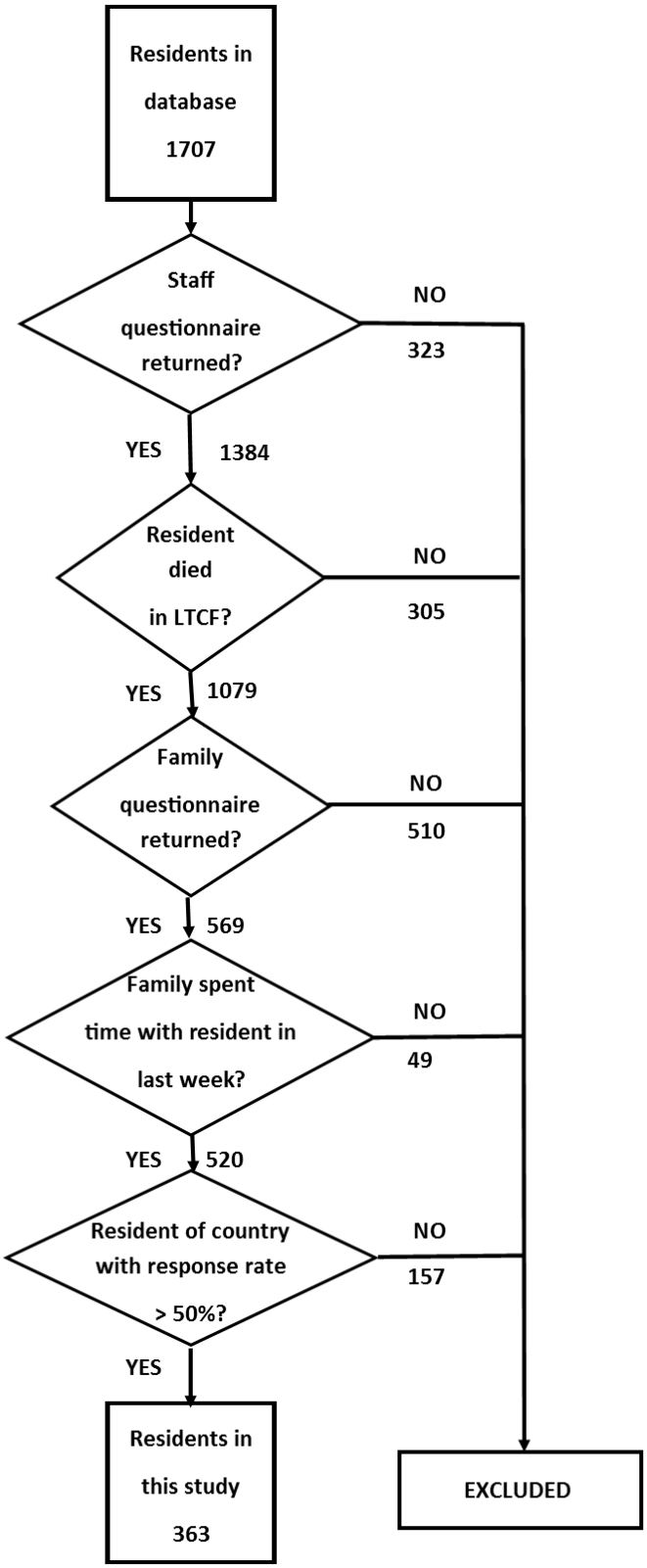
4.2 Methods

4.2.1 Study design, setting and participants

In six European countries participating in the PACE study (**PA**lliative **C**are for the **E**lderly), Belgium, Finland, the Netherlands,Italy, Poland and England, a cross-sectional survey was undertaken to describe the palliative care and end-of-life care delivery in long-term care facility residents. In this paper, 'long-term care facility' refers to 'collective institutional settings where care, on-site provision of personal assistance of daily living and nursing care, and on-site or off-site provision of medical care is provided for older people living there [(7), (8)]. Long-term care facilities were recruited by means of proportionally stratified random sample to guarantee nation-wide representativeness. All residents who died in three months before recruitment were retrospectively included. The study methods are described in detail in the published study protocol[(9)].

For each deceased resident, structured, after-death questionnaires were sent to the nurse or care assistant most involved in the residents daily care (staff questionnaire) and to a relative or other person, identified by the long-term care facility administration as the person most involved in the resident's care (family carers questionnaire). We selected the residents with a returned staff questionnaire, who died in their long-term care facility, with a returned family carer questionnaire, of whom the family carer spent time with the resident in the last week of life, and who resided in Belgium, Finland or the Netherlands; countries for which the staff and family carer response rate exceeded 50 %. (Figure 1).

Figure 1. Inclusion process for this study



4.2.2 Data collection and measurements

4.2.2.1 Symptom burden

Staff and family carers scored the residents' symptom burden by means of the EOLD-CAD (End-Of-Life in Dementia - Comfort Assessment in Dying)[10], developed and recommended[11] for use in end-of-life care for residents with and without dementia. The EOLD-CAD consists of a list of 14 symptoms, scored as "not at all", "somewhat" or "a lot" present. These scores were numerically transformed with higher scores reflecting higher comfort. Burdensome symptoms received a score of 3 for "not at all" to 1 for "a lot". Signs of comfort like peace, calm and serenity were reverse coded with a score of 3 for "a lot" to 1 for "not at all" and are, as a consequence, interpreted as lack of peace, lack of calm and lack of serenity. Four EOLD-CAD subscales have been validated. The physical distress subscale is a summation of the scores for discomfort, pain, shortness of breath and restlessness; emotional distress a summation of the anxiety, fear, crying and moaning scores; the dying symptoms subscale is a summation of choking, gurgling, difficulty swallowing and shortness of breath. Scores of these subscales ranged from four to twelve. The wellbeing subscale, finally, is the summation of the reverse coded serenity, peace and calm scores, with a subscale score ranging from 3 to 9.

4.2.2.2 Covariates

Functional and cognitive status was rated by the Bedford Alzheimer Nursing Severity scale (BANS S), developed for grading dementia[12] severity and comprising cognitive and functional items. Higher scores indicate higher functional disability and dependency. A resident "with dementia" was defined as a resident to whom the nurse and/or the physician referred to as a resident with

dementia. Cause of death was determined using a predefined checklist. Sentinel events were identified by the probe question if the resident, during the last month of life, suffered from one or more of the diseases or events mentioned in the checklist.

4.2.2.3 Statistical analysis

On the group level, descriptive statistics were used to assess resident, staff and carer characteristics and to calculate mean scores for all EOLD-CAD symptoms, subscales and total scores. The score difference was calculated by paired substraction of the family carer's score from the staff's score per individual resident. The mean paired difference was calculated over the total sample. To assess factors associated with mean paired score differences between staff and carers, a multilevel multinomial logistic regression model was built. At first, we developed a preliminary model (**appendix 1**) for each EOLD-CAD subscale, with the subscale score difference between staff and carers as dependent variable and residents, staffs and carers characteristics as independent variable. Country was included as fixed effect to compare data between countries, long-term care facility was defined as a random effect. Subsequently, we left out the independent variables without significant association with any subscale score difference, and the cause of death because of the overlap with the sentinel events and to reduce the number of categories in the model. We took the Holm-Bonferoni correction for multiple analysis into account. Associated factors were calculated for the entire survey population.

On the individual resident level analysis, interrater agreement was calculated with the kappa coefficient, showing the interrater agreement beyond chance. Kappa coefficients below 0.2 are considered as slight agreement, between 0.2 and 0.4 as fair agreement, between 0.4 and 0.6 as moderate agreement[13]. We also calculated the percentage of perfect match, where the individual

rating by staff and family carer per symptom was identical on the 3-point scale. Statistical analyses were performed in SPSS 24.

4.2.2.4 Ethics

The research teams in all participating countries obtained ethical approval from their respective ethics committees. All respondents remained anonymous and participated voluntarily. Returning the questionnaire was considered as consent to participate.

4.3 Results

4.3.1 Response rate and study population

Staffs' response rates were 85.1% for Belgium, 95.1% for Finland and 67.5% for the Netherlands; family carers' response rates were 66.1 % for Belgium, 52.3 % for Finland and 64.3 % for the Netherlands. This analysis included the scores for 145 Belgian, 101 Finnish and 117 Dutch residents.

4.3.2 Resident, staff and carer characteristics

Mean resident's age at the time of death was 87.4 (± 7.5) years. In 69.7 % of cases, the resident had dementia, and dementia was designated as the cause of death in 29.5% of cases. The most prevalent sentinel events were eating or drinking disorders in 29.2%, pneumonia in 28.4% and a febrile episode other than pneumonia in 25.3% of cases (Table 1).

Staff's mean age was 42.9 (± 10.9) years, with a mean experience in care of 13.8 years. In 72.0% of cases, the respondent was a registered nurse and 28% had an other function, mainly as an assistant-nurse or care assistant.

The family carer's mean age was 62.2 (± 10.4) years. The time spent in the residents presence during the last week of life was up to 7 hours for 27.3% of the carers, 50.9 % spent more than 15 hours in the resident's presence.

In the non-respondent analysis (**Appendix 2**) only the prevalence of dementia showed a significant difference, with 77% in the residents without family carer's response versus 68,8%. No other differences in resident and staff characteristics were found, and no significant differences in the staff's symptom ratings were found.

Table 1. Characteristics of residents, staff and family carers

Resident characteristics (N=363)		**n**	**%**
Country	Belgium	145	39.9
	Finland	101	27.8
(missing n=0)	The Netherlands	117	32.2
Residents' *mean age (SD) (missing n=26)*		87.4 (7.5)	
Mean length of stay in years (SD) *(missing n=30)*		2.9 (3.1)	
Mean total BANS-S score[a] (SD) *(missing n=1)*		19.0 (4.4)	
Dementia status[b]	Yes	253	69.7
(missing n=0)	No	110	30.3
Sentinel events in the last month of life	None	26	7.2
	Pneumonia	103	28.4
	Febrile episode (≠ pneumonia)	92	25.3
	Eating/drinking disorder	106	29.2
	Stroke	4	1.1
	Cancer	12	3.3
(missing n=0)	Other (fall, fracture)	20	5.5
Staff characteristics (N=363)		**n**	**%**
Staffs' mean age (SD*) (missing n=5)*		42.9 (10.9)	
Mean nursing care experience in years (SD) (missing n=12)		13.8 (10.1)	
Current function	Registered nurse	260	72.0
(missing n=2)	other	101	28.0
Palliative care training	None	86	23.8
	Yes, as part of pre-registration nurse training	105	29.1
	Yes, additional palliative care training	145	40.2
(missing n=2)	Other	25	6.9
Family carer characteristics(N=363)		**n**	**%**
Family carers' mean age (SD) (missing n=5)		62.2 (10.4)	
Relationship to Resident	Residents generation[c]	59	16.4
	Childs generation[d]	269	74.7
(missing n=4)	Grandchilds generation + othere[e]	32	8.9
Hours spent with resident in last week of life	≥ 28	92	25.3
	15-28	93	25.6
	8-14	79	21.8
(missing n=0)	≤7	99	27.3
Was the residents death expected?	Yes	151	41.9
	No	176	48.9
(missing n= 3)	Relative didn't know	33	9.2

[a] Bedford Alzheimer Nursing Severity Scale (BANS-S). 7 items scale, score range 7 -24.Higher scores indicate higher functional disability and dependency

[b] in this survey, a resident "with dementia" is a resident which is designated as "suffering from dementia" by the nurse, the physician or both.

[c] spouse, partner, sibling [d] child, nephew, niece [e] grandchild, legal representative, other

4.3.3 EOLD-CAD scores on population level and associated factors

The staff's versus family carer's score were 31.61 vs. 29.81 for total EOLD-CAD, 8.64 vs. 7.62 for the physical distress subscale, 9.76 vs. 9.56 for emotional distress, 8.95 vs. 8.25 for dying symptoms and 6.29 vs. 6.16 for wellbeing, with higher scores reflecting better comfort. Staff scores were significantly higher, assessing better comfort for the total EOLD-CAD score and for the physical distress and dying symptom subscales compared to family carer's scores ($P < 0.001$).

The mean symptom scores and 95% confidence intervals by staff and family carers are presented in Figure 2.

Most mean scores by staff were situated between 2 and 3, corresponding to symptom burden between "somewhat" and "not at all". The exception was the mean score of 1.94 for swallowing difficulties, which was the most burdensome symptom as scored by staff.

Five of the symptom scores by the family carers were situated between 1 and 2, corresponding with symptom burden described as "a lot" and " somewhat": 1.79 for difficulty swallowing, 1.83 for discomfort, 1.88 for pain, 1.92 for shortness of breath, and 1.93 for restlessness. Other symptoms were rated between 2 ("somewhat") and 3 ("not at all").

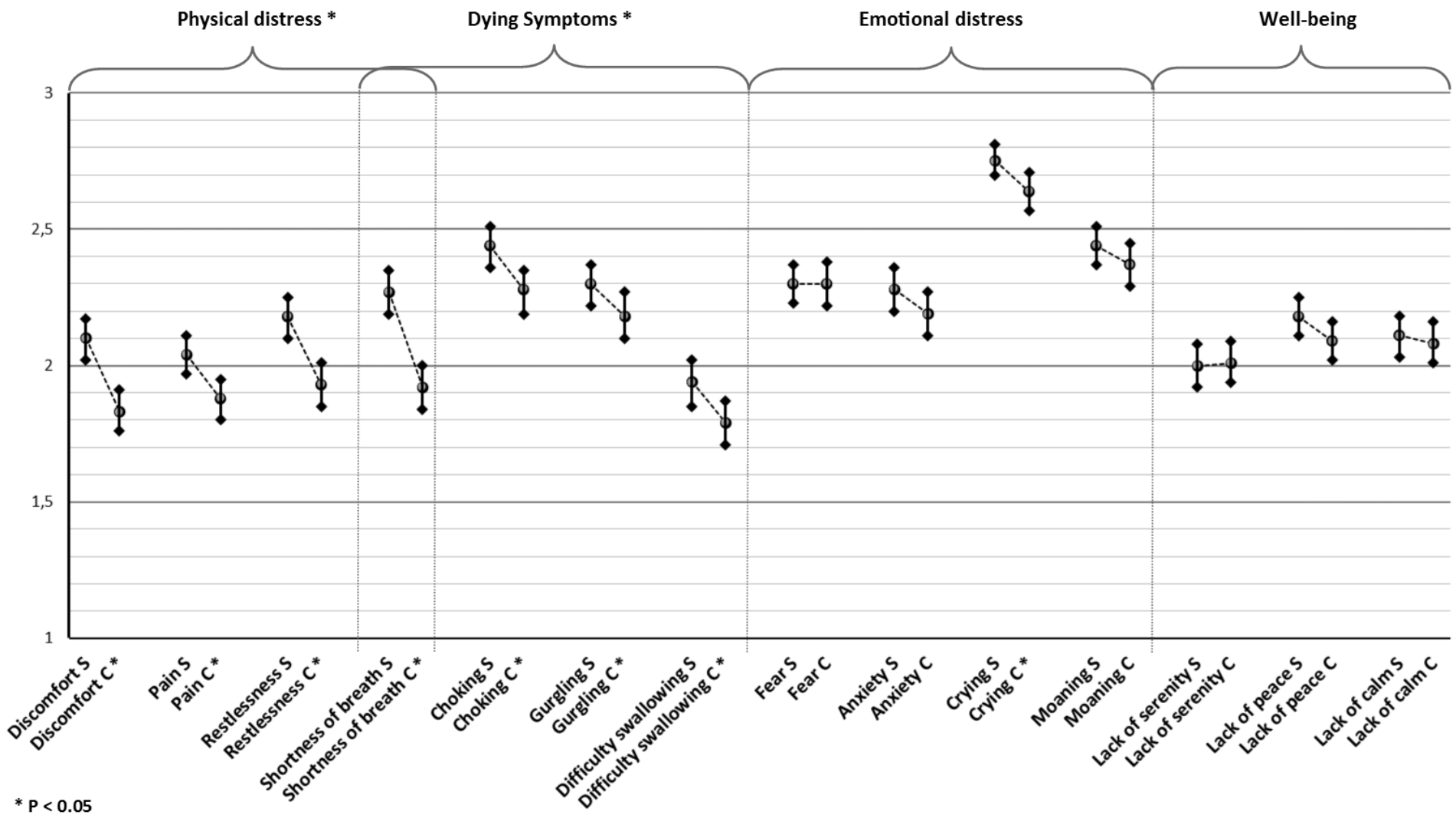
Most missing values occurred for discomfort (49), anxiety, moaning, lack of calm (34), lack of peace (33), lack of serenity (32) in the family carers' questionnaires and for discomfort (13) lack of serenity (12), lack of calm, fear, choking, difficulty swallowing (9) in the staffs' questionnaires.

On the group level, mean paired symptom scores (figure 2) differed significantly between staff and family carers for shortness of breath (0.35), discomfort (0.26), restlessness (0.25), pain (0.16), choking (0.16), difficulty swallowing (0.15) and crying (0.12). For all these symptoms, staff perceived higher levels of comfort than the family carers. All of the staff mean EOLD-CAD subscale scores and the total score surpassed the family carers' scores, albeit with small mean score differences, ranging from 6 to 17.5 % of the score range.

Length of stay, dementia status, the family carers expectation of the residents death and the included staff characteristics did not show any significant association with the subscale score differences in the preliminary model (Appendix 1). Country, resident age, sentinel events in the month prior to death and the family carer's relationship to the resident remained as independent variables.

On group level, total EOLD-CAD score differences decreased by 0.18 [95%CI: -0.3 - -0.1] point per year increase in residents age and increased by 4.74 points when the relative was a child, niece or nephew of the resident compared to family carers from the residents own generation (Table 2). In this case, the difference in the emotional distress subscale score also increased by 1.33 [0.5- 2.2] point when the relative was a child or nephew of the resident. Score differences between staff and family carers showed no other significant associations.

Figure 2. Mean EOLD-CAD symptom scores by staff (S) and family carers (C) and 95% CI



* P < 0.05

Symptom scores: 1: a lot, 2:somewhat; 3: not at all. Higher scores reflect more comfort.

Table 2: Associated factors with symptom score differences between staff and family carers

EOLD-CAD (SUB-)SCALES		PHYSICAL DISTRESS (n=273)		EMOTIONAL DISTRESS (n=288)		WELLBEING (n =292)		DYING SYMPTOMS (n =285)		TOTAL SCORE (n =255)	
		COEFF [95% CI]	P-Value	COEFF [95% CI]	P-Value	COEFF [95% CI]	P-Value	COEFF [95% CI]	P-Value	COEFF [95% CI]	P-Value
Country	The Netherlands	0.05 [-0.60 – 0.70]	0.882	0.44 [-0.21 – 1.09]	0.187	0.25 [-0.47 – 0.96]	0.498	0.24 [-0.51 – 0.99]	0.534	0.32 [-1.59 – 2.22]	0.742
	Finland	-0.78 [-1.43 - -0.13]	0.018	-0.06 [-0.72- - 0.60]	0.847	-0.23 [-0.94 – 0.48]	0.528	-0.56 [-1.31 – 0.18]	0.138	-2.34 [-4.27 - -0.42]	0.017
	Belgium	Ref.	.	Ref.	.	Ref.	.	Ref.	.	Ref.	.
Residents age		-0.04 [-0.08 - -0.00]	0.031	-0.04 [-0.08 – 0.00]	0.049	-0.01 [-0.05 – 0.4]	0.741	-0.07 [-0.11 - -0.02]	0.005	-0.18 [-0.30 - -0.06]	**0.003**
Sentinel event	Other	-1.20 [-2.66 – 0.25]	0.104	-0.01 [-1.51 – 1.48]	0.986	-1.15 [-2.76 – 0.47]	0.163	-0.96 [-2.66 – 0.74]	0.269	-3.07 [-7.32 – 1.18]	0.156
	cancer	-1.35 [-3.04 – 0.35]	0.118	-1.59 [-3.32 – 0.14]	0.071	-1.62 [-3.51 – 0.28]	0.094	-1.28 [-3.27 – 0.70]	0.205	-5.61 [-10.47 - -0.76]	0.024
	Stroke	0.95 [-1.73 – 3.63]	0.485	0.47 [-2.30 – 3.24]	0.739	-1.63 [-4.66 – 1.41]	0.292	-0.75 [-3.91 – 2.41]	0.642	-2.02 [-9.62 – 5.59]	0.602
	Eating/drinking disorder	-1.12 [-2.22 - -0.2]	0.046	-0.42 [-1.51 – 0.67]	0.447	-0.57 [-1.77 – 0.62]	0.346	-0.46 [-1.72 – 0.82]	0.483	-2.33 [-5.59 – 0.93]	0.161
	Febrile episode	-1.45 [-2.59 - -0.32]	0.012	-0.25 [-1.39 – 0.88]	0.658	-0.78 [-2.02 – 0.46]	0.217	-1.21 [-2.51 – 0.10]	0.069	-3.64 [-7.00 - -0.29]	0.033
	Pneumonia	-1.31 [-2.42 - -0.21]	0.020	-0.90 [-2.00 – 0.20]	0.106	-0.85 [-2.06 – 0.36]	0.167	-1.47 [-2.76 - -0.18]	0.025	-4.07 [-7.38 - -0.77]	0.016
	None	Ref.	.	Ref.	.	Ref.	.	Ref.	.	Ref.	.
Relatives relation	Grandchilds generation [c]	0.53 [-0.65 – 1.70]	0.378	0.16 [-1.04 – 1.36]	0.789	0.71 [-0.55 – 1.97]	0.269	1.51 [0.13 – 2.88]	0.032	3.71 [0.25 – 7.17]	0.036
	Childs generation [b]	0.94 [0.09 – 1.78]	0.030	1.33 [0.46 – 2.22]	**0.003**	0.69 [-0.25 – 1.62]	0.148	1.27 [0.27 – 2.26]	0.013	4.74 [2.23 – 7.26]	**< 0.001**
	Residents generation [a]	Ref.	.	Ref.	.	Ref.	.	Ref.	.	Ref.	.

[a]: Spouse, partner, sibling. [b]: Child, nephew/niece. [c]: Grandchild, grandnephew/grandniece, legal representative, friend, neighbour

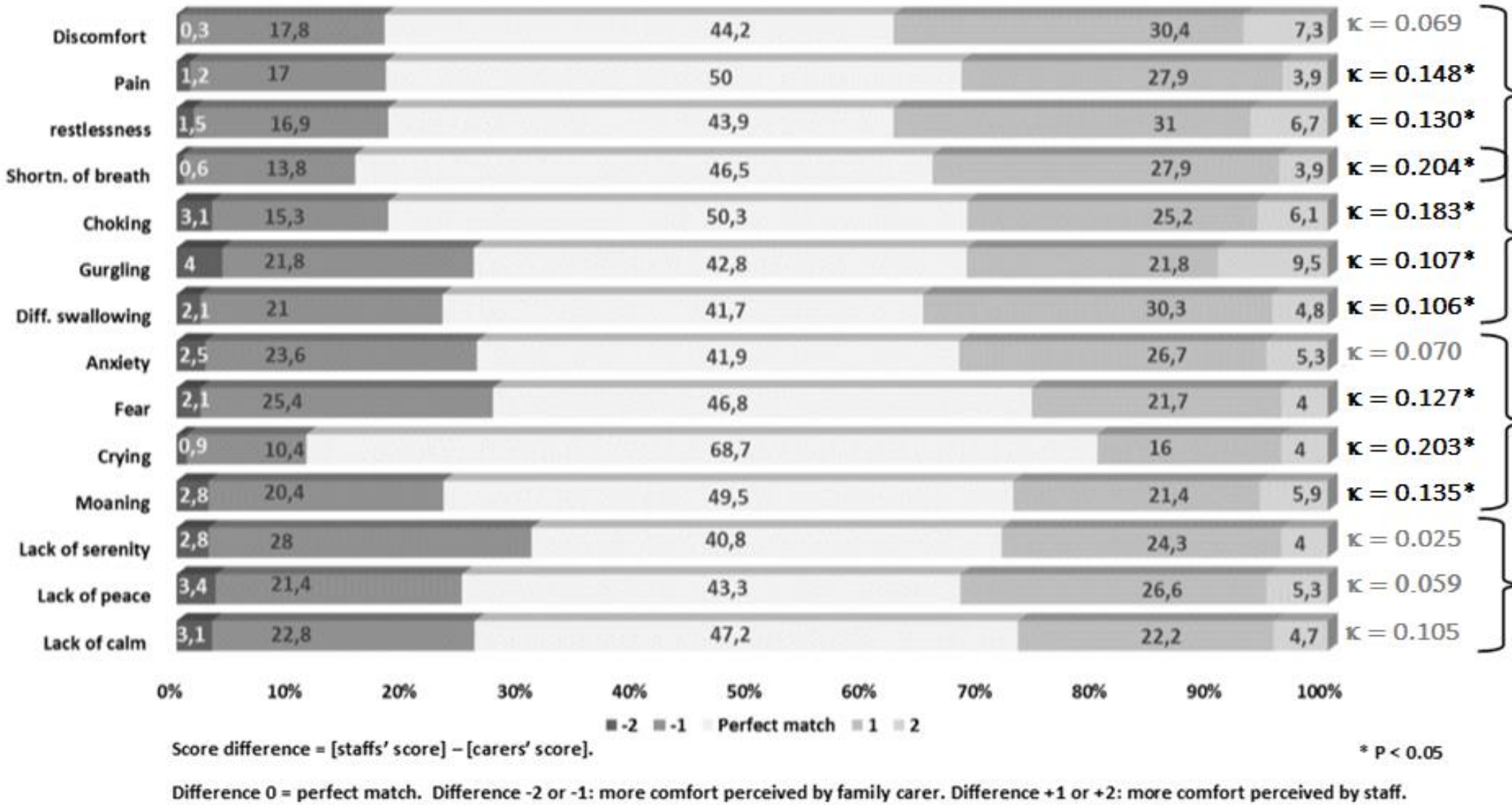
Taken the Holm-Bonferoni correction for multiple analysis into account, the boundary for significance was set at a P value below 0.004. (0.05/14= 0.004). The significant results are indicated in bold.

4.3.5 EOLD-CAD score differences and perfect match at resident level

The distribution of score differences and the extent to which there was a perfect match between staff and family carers is shown in **Figure 3**.

On an individual resident level, the percentage of the perfect match and the interobserver agreement beyond chance was 50% in cases for pain (κ-coefficient: 0.148), 43.9 % for restlessness (κ: 0.130), 46.5 % for shortness of breath (κ: 0.204), 50.3 % for choking (κ: 0.183), 42.8 % for gurgling (κ: 107), 41.7 % for difficulty swallowing (κ: 0.106), 46.8 % for fear (κ: 0.127), 68.7 % for crying (κ: 0.203) and 49.5 % for moaning (κ: 0.135). For the remaining symptoms, the interobserver agreement between staff and family carers was smaller and not statistically significant.

Figure 3: Distribution of score differences between staff and family carers in percentages



Score difference = [staffs' score] – [carers' score].

* P < 0.05

Difference 0 = perfect match. Difference -2 or -1: more comfort perceived by family carer. Difference +1 or +2: more comfort perceived by staff.

4.4 Discussion

4.4.1 Main findings

On a group level, family carers systematically scored lower comfort for the total EOLD-CAD score, the physical distress and dying symptoms subscale scores, compared to staff. The differences in mean scores seem very small, but as the scores 3 to 1 correspond to categories “not at all” to “a lot”, they are clinically relevant. For the psychological distress and well being subscales, no significant differences were found.

Discrepancies between staff and family carers were larger for family carers from the childrens’ generation compared to family carers from the residents’ own generation, and with the increasing age of the dying resident.

On the residents level, the extent of perfect matches for the individual symptoms in the EOLD-CAD ranged from 40.8 to 68.7 %, interrater agreement beyond chance between staff and family carers was slight to fair.

4.4.2 Strengths and limitations

To our knowledge, this is the first international study directly comparing staff and family carer reported ratings of a broad range of symptoms at the end of life of long-term care facility residents. Compared to other literature studying quality of life and quality of dying in dying residents, the large study sample is an additional strength of this study. As in any retrospective survey, some limitations have to be acknowledged. The risk of recollection bias was reduced by limiting the inclusion period to three months prior to the data collection, by requesting that the staff member most involved in the care of the deceased resident completed the staffs questionnaire, and that the

respondant consulted the resident's nursing records. Moreover, the EOLD-CAD rates symptom burden in clearly distinguishable categories and was validated for post-mortem research purposes. Since the return of a family carer's questionnaire was an inclusion criteria, selection bias can not be excluded. However, earlier research has established that selection bias based on relative's participation could result in differences in nursing care outcomes such as satisfaction with care, but not in resident outcomes, more specifically in EOLD-CAD scores[14].

We decided to include countries in which both the staff and the family carer's response rate exceeded 50 % for the residents who died in their long-term care facility for reasons of reliability. Staff function could only be categorised as either registered nurses or other functions, to allow comparison between countries and, lastly, the number of missing values for certain symptom ratings has to be acknowledged.

4.4.3 Relation to other studies and possible explanations

On individual resident level, the interrater agreement between staff and family carers was slight to fair. As in our study, van der Steen et al. found poor agreement in individual ratings, concomitantly with little systematic difference[5]. No other studies, focussing on staff- family carers interrater agreement, were found.

At group level, the staffs' symptoms scores generally reflected a higher perception of comfort compared to the family carers' scores. The mean score differences were not significant in the psychological distress and well being subscale scores, but in the physical distress, dyings symptoms subscales and the total EOLD-CAD score, staff scores significantly reflected slightly higher perception of comfort.

Three possible explanations are suggested: staff is too optimistic in their appraisal of symptom burden; family carers are too pessimistic or both are present.

As far as the physical distress and dying symptoms are concerned, the research team believe that overestimation of symptom burden by family carers is the most probable. In studies comparing patient and staff symptom ratings, both overestimation[15] and underestimation[4, 16] by staff has been described. However, Bahrami et al.[17] established that agreement between patients and nurses was higher in describing the physical aspects of quality of life, in particular in nurses who have greater clinical experience. As the age distribution and nursing experience of the staff respondents suggest, this effect is likely in our study. Moreover, formal training in end-of-life care might mitigate staff interpretation of symptoms such as Cheyne-Stokes-like breathing, death-rattle, gurgling and swallowing difficulties as normal dying symptoms, whereas families, who lack formal training might interprete these symptoms as burdensome[34]. In our findings also, the discrepancy on individual level was the highest for gurgling.

All the more, when family carers visit a resident in the dying process, it is likely that they are emotionally overwhelmed. Similar emotional reactions are reported in third-year nursing students' experience[18] in the care for the dying, who described the sudden physical deterioration prior to death as unexpected and shocking, although the patients death was expected.

The difference in clinical experience and in witnessing dying might explain the discrepancy in the physical distress and dying symptom subscale scores, but may also explain our finding that score differences between family carers and staff in the residents childrens generation exceed the score differences between staff and family carers in the residents generation (4.74; 95% CI 2.23 – 7.26], presuming that family carers of the residents generation have acquired more experience in witnessing dying than carers of the next generation. However, these hypotheses need furtherresearch.

For the psychological distress and wellbeing subscale scores, the interpretation is less clear. Compared to patients, both staff[15] and family carers[19] have been found to overrate psychological and existential symptoms, which can explain the non-significant subscale score differences when comparing staff and family carers.

The shortage of discernible, objective signs to determine the presence of certain symptoms can lead to different interpretations of the symptom prevalence and hence to score differences. In this respect, the missing scores per symptom, are interesting. Most missing values occurred for physical symptoms such as discomfort and lack of calm in both the family carers' and staff questionnaires, possibly because of the unclear definition and the difficult distinction with other symptoms in the EOLD-CAD. This is consistent with other research, that stated that symptom score differences were found to be bigger for less observable symptoms[20-25] or psychological symptoms[16, 26].

4.4.4 Implications for clinical practice and research

At a group level, staff and family carers showed no significant differences in psychological distress and wellbeing subscale scores. For physical distress, dying symptoms and the total EOLD-CAD scores, there was a slight but systematically lower estimation of symptoms by staff, compared to family carers. When this slight difference is taken into account, both staff's and family carer's symptom ratings can be used for regular monitoring of patient outcomes.

At an individual level, the low interrater agreement shows that the family carers and staff view resident's comfort differently and that both perspectives on symptom burden are equally important.The discrepancy in perception of symptoms and suffering can give rise to conflicts between professional staff and disappointed family carers, while they believe their relatives are not sufficiently or effectively taken care off. Long-term care facility staff should be aware of possible

differences in symptom assessment by staff and family carers. They should inform relatives pre-emptively of possible symptoms, explain the burden they do (or do not) cause, the treatment possibilities and should regularly discuss the interpretation, burden and treatment of symptoms with family carers. Symptom assessment by both groups could be more congruent when symptoms or symptom behaviour are unambigiously defined. The parallel use of simple, validated measuring tools for symptom assessment should be stimulated and supported by training sessions for nursing staff and bedside teaching for family carers and long-term care facility volunteers. A shared perspective in symptom assessment might improve care and treatment decisions with regard to burdensome symptoms and will facilitate patient and family centered care in long-term care facilities, resulting in better comfort

Further qualitative research is needed to understand the discrepancies between staff and family carers in symptom ratings. Intervention studies, where symptoms are scored by both groups and discussed regularly, should investigate if score differences decrease over time.

4.5 Conclusion

Staff rate comfort in dying long-term care facility residents higher than the family carers , especially in the physical distress and dying symptom subscales. Score differences between staff and family carers were larger with family carers of the resident's children's generation.

Family carers may contribute in symptom assessment for clearly observable symptoms but need regular discussions with staff to understand the residents' symptom burden.

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Appendix 1: Associated factors with symptom score differences by staff and carers (preliminary model)

EOLD-CAD SUBSCALES		PHYSICAL DISTRESS (n=258)		EMOTIONAL DISTRESS (n=274)		WELLBEING (n =278)		DYING SYMPTOMS (n =271)	
		COEFF [95% CI]	P-Value	COEFF [95% CI]	P-Value	COEFF [95% CI]	P-Value	COEFF [95% CI]	P-Value
Country	The Netherlands	-0.15 [-0.97 – 0.67]	0.725	0.26 [-0.53 – 1.06]	0.513	0.048 [-0.39 – 1.36]	0.280	-0.35 [-1.25 – 0.56]	0.454
	Finland	-0.69 [-1.45 – 0.07]	0.076	-0.35 [-1.10 – 0.41]	0.367	-0.36 [-1.19 – 0.46]	0.387	-0.98 [-1.84 - -0.12]	0.025
	Belgium	Ref.	.	Ref.	.	Ref.	.	Ref.	.
Residents age		-0.05 [-0.09 - -0.01]	0.025	-0.05 [-0.09 - -0.01]	0.023	-0.01 [-0.06 – 0.04]	0.716	-0.07 [-0.12 - -0.03]	0.003
Length of stay		0.04 [-0.05 – 0.13]	0.402	0.06 [-0.04 – 0.15]	0.226	0.04 [-0.06 – 0.14]	0.467	0.01 [-0.09 – 0.11]	0.898
Dementia status	No	0.20 [-0.51 – 0.90]	0.587	0.33 [-0.39 – 1.04]	0.367	0.38 [-0.40 – 1.17]	0.336	0.14 [-0.68 – 0.96]	0.746
	Yes	Ref.	.	Ref.	.	Ref.	.	Ref.	.
Sentinel event	Other	-1.44 [-3.01 – 0.12]	0.071	0.01 [-1.56 – 1.58]	0.988	-1.15 [-2.88 – 0.58]	0.191	-1.34 [-3.14 – 0.46]	0.143
	cancer	-1.89 [-3.88 – 0.09]	0.061	-2.41 [-4.40 - -0.42]	0.018	-2.27 [-4.48 - -0.04]	0.046	-2.39 [-4.68 - -0.09]	0.041
	Stroke	0.53 [-2.29 – 3.35]	0.710	0.31 [-2.59 – 3.20]	0.836	-2.19 [-5.39 – 1.02]	0.180	-0.51 [-3.80 – 2.78]	0.761
	Eating/drinking disorder	-1.34 [-2.56 - -0.125]	0.031	-0.51 [-1.67 – 0.65]	0.384	-0.60 [-1.90 – 0.71]	0.367	-1.02 [-2.40 – 0.37]	0.149
	Febrile episode	-1.66 [-2.91 - -0.41]	0.009	-0.22 [-1.42 – 0.98]	0.722	-0.62 [-2.26 – 0.43]	0.181	-1.65 [-3.06 - -0.24]	0.022
	Pneumonia	-1.40 [-2.60 - -0.19]	0.023	-0.77 [-1.93 – 0.39]	0.191	-0.91 [-2.21 – 0.39]	0.169	-1.68 [-3.05 - -0.30]	0.017
	None	Ref.	.	Ref.	.	Ref.	.	Ref.	.
Cause of death	Other	-0.53 [-1.72 – 0.66]	0.381	-0.45 [-1.65 – 0.76]	0.466	-0.91 [-2.24 – 0.41]	0.176	-0.88 [-2.27 – 0.52]	0.217
	dementia	-0.33 [-1.51 – 0.85]	0.583	-0.61 [-1.80 – 0.57]	0.308	-0.10 [-1.39 – 1.20]	0.880	-0.59 [-1.95 – 0.77]	0.392
	respiratory disease	-0.84 [-2.20 – 0.53]	0.228	-1.71 [-3.08 - -0.35]	0.014	-0.62 [-2.11 – 0.87]	0.412	-1.19 [-2.73 – 0.36]	0.132
	Cerebro-/cardiovascular	-0.40 [-1.54 – 0.74]	0.493	-0.91 [-2.06 – 0.24]	0.119	-0.50 [-13.77 - -0.77]	0.438	-0.64 [-1.97 – 0.69]	0.345
	Cancer	Ref.	.	Ref.	.	Ref.	.	Ref.	.
Staff age		-0.01 [-0.03 – 0.02]	0.576	0.00 [-0.02 – 0.03]	0.825	-0.00 [-0.3 – 0.3]	0.934	0.02 [-0.01 – 0.05]	0.264
Staff function	Other	0.37 [-0.38 – 1.12]	0.329	-0.17 [-0.90 – 0.56]	0.652	-0.32 [-1.14 – 0.50]	0.442	0.69 [-0.14 – 1.51]	0.102
	Nurse	Ref.	.	Ref.	.	Ref.	.	Ref.	.
Palliative care training	Other	0.07 [-1.23 – 1.38]	0.912	-0.65 [-1.96 – 0.66]	0.329	0.50 [-0.92 – 1.92]	0.486	-1.22 [-2.70 – 0.25]	0.104
	Additional palliative care training	0.15 [-0.63 – 0.93]	0.707	-0.60 [-1.38 – 0.18]	0.132	0.20 [-0.65 – 1.06]	0.639	-0.69 [-1.58 – 0.19]	0.125
	As part of pre-registration nurse training	0.35 [-0.47 – 1.17]	0.402	-0.29 [-1.10 – 0.51]	0.474	0.17 [-0.71 – 1.06]	0.190	-0.28 [-1.20 – 0.65]	0.554
	None	Ref.	.	Ref.	.	Ref.	.	Ref.	.
Relatives relation	Grandchilds generation + other [c]	0.68 [-0.55 – 1.92]	0.275	0.41 [-0.83 – 1.66]	0.515	0.84 [-0.48 – 2.16]	0.212	1.68 [0.27 – 3.10]	0.020
	Childs generation [b]	0.91 [0.04 – 1.77]	0.041	1.46 [0.57 – 2.37]	0.001	0.64 [-0.32 – 1.61]	0.190	1.20 [0.19 – 2.21]	0.020
	Residents generation [a]	Ref.	.	Ref.	.	Ref.	.	Ref.	.
Relative expected death?	Relative didn't know	-0.34 [-1.38 – 0.69]	0.514	-0.26 [-1.27 – 0.76]	0.615	-0.11 [-1.22 – 1.00]	0.843	0.03 [-1.16 – 1.22]	0.961
	No	0.02 [-0.57 – 0.61]	0.942	-0.15 [-0.74 – 0.44]	0.616	0.15 [-0.50 – 0.81]	0.639	-0.65 [-1.33 – 0.02]	0.056
	Yes	Ref.	.	Ref.	.	Ref.	.	Ref.	.

[a]: Spouse, partner, sibling. [b]: Child, nephew/niece. [c]: Grandchild, grandnephew/grandniece, legal representative, friend, neighbour

Appendix 2: non-respondent analysis from residents with and without carers' response

Resident characteristics (N=629)		Without carers' response	With carers' response	P-value[1]
Country	Belgium	35.1%	39.4%	0.229
	Finland	35.1%	28.6%	
(missing n=0)	The Netherlands	29.8%	32.0%	
Residents' mean age (SD) *(missing n=37)*		86.6 (8.3)	87.2 (7.6)	0.363
Mean length of stay in years (SD) *(missing n=46)*		1.1 (1.2)	1.1 (1.1)	0.861
Mean total BANS-S score[a] (SD) *(missing n=3)*		19.4 (4.4)	19.0 (4.4)	0.210
Dementia status[b]	Yes	77.0%	69.8%	0.050
(missing n=2)	No	23.0%	30.2%	
Sentinel events	None	9.0%	8.1%	0.614
	Pneumonia	24.1%	28.1%	
	Febrile episode (≠ pneumonia)	20.8%	25.3%	
	Eating/drinking disorder	36.3%	28.9%	
	Stroke	0.8%	1.3%	
	Cancer	3.3%	3.1%	
(missing n=0)	Other (fall, fracture)	5.7%	5.2%	
Cause of death	dementia	25.2%	29.4%	0.053
	respiratory disease	11.3%	15.4%	
	cerebro-/cardiovascular	17.6%	21.5%	
	cancer	10.9%	8.2%	
(missing n=14)	other	34.9%	25.5%	
Staff characteristics (N=363)				
Staffs' mean age (SD) *(missing n=5)*		44.0 (10.8)	43.1 (10.9)	0.299
Mean nursing experience in years (SD) *(missing n=21)*		13.8 (10.5)	13.8 (10.1)	0.978
Current function	Registered nurse	90.1%	90.3%	0.939
(missing n=6)	other	9.9%	9.7%	
Palliative care training	None	25.3%	22.9%	0.758
(missing n=8)	Yes, as part of pre-registration nurse training	30.3%	30.3%	
	Yes, additional palliative care training	44.4%	46.8%	
CAD EOLD scores				**P value[2]**
Discomfort (missing n = 19)		2.04 (0.68)	2.11 (0.64)	0.182
Pain (missing n = 9)		2.04 (0.61)	2.04 (0.63)	0.916
Restlessness (missing n = 10)		2.16 (0.70)	2.19 (0.69)	0.621
Shortness of breath (missing n = 9)		2.26 (0.77)	2.28 (0.73)	0.684
Choking (missing n = 10)		2.42 (0.74)	2.46 (0.70)	0.464
Gurgling (missing n = 9)		2.26 (0.75)	2.31 (0.71)	0.365
Difficulty swallowing (missing n = 10)		1.86 (0.79)	1.94 (0.74)	0.179
Fear (missing n = 12)		2.25 (0.69)	2.30 (0.66)	0.373
Anxiety (missing n = 14)		2.28 (0.68)	2.29(0.69)	0.845
Crying (missing n = 10)		2.69 (0.56)	2.75 (0.51)	0.122
Moaning (missing n = 8)		2.40 (0.69)	2.45 (0.62)	0.316
Serenity * (missing n = 17)		2.01 (0.65)	1.99 (0.68)	0.747
Peace * (missing n = 11)		2.11 (0.65)	2.17 (0.66)	0.265
Calm * (missing n = 12)		2.10 (0.64)	2.11 (0.64)	0.770

[a] Bedford Alzheimer Nursing Severity Scale (BANS-S). 7 items scale, score range 7 -24.Higher scores indicate higher functional disability and dependency

[b] in this survey, a resident "with dementia" is a resident which is designated as "suffering from dementia" by the nurse, the physician or both.

[1] Calculated with chi-squared test. [2] Calculated with independent samples T-test * reverse coded

Chapter 5: Development and validation of the SATISFIE - scale (*S*ymptom *A*ssessment *T*o *I*mprove *S*ymptom control *F*or *I*nstitutionalized *E*lderly)

Maaike De Roo[1], Marc Tanghe[2], Nele Van Den Noortgate[1], Ruth Piers[1].

1 Ghent University Hospital, Department of Geriatrics, Ghent, Belgium.

2 End-of-Life Care Research Group, Ghent University, Ghent, Belgium.

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Abstract

Objectives

To validate a newly developed multiple symptom self-assessment tool in nursing homes.

Design

Thirty prevalent symptoms, identified in literature, were classified by a two-round Delphi procedure to a top 10 of most relevant, burdensome symptoms. Since no existing symptom scale fully covered this top 10, we developed a new scale, consisting of a horizontal numerical scale for the top 10 symptoms, with the possibility to add and rate 3 other symptoms. This scale was validated.

Setting & Participants

Hundred seventy four participants, mean age 85 (± 5.94) years, were recruited in 7 nursing homes (86%) and in 3 acute geriatric wards (14%).

Methodology

To test the construct validity, participants with and without a palliative status were enrolled. Participants completed the SATISFIE (Symptom Assessment To Improve Symptom control For Institutionalized Elderly) scale on day 0 and day 1 (intra-rater reliability). Nurses completed the scale on day 0 (inter-rater reliability).

Descriptive statistics described the characteristics of the study population and symptom scores. Differences in symptom scores between palliative and non-palliative participants were analysed with the Mann-Whitney U test. Intra-rater and inter-rater reliability were calculated by means of an intraclass correlation coefficient. Factor analysis searched for possible symptom clusters. Feasibility was evaluated by measuring the assessment time and by a questionnaire for the nurses.

Results

In the non-palliative group (n=130), the highest self-rated median scores were pain on day 1 (median 3, range (IQR) 0-5) and pain on day 2. In the palliative group (n=44), the highest median self-rated scores were fatigue on day 1 (median: 5 (IQR 0-6)), lack of energy on day 1 and 2, (both median 5 (IQR 0-8)); and depressed feeling on day 2, (median 3 (IQR 0-5)).

Nurses' assessments median scores were the highest for depressed feeling, (median 5 (IQR 1-7)), fatigue, (median 4.5 (IQR 0-6.5)), and lack of energy, (median 3 (IQR 0-6)), in the palliative group. In the non-palliative group, none of the median scores was 3 or more.

Intraclass correlation coefficients (ICC) for intra rater reliability varied between 0.65 and 0.89,. for inter-rater reliability (patients-nurses) between 0.18 and 0.63.

Mean assessment time for nurses was 2.0 minutes (SD=1.01). For participants, it decreased from 10.5 minutes (SD=5.41) at the first to 7.5 minutes (SD=3.72) at the second assessment.

Nurses qualified the SATISFIE instrument as useful, applicable in daily practice and sufficiently comprehensible for the patients.

Conclusion

The SATISFIE scale is a valid and feasible instrument for regular, multiple symptom assessment in institutionalized older persons.

Key words

symptom assessment, symptom assessment tool, frail older persons, nursing home, symptom control

5.1 INTRODUCTION

With the rising proportion of older people in our society, more and more people die at older age, after a period of chronic health problems[1, 2]. As a consequence, an increasing amount of people require care toward the end of life[3]. Palliative care aims to relieve pain and other distressing symptoms by the means of "early identification and impeccable assessment[4]. For adequate symptom assessment, valid and feasible instruments are needed. Traditionally, the development and validation of symptom scales for a palliative care population have predominantly taken place in cancer patients[5, 6]. However, attention to non-cancer populations and the elderly population in particular is growing, especially in the domain of pain assessment[3]. Studies concerning pain assessment in dementia indicate that self-assessment is valid and even preferable for patients with moderate to severe dementia[7-9].

Nonetheless, symptom assessment and control are broader than pain only. Currently, several symptom assessment scales are available. An overview is given in Appendix 1. To our knowledge, however, only two instruments have been specifically tested in and adapted for an older population: the Symptom Assessment Scale for Elders (SAS-E)[10] and the MIDOS tool (MInimal Documentation System for palliative care)[11], a German version of the Edmonton System Assessment Scale[12].

This study aims to present and validate an instrument for self-rated symptom assessment in an elderly palliative population. Furthermore, this study describes the prevalence of symptom distress in a population of older persons.

5.2 METHODS

5.2.1 Development of a new instrument

In a first step, a Medline-search, which searched for terms “symptom control, measuring symptoms, measuring tool, symptom scale”, combined with “end-of-life, palliative patient, palliative care, palliative elderly or geriatric patient” withheld 100 symptoms, prevalent in an older population. After removing overlapping and non-relevant symptoms, a list of 30 symptoms remained, which was presented in alphabetical order to an expert panel, consisting of 7 physicians and 6 nurses working in geriatric and palliative care settings, and familiar with the use of assessment instruments. The experts scored these 30 symptoms for frequency (1=rarely 2=sometimes 3=often 4=very often) and distress (1=light 2=average 3=serious). The frequency and distress scores per symptom were multiplied, resulting in a total score, ranging from 1 to 12. Symptoms were ranked by median and in case of ex aequo, also by mean score from high to low. The top-30 symptom list is presented in appendix 2. Above all, we did not want the assessment instrument to be too burdensome[8] for this frail population. Therefore we selected the top 10 of most relevant symptoms. Since, in the Dutch language, the terms “concentration problems” and “being confused” are often used concurrently, we combined them into the item “confusion” which we defined as problems with concentration or memory. As a consequence, fatigue, which was ranked as the eleventh symptom, was also included in the ten item symptom list, resulting in the SATISFIE scale which scores breathlessness, depressed feeling, feeling nervous, pain, respiratory secretions, swallowing problems, lack of appetite, fatigue, confusion, lack of energy.

A second step was to examine whether these ten symptoms are part of existing symptom scales. After comparison of these ten items with the assessment instruments found in literature (Appendix 1), we concluded that none of the existing instruments contained all ten items. Some instruments had less than ten items, other instruments were much longer and contained additional symptoms.

Therefore, it was decided to develop a new scale containing the top 10 symptoms. Additionally, we offered the possibility to add three symptoms which patients might experience but are not included in our top 10. A horizontal numerical scale was chosen, with 0 being “not at all” and 10 being “worst possible”. This type of scale is widely used and proven to be a well-understood and easy to complete[6, 7, 13, 14]. The final instrument is shown in Figure 1.

SATISFIE INSTRUMENT

Birth Year: Filled in by **O** Patient
Initials **O** Caregiver
Date of assessment

Not at All **Worst possible**

Breathlessness
0 1 2 3 4 5 6 7 8 9 10

Depressed feeling
0 1 2 3 4 5 6 7 8 9 10

Feeling nervous
0 1 2 3 4 5 6 7 8 9 10

Pain
0 1 2 3 4 5 6 7 8 9 10

Respiratory secretions
0 1 2 3 4 5 6 7 8 9 10

Swallowing problems
0 1 2 3 4 5 6 7 8 9 10

Not at All **Worst possible**

Lack of appetite
0 1 2 3 4 5 6 7 8 9 10

Fatigue
0 1 2 3 4 5 6 7 8 9 10

Confusion
0 1 2 3 4 5 6 7 8 9 10

Lack of energy
0 1 2 3 4 5 6 7 8 9 10

Other:
0 1 2 3 4 5 6 7 8 9 10

Other:
0 1 2 3 4 5 6 7 8 9 10

Other:
0 1 2 3 4 5 6 7 8 9 10

Assessment time:……..min.

Symptom	Description
Breathlessness	**Being breathless, difficulty breathing, gasping.**
Depressed feeling	**Feeling depressed, feeling moody, not interested or not enjoying things around you**
Feeling nervous	**Being restless, being nervous, being agitated, wriggle**
Pain	**Physical pain**
Respiratory secretions	**Secretion, slimes, expectorations in your throat**
Swallowing problems	**Difficulty swallowing**
Lack of appetite	**Less/No appetite/thirst**
Fatigue	Always in need of sleep, sleeping all the time, being exhausted, no energy
Confusion	Problems with concentration or memory, not able to concentrate, always distracted, disoriented
Lack of energy	Weakness in the legs, feeling weak, muscle weakness

5.2.2 Validation study sample

Since a change of 1.0 in a symptom VAS score is considered as clinically relevant, sample sizes of 96 and 48 achieve 80 % power to detect a clinically relevant difference between the two groups with a significance level of 0.05, using a two sided two-sample t-test. Participants were recruited from 7 residential long-term care facilities and 3 acute geriatric wards and were included when aged 70 years or more, able to sign informed consent and having a Mini Mental State Examination score of 18/30 or more). For validation, we hypothesized that overall symptom burden in a palliative population would exceed the symptom burden of a non-palliative population. Participants were classified as palliative when the medical record mentioned a palliative care oriented nursing plan or a formal decision to forego life-sustaining treatments, reflecting dying is expected and care focuses rather on comfort than cure. Other participants were considered as a non-palliative group. The ethical committee of Ghent University Hospital (Belgium) approved the study protocol. Informed consent was obtained from all participants.

5.3.3 Psychometric properties and statistics

In presence of the researchers, who briefly explained the use of the scale, participants performed symptom self-assessment with the SATISFIE-instrument on two consecutive days. After scoring of the 10 listed symptoms, participants were asked if they suffered from other symptoms, without limiting the number of additional symptoms, although the printed version only had room to add three symptom scores. These additional symptoms were also scored on a level from 0 to 10. Nurses only completed the assessment on day 1.

Descriptive statistics describe the characteristics of the study population and symptom scores. To evaluate the concurrent validity of the SATISIFIE-instrument, we analysed the symptom scores differences between the palliative and non-palliative group participants with the help of the non-parametric Mann-Whitney U test. Test-retest or intra-rater reliability was calculated by means of an intraclass correlation coefficient

(variability between the participants' score on the first and the second day), as was the inter-rater reliability (difference between participants' and nurses' rating on the first day). In order to verify if reduction of the number of symptoms in the scale is needed, possible symptom clusters were detected by means of factor analysis. Feasibility was evaluated with the help of the assessment time and a questionnaire for the nurses. All analyses were performed with IBM SPSS Statistics software Version 20.0 (IBM Corp., 2011, Armonk, NY). The significance level was set at 0.05.

5.3 RESULTS

5.3.1 Characteristics of the validation sample

174 participants were included in this study. Mean age of the total group was 85 years (SD=5.94 years). The majority of the participants were female (69%). One hundred and fifty participants resided in a long-term care facility (86%), 24 participants were recruited from an acute geriatric ward in a hospital (14%). Mean Mini Mental State Examination (MMSE) score was 23.8/30 (SD=3.21). MMSE scores were only obtained in 111 out of 174 participants as some care facilities only perform a MMSE test when cognitive problems are suspected.

130 participants were in the non-palliative group, 44 in the palliative group. Four participants did not consent to take part in the second assessment and dropped out.

5.3.2 Median symptom scores

In the non-palliative group, the highest self-rated median scores were pain on day 1 with a median score 3 (Interquartile range (IQR) 0-5) and pain on day 2. None of the other median scores was higher than 3 (Table

1). In the palliative group, the highest median self-rated scores were fatigue on the first day, median score 5 (IQR 0-6) and lack of energy on day 1 and 2, both median score 5 (IQR 0-8); and depressed feeling on day 2, median score 3 (IQR 0-5) (Table 1). As for the nurses' assessment, median scores were the highest for depressed feeling, median score 5 (IQR 1-7), fatigue, median score 4.5 (IQR 0-6.5), and lack of energy, median score 3 (IQR 0-6), all in the palliative group (Table 1). In the non-palliative group, none of the median scores was 3 or more (Table 1). All median symptom scores from the palliative group were higher than or equal to the median scores of the non-palliative group (Table 1). Breathlessness, lack of appetite, fatigue and lack of energy were significantly higher in the palliative group in both assessments by the participants, respiratory secretions was significantly higher in assessment 1 and swallowing problems in assessment 2. In the assessment by the nurses, all symptoms were significantly higher in the palliative group, except for pain, lack of appetite and confusion.

Table 1 Median symptom scores

	Assessment by patient Day 1			Assessment by nurse			Assessment by patient Day 2		
	Non-palliative group (n=130)	Palliative group (n=44)	p-value	Non-palliative group (n=130)	Palliative group (n=44)	p-value	Non-palliative group (n=128)	Palliative group (n=42)	p-value
Breathlessness	0 (0-2)	2 (0-5.5)	**0.002**	0 (0-3)	2 (0-6)	**0.004**	0 (0-2)	1.5 (0-6)	**0.003**
Depressed feeling	2 (0-5)	2 (0-5)	0.395	1 (0-4)	5 (1-7)	**<0.001**	2 (0-5)	3 (0-5)	0.146
Feeling nervous	2 (0-5)	2 (0-5)	0.448	0 (0-2)	2 (0-6)	**0.008**	2 (0-5)	2 (0-5)	0.607
Pain	3 (0-5)	1.5 (0-6.5)	0.630	2 (0-4)	2 (1-5)	0.322	3 (0-6)	0 (0-5)	0.106
Respiratory secretions	0 (0-2)	0 (0-4)	**0.033**	0 (0-0)	0 (0-1)	**0.025**	0 (0-2)	0 (0-5)	0.138
Swallowing problems	0 (0-0)	0 (0-2)	0.089	0 (0-0)	0 (0-4.5)	**<0.001**	0 (0-0)	0 (0-4)	**0.005**
Lack of appetite	0 (0-0)	0 (0-5)	**0.011**	0 (0-2)	0 (0-6.5)	0.113	0 (0-2)	1 (0-5)	**0.006**
Fatigue	0 (0-2)	5 (0-6)	**<0.001**	1 (0-3)	4.5 (0-6.5)	**0.002**	0 (0-2)	2 (0-5)	**0.001**
Confusion	0 (0-0)	0 (0-0)	0.365	0 (0-2)	0 (0-2.5)	0.342	0 (0-0)	0 (0-1)	0.212
Lack of energy	0 (0-5)	5 (0-8)	**0.007**	0 (0-5)	3 (0-6)	**0.004**	0 (0-5)	5 (0-8)	**0.001**

5.3.3 Additional symptoms

At the first measurement, 18 participants mentioned 23 additional symptoms, at the second measurement, 15 participants added 16 extra symptoms. Information about additional symptoms is presented in appendix 3.

5.3.4 Psychometric properties

Intraclass correlation coefficients (ICC) between assessment 1 and 2 varied between 0.65 and 0.89 per assessed symptom, indicating good test-retest reliability (Table 2). There was a poorer correlation between the scores of patients and the nurses (ICC for inter-rater reliability varied between 0.18 and 0.63), with slightly bigger mean differences (Table 2).

Cronbach's α was 0,76. Factor analysis (results shown in Appendix 4) revealed the presence of 3 possible clusters. These clusters explained 57 % of the variability.

The mean assessment time for nurses was 2.0 minutes (SD=1.01), whereas it was 10.5 minutes (SD=5.41) for participants at the first assessment and 7.5 minutes (SD=3.72) at the second.

The nurses' questionnaire about usability and feasibility revealed nurses' agreement that there is need for an instrument and that the proposed instrument contains important symptoms for this population. Furthermore, they considered the instrument sufficiently comprehensible for the patient, and found it feasible to fill in the scale within their daily activities.

Table 2: Test-retest reliability and inter-rater reliability

	ICC Assessment 1 – Assessment 2 (n=170)			ICC Assessment 1 – Assessment nurses (n=174)		
	ICC	p-value	Mean difference	ICC	p-value	Mean difference
Breathlessness	0.890	**<0.001**	0.00	**0.627**	**<0.001**	-0.07
Depressed feeling	0.796	**<0.001**	0.08	**0.358**	**<0.001**	-0.02
Feeling nervous	0.855	**<0.001**	0.11	**0.356**	**<0.001**	0.95
Pain	0.823	**<0.001**	0.11	**0.392**	**<0.001**	0.51
Respiratory secretions	0.896	**<0.001**	-0.04	**0.430**	**<0.001**	0.64
Swallowing problems	0.739	**<0.001**	-0.02	**0.564**	**<0.001**	0.12
Lack of appetite	0.875	**<0.001**	-0.04	**0.622**	**<0.001**	-0.25
Fatigue	0.859	**<0.001**	0.09	**0.596**	**<0.001**	-0.36
Confusion	**0.650**	**<0.001**	-0.14	**0.181**	**0.008**	-0.52
Lack of energy	0.879	**<0.001**	0.14	**0.624**	**<0.001**	0.48

ICC= intraclass correlation coefficient

5.4 DISCUSSION

This study describes the development and validation of the new SATISIFIE-instrument. As research states that symptom prevalence and intensity increases near end-of-life[15-17], we hypothesized that overall symptom burden in the palliative population would exceed the symptom burden of the non-palliative one in a group of communicative elders. The observed differences between these two groups support our hypothesis: the median symptoms scores appeared to be higher in the palliative group than in the non-palliative group, except for pain (assessment 1 and 2), showing good construct validity.

In contrast to other symptoms, pain scores appeared to be higher in the non-palliative group compared to the palliative residents. This could be explained by the fact that the palliative participants were already enrolled in a palliative care program, or by the symptom awareness, influenced or even induced by the palliative status itself. For the general public after all; pain control is experienced as one of the main goals of palliative care. Consequently, caregivers, patients and relatives will be more attentive to pain, thus increasing the level of pain control. In the non-palliative group, however, pain was slightly underestimated by the caregivers, as regularly reported in other studies[8, 18, 19]. This study also revealed high scores for fatigue and lack of energy in the palliative group, and nervous and depressed feelings in both patient groups.

These findings, again, plead for regular and systematic overall symptom assessment in nursing home residents.

In a qualitative research[11], studying nurses' experiences with a palliative care symptom assessment scale, nurses reported that the task of rating a symptom creates a certain awareness of the symptoms existence. Another study[20] about dying trajectories for nursing home residents also emphasized the importance of systematic overall symptoms assessment by means of validated instruments. Expanded awareness of the complete symptom burden can influence treatment and care decisions, thus improving nursing home residents' well-being. Although treatment of the assessed symptoms is often difficult, or in some cases even impossible (as for example in fatigue), the caregivers' awareness of symptom burden provides deeper insight in the residents' experience of daily life, perhaps resulting in a more compassionate approach in contact and care giving activities. To what extent this might be beneficiary for the residents remains unclear, but a significant decrease in depression among cancer patients, simply by systematic assessment, was reported[21].

Intraclass correlation coefficients (ICC) between 2 consecutive days indicated good test-retest reliability for the different items of the scale. This indicates the stability of the SATISFIE instrument. Moreover, the small numbers in mean difference, varying between positive and negative, revealed no systematic overestimation or underestimation between 2 patient's assessments.

Inter-rater ICC scores were slightly better for physical, purely observable symptoms than for the psychological ones. Depressed feelings were overestimated by the nurses, whereas lack of energy was underestimated by the nurses in the palliative group. In the non-palliative group, depressed feelings and feeling nervous were rather underestimated by the nurses. This way, the SATISFIE scale reflects the reality that nurses symptom estimation often diverges from patients' assessment. Consequently, our findings firmly support the guidelines that symptoms should preferably, whenever possible, be assessed and reported by patients themselves[8, 9, 19, 22].

Factor analysis showed no symptoms with completely parallel variations in score, but revealed the presence of 3 possible clusters. However, some clusters showed overlap, since some symptoms were attributed to several clusters. Additionally, from a clinical point of view, all separate symptoms are relevant to the residents. Consequently, we decided to maintain the 10 items without leaving a symptom out of the assessment tool.

The assessment time and a nurses' feasibility questionnaire revealed that the instrument was feasible, both in nurses' and patients' experience. However, vigilance remains necessary to avoid patients[8] and nurses getting overburdened by demanding, time-consuming assessment instruments.

5.4.1 Strengths and limitations

The SATISFIE instrument is, to our knowledge, the first instrument, developed and validated in a nursing home setting, for general use, independent of any specific disease. It also is the first in this context, designed for the self-rated broad symptom assessment of communicative elders. The main goal of this instrument is not to provide in-depth insight of all individual symptoms, but to draw attention to the most prevailing ones, especially those with high burden, in order to optimize symptom control. The validation study provided new insight into the symptom burden elders are dealing with and enables improvement of quick, regular symptom assessment. This way, relevant symptom control for this population can be adapted, and for some unexpected symptoms even initiated.

In our opinion, the instrument's main strength is its ability to assess a broad range of symptoms in a feasible way. The one-page lay-out offers the opportunity to get acquainted with the residents actual global symptom burden in a single swift glance, which makes the information more available and useful for symptom evolution follow-up[11]. The instrument is regarded as feasible and comprehensible for caregivers and, more importantly, for communicative elderly. The time needed to complete the instrument diminished during the second measurement. We expect it to decrease further as residents get familiar with the instrument.

The SATISFIE assessment scale covers all domains of palliative care, as stated by the WHO, except spiritual aspects. This might be considered as one of the instrument's limitations. Correlations between meaning in life and physical symptoms, although moderate, were established[23]. Therefore, the inclusion of a spiritual burden, such as for example "lack of meaning in life" or "feeling of meaninglessness" and validation of the adapted instrument is planned in the near future. This might refine the instrument for symptoms which are currently perhaps wrongly categorized as feelings of depression.

Inclusion of patients with lower MMSE scores is definitely another future validation research perspective. Since we aimed to develop an instrument for communicative elders, we included participants with MMSE >18. Consequently, we have no information about applicability of the SATISFIE instrument in a more cognitively impaired population.

Validation almost exclusively took place in nursing homes. Therefore, this study is only an initial validation of this instrument, to be confirmed in new studies which will additionally be organized in other care settings, such as (palliative) community care and hospital settings. Furthermore, the gathering of additional information on residents comorbidity and disease status could provide interesting insights into the assessed symptoms.

5.4.2 Nursing practice implications

In order to deliver high-quality palliative and comfort care for nursing home residents, it is of the most importance that symptoms are regularly and systematically assessed in clinical practice. The focus of this assessment should be broader than pain exclusively, and assessment should, whenever possible, be executed by patients themselves. Therefore, symptom assessment instruments should be easily understandable, and quick and easy to complete. SATISFIE is a tool specially designed for these purposes. In addition, the SATISFIE scale can also be used for research purposes.

5.5 CONCLUSION

Older patients are able to rate their symptoms with the help of the newly developed SATISFIE instrument.

This is important, since this study showed that nurses underestimate some of their patients' symptoms.

Appendix 1

Symptoms "TOP 10"	SAS[24]	SAS - E[10]	ESAS[25]	MSAS[26]	C-MSAS[5]	CAMPAS-R[27]	CSS[28]	MDASI[29]	SEI[30]
Pain	Pain	Pain	Pain	Pain	Pain	Pain	Pain	Pain	Pain
Feeling nervous				Feeling nervous Feeling irritable	Feeling nervous				Restlessness
Breathlessness	Breathing problems	Breathing problems	Shortness of breath	Shortness of breath	Shortness of breath	Breathlessness	Shortness of breath	Shortness of breath	Difficulty in breathing
Depressed feeling			Depression	Feeling sad	Feeling sad	Depression/ feeling low		Sad	
Confusion*				Difficulty concentrating	Difficulty concentrating		Problems remembering things	Problems remembering things	Poor concentration Poor memory
Swallowing problems				Difficulty swallowing					Difficulty in swallowing
Lack of energy				Lack of energy	Lack of energy		Lack of energy		
Respiratory secretions									
Lack of appetite	Appetite problems		Appetite	Lack of appetite	Lack of appetite		Lack of appetite	Lack of appetite	Anorexia
Fatigue	Fatigue	Fatigue	Fatigue			Fatigue/tiredness		Fatigue/tiredness	Fatigue
Symptoms NOT in our "TOP 10"	Bowel problems	Bowel problems	Anxiety	Change in the way food tastes	Constipation	Anxiety/ feeling tense	Constipation	Distressed/upset	Abnormal urinary elimination
	Difficulty sleeping	Bladder problems	Drowsiness	Changes in skin	Difficulty sleeping	Carer Anxiety/ feeling tense	Coughing	Disturbed sleep	Changes in appearance
	Nausea	Difficulty sleeping	Nausea	Constipation	Dry mouth	Carer depression or feeling low	Dizziness	Drowsy/sleepy	Constipation or diarrhoea
			Well-being	Cough	Feeling drowsy	Nausea	Nausea	Enjoyment of life	Coughing
				Diarrhea	Nausea	Vomiting	Vomiting	General activity	Dizziness
				Difficulty sleeping	Weight loss		Weak or sore muscles	Mood	Hearing changes
				Dizziness	Worrying			Nausea	Insomnia
				Dry mouth				Numbness/tingling	Nausea
				Feeling bloated				Relations with other people	Neurological changes in extremities
				Feeling drowsy				Vomiting	Poor vision
				Hair loss				Walking	Voice changes
				"I don't look like myself"				Work (including around the house)	Vomiting
				Itching					
				Mouth sores					
				Nausea					
				Numbness/tingling in hands or feet					
				Problems with sexual interest or activity					
				Problems with urination					
				Sweats					
				Swelling of arms or legs					
				Vomiting					
				Weight loss					
				Worrying					
Room for extra symptoms	2	2	1	3	none	3	none	none	none

* Confusion: problems with concentration or memory

Appendix 2: Top 30 of expert-scored symptoms

	Symptom	Median score (/12)	Mean score (/12)	SD	Min score	Max score
1	Pain	12	10.27	2.15	6	12
2	Feeling nervous	9	8.45	3.14	4	12
3	Breathlessness	9	8.08	2.94	4	12
4	Depressed feeling	8	8	3.77	1	12
5	Swallowing problems	8	6.91	3.59	1	12
6	Concentration problems	6	7.27	3.50	2	12
7	Being confused	6	7	3.23	3	12
8	Lack of energy	6	6.83	3.83	1	12
9	Respiratory secretions	6	6.73	1.95	4	9
10	Lack of appetite	6	6.64	3.85	1	12
11	Fatigue	6	6.58	3.97	1	12
12	Difficulty sleeping	6	6.18	3.40	1	12
13	Constipation	6	6.08	2.61	1	9
14	Urination problems	6	6	2.15	2	9
15	Oedema	6	5.83	3.22	1	12
16	Anxiety	6	5.67	3.45	1	12
17	Pressure sores	6	5.64	3.33	1	12
18	Worrying	5	5.83	4.28	1	12
19	Nausea	5	5	3.38	1	9
20	Faecal incontinence	5	4.91	2.21	1	9
21	Fever	4	4.33	2.15	1	9
22	Cough	4	3.64	2.98	1	9
23	Feeling irritable	3	4	3.44	1	12
24	Itching	3	3.08	1.83	1	6
25	Vomiting	3	3	2.05	1	6
26	Diarrhoea	2	3.25	2.60	1	9
27	Trembling	2	2.92	2.15	1	6
28	Bellyache/abdominal cramps	2	2.75	1.96	1	6
29	Reflux	2	2.58	1.73	1	6
30	Tingling in hands or feet	1	1.83	1.19	1	4

Appendix 3 Additional symptom reports.

Additional symptoms per participant

Number of participants	Assessment by patient on Day 1	Assessment 2 patient on Day 2	Assessment by caregiver
With 1 extra symptom	14	14	3
With 2 extra symptoms	3	1	
With 3 extra symptoms	1		
Total number extra symptoms	23	16	3

Additional symptoms mentioned

Symptom	Day 1	Day 2	Caregivers	Total	Corresponding symptom out of "Top 30"
Sleeping problems	2	3		5	Difficulty sleeping
Pollakiuria, urinary loss	3	1		4	Urination problems
Vision problems	3	1			
Loss of fine motricity, unable to do use hands	2	2		4	
Voice loss	2	1		3	
Irritating cough	2			2	Cough
Skin problems, psoriasis	2			2	
Headache, painful knees	1	1		2	Pain
Hiccups	1	1		2	
Walking problem	1	1		2	
Thinking about death, melancholy		2		2	Anxiety, worrying
Audition problem	1			1	
Problem with dentures	1			1	
Spasms	1			1	Bellyache/ Abdominal cramps
Loss of independence and own will	1			1	
Dizziness		1		1	
Difficult legs (due to varicose veins)		1		1	
Bowel movement problems		1		1	Constipation, faecal incontinence, diarrhoea
Mood swings			1	1	
Jealousy, demanding attention			1	1	
Need for motivation			1	1	

Appendix 4 factor analysis

Reliability

Scale: ALL VARIABLES

		N	%
Cases	Valid	151	86,8
	Excluded[a]	23	13,2
	Total	174	100,0

a. Listwise deletion based on all variables in the procedure.

Reliability Statistics

Cronbach's Alpha	N of Items
,758	10

Factor Analysis

Descriptive Statistics

	Mean	Std. Deviation
Breathlessness	1,68	2,707
Depressed feeling	2,96	3,006
Feeling nervous	2,93	3,153
Pain	3,24	3,334
Respiratory secretions	1,45	2,584
Swallowing problems	,94	2,004
Lack of appetite	1,72	2,969
Fatigue	1,80	2,742
Confusion	,60	1,588
Lack of energy	2,68	3,330

5.6 REFERENCES of this chapter

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Chapter 6: General discussion and conclusions

6.1 Summary of the main findings

In this PhD thesis, we studied the current status of pharmacological symptom treatment and assessment of symptoms by comparing end-of-life care in nursing homes of six European countries.

Regarding the pharmacological treatment during the last three days of life, we compared the prevalence of opioids, antipsychotics and hypnotics between countries and studied factors associated with end-of-life medication prescription (chapter 2). We defined opioid underuse as the absence of an opioid prescription for residents suffering from pain and/or dyspnea and explored the prevalence of opioid underuse in 6 European countries, searched for associated characteristics related to the resident, the nursing home and the organization of care (chapter 3).

In relation to symptom assessment, we compared symptom ratings between family caregivers and professional staff, and factors associated with differences between raters (chapter 4). We also developed a self-rated multi-symptom assessment tool (the SATISFIE instrument) for regular symptom assessment in a nursing home resident population. We validated SATISFIE by comparing the symptom scores of residents with and without a palliative status (chapter 5).

6.1.1 Pharmacological treatment of symptoms

As described in chapter 2, we found significant differences between six European countries in opioid, antipsychotic and hypnotic use in the last three days of life of nursing home residents. These differences between countries remained after multiple statistical adjustment for nursing home and resident characteristics. Country differences ranged from 4.8 % in Finland to 22.4 % in Italy for antipsychotics, from 7.8 % in Finland to 47.9% in the Netherlands for hypnotics, but most strikingly for opioids we found a range from 18.5 % in Poland to 77.9 % in the Netherlands. We also found a difference in pharmacological end-of-life symptom treatment between cancer and non-cancer patients. Dying of cancer tripled the odds of opioid prescription and doubled the odds of hypnotic prescription in nursing home residents' end-of-life.

When focusing on opioid prescription in residents with pain and/or dyspnea (chapter 3), we found that 86,2% of residents who died in the nursing home had symptoms that are treatable with opioids in the dying phase; of which 34.4% had pain, 10.6% had dyspnoea, 55.0% had both symptoms. Opioids were less often used to treat shortness of breath compared to treatment of pain in the terminal phase. Potential opioid underuse in the dying phase of nursing home residents differed considerably between participating countries, ranging from 19.2 % in the Netherlands to 79.1 % in Poland. Regardless of country, having assessed pain was the only factor significantly associated with less risk for potential opioid underuse, whereas having had a formal pain assessment tripled the odds of opioid prescription. We repeated the same analysis in the small population sample where the physician recognised the terminal phase, the odds of potential opioid underuse were significantly higher in residents with dyspnoea but without pain (OR 3.90; 95 % CI: 1.18 – 12.88) compared to those with dyspnoea and pain. Odds of potential opioid underuse were

also higher for residents dying of dementia (OR 5.90; 95 % CI: 1.29 – 27.02) and of cerebro- and cardio-vascular disease (OR 11.40; 95 % CI: 2.59 – 50.16), compared to residents dying of cancer. The association between lack of pain assessment and potential opioid underuse remained, but was no longer statistically significant.

6.1.2 Symptom assessment

In chapter 4 we compared symptom scores assessed by family carers and professional staff in nursing home residents' end of life. On a group level, family caregivers' perception of symptom burden was significantly higher than staffs' perception for the total symptom burden, physical distress and dying symptoms in nursing home residents' last days of life. There was no difference in the perception of emotional distress or well-being. Discrepancies between staff and family carers were larger if family carers were from the children's generation compared to family carers from the residents' own generation, and with younger age of the dying resident. On the residents' level, the extent of perfect match, where professional staff and family caregiver gave the same score for an individual symptom, ranged from 40.8 to 68.7 %; interrater agreement beyond chance between staff and family carers was slight to fair.

To test the validity of the SATISFIE symptom assessment tool in a nursing home population, we compared patients' symptom scores in palliative and non-palliative patients in chapter 5. We considered a patient as palliative when the patient's medical record mentioned a palliative care oriented nursing plan or a formal decision to forego life-sustaining

treatments. Other participants were considered as a non-palliative group. The median symptoms scores appeared to be higher in the patient group with a palliative care status than in the patient group without a palliative care status, as was hypothesized. In contrast to other symptoms, pain scores appeared to be higher in the non-palliative care group compared to the residents with a palliative care status.

We also compared patients' and nurses' scores: in the non-palliative group, pain and depressed feelings were rated slightly lower and fatigue higher by the nurses compared to the patients' scores. In the palliative group, depressed feelings were rated higher, and fatigue and lack of energy slightly lower by the nurses, compared to the patients' scores.

6.2 Methodological considerations, strengths and limitations of all studies

6.2.1. International cross-sectional study of nursing home deaths

In chapters **2 to 4**, we analysed data from the cross-sectional Pace I study.

In 6 European countries (Belgium, the Netherlands, England, Finland, Poland and Italy), nursing homes were designated by stratified random sampling. Each nursing home reported all residents, deceased in the previous three-month period. For each deceased resident, structured questionnaires were sent to the nurse most involved in care, the treating physician, the nursing home management, and a family member, designated by the nursing home management. The nursing home management also completed a structured questionnaire on nursing home characteristics.

The international design of the study, resulting in the first, large-scale international database enabling comparative research in nursing homes residents' symptom burden and pharmacological symptom treatment in 6 European countries, is the most important strength. The selection of the participating countries enabled a good spread of geographic regions, countries with different economic growth, different health care systems and different levels of palliative care[1]. Due to the stratified random selection, optimal representativeness was reached in the studied countries. To guarantee the quality of the data, strict collection procedures were described in a quality assurance manual. Prior to the gathering of data, all researchers received training. The extensiveness of the data is another important strength of the study, which includes measurements of outcomes (e.g. symptom burden in the last days of life), care processes (e.g. medication use) and nursing home characteristics (e.g. availability of opioids); enabling the analysis of associations between outcomes and processes and the formulation of hypothesis.

With exception of England, with only satisfactory response rates, our data collection resulted in high response rates in all countries for nurses and family caregivers. Moreover, the pseudonymised data provided by the nurse, the family caregiver, the physician and nursing home administration could be linked to the deceased resident. This multi-perspective data provision increased the reliability of the data and enabled us to look for broad associations.

The retrospective post-mortem design has been identified as an appropriate design to evaluate end-of-life treatment and care as it enables to identify a representative sample of deaths[2].

Moreover, by retrospectively studying deceased residents we aimed to gain insight into palliative care, the dying process and terminal care, in contrast with studies were dying residents are excluded. More specifically, by focusing our studies on the last week of life, where palliative care should focus on terminal care in which comfort and efficient relief of symptoms remain the main goals of care. In this context, the use of comfort medication such as opioids, antipsychotics and hypnotics is considered to be more suitable in this stage than in previous stages of the disease trajectory.

In relation to symptom assessment, this is the first multicenter study using a large European nursing home population to compare symptom assessment between nurses and family caregivers. We only found one previous study[3] with direct, multiple-symptom rating comparisons between family carers and staff in nursing homes with 48 staff-family caregiver dyads.

Some limitations must be acknowledged.

The cross-sectional design only enabled us to compare and describe characteristics of pharmacological treatment and assessment of symptoms and to find associated factors. It enabled us to formulate some hypotheses regarding possible explanations for our findings but did not allow to identify cause-effect-relations.

A retrospective study design is susceptible for recall bias. Professional staff and family caregivers were asked to report on symptom burden of residents who died up to 3 months earlier. The 3-months limit has been successfully tested in previous research[2, 4-6]. Moreover, the EOLD-CAD assessment tool was developed and validated for retrospective studies[7, 8]. For professional staff, we reduced the risk be asking that the staff questionnaire was

completed by the professional caregiver, most involved in the care of the deceased resident. For medication use in the last days of life, staff could rely based on the nursing files.

The post-mortem design enabled us to identify all nursing home deaths, and made the terminal phase obvious. In daily practice and as a result in prospective study design, the terminal phase is often not predictable or sometimes impossible to foresee. This might decrease the generalizability of the study results. Moreover, the uncertainty of the terminal phase undoubtedly interferes with possible therapeutic choices.

With regards to the symptom treatment; with the available data, we made the pragmatic choice of studying the international comparison of the prescription of opioids, antipsychotics and hypnotics in the last three days of life of nursing home residents and to investigate possible associated factors.

The design of the Pace 1 study didn't allow in-depth exploration of possible explanations of differences between countries and has some important limitations. Firstly, we weren't able to take the non-pharmacological treatment into consideration. Secondly, we only had dichotomous data on whether or not opioids, antipsychotics or hypnotics were prescribed, without further specification. Thirdly, we had no further data on the indication, the duration and the dose or dose-changes over time of the prescription. Fourthly, we did not know whether or not the nursing home staff administered the prescribed medication. Fifthly, we had no information about the prevalence of undesirable side-effects and whether or not side-effects were reported to the physician who completed our study questionnaire. Finally, we had no insight in the prescription and deprescription history during the weeks prior to the terminal phase; nor on other clinical factors that could have influenced prescription of

medication during the last days of life, like the resident's or family's preferences or refusals concerning medication use. Based on these limitations, we have no insight in the mechanisms which could have led to the underuse of pharmacological treatment. As a consequence, we can only formulate hypotheses regarding *potential* underuse of opioids.

With regard to the symptom assessment, the symptoms incorporated in EOLD-CAD tool are assessed by a 1-to-3 Likert-wise scale, corresponding with the symptom scores "not at all", somewhat" or "a lot" which could be considered a rather 'rough' estimate. This choice was made as the EOLD-CAD assessment tool was developed and validated for retrospective studies. For purposes of regular follow-up in daily nursing care, an assessment instrument with a larger score range would be more desirable, possibly decreasing the percentages of perfect match and the interobserver agreement beyond chance, but increasing the possibility of personalized, fine-tuned symptom assessment and treatment.

6.2.2. Validation study of the newly developed SATISFIE multi-symptom rating scale

In **chapter 5** we described the development and validation of the SATISFIE-rating scale. With the SATISFIE-scale, older people can rate ten frequently prevalent symptoms on a zero-to-ten numeric scale. If necessary, they can add three symptoms and rate them likewise.

The SATISFIE multi-symptom scale is, to our knowledge, the first self-rating instrument for broad symptom assessment that was developed and validated among a heterogeneous population of nursing home residents, including residents with mild to moderate dementia.

The SATISFIE assessment scale (chapter 5) covers most domains of palliative care, as stated by the World Health Organization, except spiritual care. This might be considered as one of the instrument's limitations.

Because we aimed to develop an instrument for communicative elders, we included participants with MMSE >18. Consequently, we have no information about applicability of the SATISFIE instrument in a more cognitively impaired population.

The validation-study of SATISFIE was organized in Flanders. We translated the scale in English for publication without validating the translation. Validation in other countries and languages remains necessary.

6.3. Discussion of the main findings

6.3.1 Pharmacological treatment of symptoms

Based on our data, we cannot make firm conclusions on possible misuse or overuse of pharmacological treatment of symptoms. By combining data on the individual resident's prevalence of symptoms and the absence of opioid prescription, considered as best practice in the dying phase, it was possible to operationalize potential opioid underuse. However, since we have no data with regards to other possible non- or pharmacological treatment options, we cannot make firm conclusions on the quality of care during the terminal phase of the nursing home population.

Although, the design of our study does not allow us to establish causal relations with the prevalence of pharmacological treatment of symptoms, it gives the opportunity to define some factors which could be associated with the use of pharmacological treatment of symptoms in the terminal phase. These factors are shortly discussed in the following paragraphs.

6.3.1.1 Country

Prevalence of opioid, antipsychotic and hypnotic prescription was, in our study, strongly associated with the resident's country. International comparison revealed significant differences between countries with the most striking difference for opioids (chapter 2). Even

when we focused on residents to whom opioids were indicated, because they suffered from pain or dyspnoea in the last days of life, the difference in potential opioid underuse between countries, as described in chapter 3, was remarkable; the most pronounced potential underuse of opioids was found in Italy (64.6 %) and Poland (79.1 %). Based on our data we cannot establish the reasons for these differences between countries, but other research and literature can be used to identify possible explanations. Use of opioids can be hindered by multiple factors and on different levels which were found to exist simultaneously and interactively maintain each other[21]. In Poland and Italy, fewer initiatives were taken to develop palliative care in nursing homes[9], as already stated by a European Association of Palliative Care (EAPC) taskforce[10]. The PACE 1 cross-sectional study established that, in Poland and Italy, only a minority of the deceased residents received palliative care[11]; nursing home nurses and care assistants less often agreed with the basic principles of palliative care[12] and physicians were more reluctant to propose palliation as a treatment goal [13]. While, in Poland and Italy, the nursing home residents received less opioids in the last days of life, they had the highest prevalence of antibiotics administration and received more common, potentially inappropriate treatments as artificial nutrition and/or artificial fluids, compared to nursing home residents in the other participating countries[14].

Earlier research also showed that physicians in Italy were reluctant to recognize the terminal phase and to communicate openly with patients and family members about end-of-life situations[15] and advance care planning seems less incorporated in the care [16]. An existing cultural taboo about death and dying[17] is also known to make nursing home staff feel more often incompetent to start end-of-life conversations[18]. Fear of opioids (dependence, hastening death, tolerance) is already been described as the most important barrier for opioid use[22] and is identified as a large popular conviction in some countries[23].

The difference in reimbursement of opioids between cancer patients and non-cancer patients reflects, by contrast, rather a medical, public health point of view. The reluctance to use opioids to treat dyspnoea is an attitude among health care professionals, also described in chronic lung disease physicians[24]. Misconceptions and misinformation related to opioid treatment are still widespread among the public and among health care providers. These misconceptions are not sufficiently remedied by governmental initiatives [22].

6.3.1.2 Cancer

Having cancer was also associated with the prescription of comfort medication in nursing home residents' end of life. Dying of cancer tripled the odds of opioid prescription and doubled the odds of hypnotic prescription, as we established in chapter 2. This is presumably explained by three factors. Firstly, the nurses and physicians are more aware of, or even expected that, cancer patients probably having pain or that they may be more anxious or nervous.

Secondly, as the use of opioids for non-malignant pain is still controversial[19], cancer patients are more likely to receive opioids, compared to patients with pain of other causes.

Thirdly, palliative care, with symptom treatment as a crucial component, is historically associated with cancer. Research in different healthcare settings, including nursing homes, already established that people with cancer have more easily access to palliative care[11, 20] and often receive higher quality palliative care, compared to patients with organ failure[21]. Not surprisingly, when we compared the symptom burden of older people with a palliative status against older people without (chapter 5), we found less pain in the palliative group, while other symptoms had an equal or a higher score in the palliative group.

6.3.1.3 Pain assessment

In our study, we found that receiving a pain assessment tripled the odds of opioid prescription. The absence of symptom assessment can lead to under recognition of existing pain or dyspnea, possibly resulting in undertreatment. When a symptom assessment is also omitted once the opioid treatment is initiated or adapted, caregivers lack precise information on the treatment's effectiveness and the (non-)occurrence of possible side-effects.

This result is in line with literature stating that formal pain assessment creates or enhances awareness[29], and awareness of symptoms leads potentially to better symptom treatment. The importance of regular, systematic symptom assessment for high-quality palliative care in nursing homes cannot be neglected: we calculated that the odds of opioid use in patients with indications for opioids were tripled when their pain was assessed. These findings are consistent with other research[30-33], elucidating the importance of systematic pain and symptom assessment. In daily care, experience can be an important resource to rely on, but staff need to remain critical and open-minded for evidence-based nursing practice.

6.3.1.4 Symptom burden is not associated with pharmacological treatment of symptoms

When we searched for potential opioid underuse, which we defined as the absence of an opioid prescription in the last three days of a resident's life with a nurse's score of

"somewhat" or "a lot" for the items pain or dyspnea in the EOLD-CAD-tool, we found no association between opioid prescription and the prevalence of the symptom. This cannot be explained by the lack of awareness. The scores "somewhat" or "a lot" in the EOLD-CAD proof the nurses' awareness of the prevalence of pain or dyspnea. But apparently, the awareness of the symptom's prevalence in itself, is not sufficient to initiate the use of comfort medication in end of life. Firstly, the lack of palliative care knowledge could be a possible explanation. Palliative care knowledge should foster a palliative care attitude of professional caregivers and adjust their misconceptions of opioid treatment. Lack of palliative care knowledge has been identified as a barrier for both a favorable attitude towards palliative care[22] with increased receptiveness to symptom management and to opioid treatment[23]. Not surprisingly, the research by the PACE-consortium established that in Poland and Italy, the lowest prevalence of opioid use and the highest prevalence of potential opioid underuse go hand in hand with the lowest level of palliative care knowledge, and of end-of-life factors more specifically[24], and the lowest level of staff agreement with the principles of palliative care[12]. Secondly, opioid treatment is even more hampered when the resident's health status is not recognized or not openly acknowledged as palliative. Earlier research[15] already showed that this is the case in Italy. Research by the PACE consortium confirmed this, together with the low prevalence of palliation as a treatment goal in Poland and Italy[13]. To overcome these problems, it is recommended that the early implementation of palliative care, advance care planning and terminal care should be fostered by all levels of nursing home staff, including the management boards and the coordinating organizations[25].

6.3.2 Symptom assessment

When comparing the family caregivers' reporting of symptom burden of residents' end of life with the staff's reporting, we found that, on a group level, family caregivers reported significantly higher burden than staff for the physical distress and dying symptoms. The differences in mean scores seem very small, but are clinically relevant[26], as the score range from 1 to 3 represents a range in symptom burden from "not at all" to "a lot". In contrast, we found no difference in the reported emotional distress and well-being.

As mentioned in chapter 4, the overestimation of symptom burden by family carers, compared to professional staff, is, in our opinion, the most probable explanation. When family carers visit a resident in the dying process, it is likely that they are emotionally overwhelmed by the sometimes sudden, physical deterioration prior to death. Similar emotional reactions are reported in third-year nursing students' experience[27] in the care for the dying, although the patients' death was expected. Professional caregivers, in contrast, gain experience by witnessing dying processes regularly. They learn to recognize the symptoms, to what extent they can occur and, if possible, by talking with the patients, they even learn to estimate to what extent a symptom can be burdensome for the patient. Bahrami et al.[28] found a larger agreement in describing the physical aspects of quality of life between patients and nurses in nurses with a greater clinical experience. The study by Bahrami, together with the age distribution and nursing experience of the staff respondents in our study, make our hypothesis of overestimation of symptoms by family members more plausible than their underestimation by professional staff.

Presuming that family carers of the residents' generation have acquired more experience in witnessing dying than carers of the next generation, our finding that score differences

between family carers and staff in the residents' children's generation exceed the score differences between staff and family carers in the residents generation, also supports our hypothesis: the difference in clinical experience and in witnessing dying may explain the discrepancy in the physical distress and dying symptom subscale scores between staffs and family caregivers' scores.

Moreover, formal training in end-of-life care mitigates the staff's interpretation of symptoms such as Cheyne-Stokes,-like breathing, death-rattle, gurgling and swallowing difficulties as symptoms that occur normally in the dying process, and which are not necessarily harmful or disturbing for the resident. Family caregivers who lack formal training, in contrast, might perceive these symptoms as burdensome. Hence, clinical experience possibly enables professional staff to have a better idea of the resident's symptom burden.

While it can be reassuring for residents and family caregivers that experienced staff more easily recognise possibly burdensome symptoms, this experience concomitantly represents the risk of blind spots for less common or unexpected symptoms in non-communicative residents. Experience and awareness is inherently limited, also professional caregivers don't know what they don't know. In our validation study of the SATISFIE-instrument (chapter 5), for example, the nurses' mean score for pain was higher than the patients' score in the group of patients with a palliative status, but lower than the patients' score in the non-palliative group. This illustrates the importance of regular symptom assessment.

Earlier research showed that self-assessment of symptoms is largely preferable [29-33], even in patients with moderate to severe dementia. Without detracting the gold standard of self-assessment, we questioned if symptom scores by family caregivers could equally be used as symptom scores by staff, in cases where self-assessment is no longer possible to obtain a

broader view of the resident's symptom burden. On the residents' level, the extent of perfect matches for the individual symptoms in the EOLD-CAD ranged from 40.8 to 68.7 %, interrater agreement beyond chance between staff and family carers was slight to fair. Remarkably, the highest percentages of perfect match were reached for objectively observable symptoms as crying, choking, pain, moaning, dyspnea and restlessness. This is consistent with other research, that found larger score differences for less observable symptoms[34-39] or psychological symptoms[40, 41].

Consequently, staff and family carers firstly need to discuss what they mean by each symptom and how they ascertain its presence. When they have deliberated clearly how each symptom is defined in this resident, both family carers and staff can meaningfully assess the symptoms and discuss their prevalence and the possible effect of symptom treatment regularly.

6.4. Implications of the main findings

6.4.1. Implications for further research

6.4.1.1 Pharmacological treatment of symptoms

Our study pointed to the existence of important differences in medication prescription in the last three days of life of nursing home residents between 6 European countries.

Regular analogous comparison of medication use over time could monitor whether the existing differences persevere or how countries evolve and should, where possible, lead to the proposal of international standards to orientate the end-of-life medication use. In-depth qualitative research could explore the health-care professionals' perception of appropriateness of opioid, antipsychotic and hypnotic treatment in palliative situations. Qualitative research could also explore the perceived fault lines and benchmarks between care for older people, palliative care and end-of-life care. This could also explain some differences in symptom treatment between cancer and non-cancer patients. The existing difference in prescription between cancer and non-cancer patients should be subject of further research. In every research on symptom management, this difference between cancer and non-cancer patients should be taken into account, while in-depth qualitative research should explore the mechanisms maintaining this difference.

To gain insight into the appropriateness of opioid, antipsychotic and hypnotic treatment, prospective longitudinal research is desirable in which the administered treatment, the rhythm of dose adaptations is combined with the patient's health and cognitive status, comorbidity and regular assessment of the patient's symptom burden. This research should be joined with the patient's, health professional's and family's satisfaction with care, while qualitative research should document the treatment choices and the resident's and family's satisfaction with care. An international research approach in different palliative care settings would enable international comparison and between care settings.

Further research taking the multimorbidity of the oldest old into account is needed to enlarge and refine palliative care guidelines for the fast growing frail older population.

To keep patients in the terminal phase included in this longitudinal research, advanced consent should be used, which means that patients or their legal representatives consent in advance to continue to participate in this research even if they are no longer able to give their permission at the moment that burdensome symptoms would occur.

6.4.1.2 Symptom assessment

To operationalise the family caregivers' input in symptom assessment, deeper insight in to how family caregivers and health professionals assess symptoms is needed. Symptom assessment scores should be mutually compared between all involved parties in this triangle, to gain insight in how family caregivers' and health professionals' score relate to each other and to the gold standard of the residents own score, in case the latter would become unavailable over time. Qualitative research can clarify how the involved parties experience or perceive symptoms, to gain insight in factors that explain the differences in symptom scores.

As mentioned in the limitations' section, the use of symptom assessment tools with a broader score range is preferable in daily nursing practice, and could be used in prospective longitudinal research. We performed an initial validation of the SATISFIE symptom assessment tool (chapter 5) in communicative older people.

The missing out of the domain of spiritual care in the SATISFIE assessment tool is remarkable. Possibly, the expert group was to (para)medical and the choice of the word "symptoms" can narrow the scope of the professionals, but also of the residents. The COVID-19 pandemic clearly revealed the importance of non-physical aspects of suffering in nursing

home residents, as they suffered from lack of social interaction and isolation. Perhaps, we should go back to basic model of palliative care, as formulated by Cicely Saunders, and look explicitly for physical, psychological, social and spiritual suffering, and present a list of possible symptoms that covers all domains to an expert panel which is expanded to occupational therapists, animators, spiritual caregivers and residents' representatives. We should question the residents about possible suffering, which can be understood more broadly than symptom burden.

This adapted SATISFIE scale still has to be validated in the nursing home population with particular attention to the extent to which it is useful in residents with moderate or more severe dementia. Therefore, inclusion of residents MMSE scores below 18 is necessary.

Our validation of the SATISFIE assessment tool almost exclusively took place in nursing homes and is to be confirmed in new studies which will additionally be organized in other care settings, such as (palliative) community care and hospital settings. Furthermore, the gathering of additional information on residents' comorbidity and disease status could provide interesting insights into the assessed symptoms.

6.4.2. Implications for health care policy and education

6.4.2.1 Pharmacological treatment of symptoms

In our research, country is an important associated factor in end-of life medication use for antipsychotics, hypnotics and certainly opioids. As the WHO advocates, palliative care delivery should shift from prognosis- or diagnosis-based models to needs-based care delivery[42]. Validated tools should be largely implemented for detection of palliative care needs, including symptom burden to guide the use of pharmacological treatment of symptoms. In the context of nursing home residents, a more specific tools such as The End of Life in Dementia (EOLD) scale[8], which is completed by the health-care provider and assessing satisfaction with care, symptoms, and comfort at the end of life is more suitable[7]. The outcomes of these measures should be used to guide comfort medication use in a palliative context. The large variation between countries suggest that each country will require its own policies to meet those international standards.

To adjust the misconceptions and misinformation related to opioid treatment, information campaigns should strengthen the health care literacy of the population as a whole, and of health care workers in particular. These campaigns should be specifically tailored to the information needs of each country, and should not only cover comfort medication use, but also inform about the goals and possibilities of palliative care, end-of-life care and advance care planning.

Palliative guidelines need to be enlarged or refined for chronic, incurable non-cancer diseases and for older patients, based on ongoing research. They should take the multi-morbidity, their specific responsiveness, their vulnerability for side effects and the specific context of end of life into the nursing home into account. In palliative care, medication is often used differently, compared to curative medicine. Differences of medication

prescription and use in palliative medicine, compared to curative medicine should be integrated in the guidelines and taught in the medical curriculum. Due to the often-restricted prognosis, undesired side effects in the long-term are less taken into account, while off-label use of medication, based on clinical experience, is not uncommon. should also be taken in account in the development of palliative care guidelines.

Positive attitudes towards palliative care and knowledge about effective pharmacological treatment of symptoms merit more attention in the education of (assistant) physicians and nurses as well as in postgraduate education. It has already been advocated that a range of continuing professional education opportunities are also needed for registered health professionals to increase their symptom assessment and medication management competencies, particularly related to administering opiates[43]. Well-trained physicians, will be less reluctant to choose for palliation as a treatment goal and will be more confident to discuss palliative care and end-of-life, while they experience that they can meaningfully contribute to the patients well-being. Consequently, it offers them the possibility to continue their professional relation with patients and their families, which can alleviate the feeling they let down or abandon their patients. Palliative care training can encourage nurses to discuss goals of care with patients and their families, help families to cope with their concerns and can explain the rationale why certain treatment and care activities are no longer undertaken while others are intensified to optimise the patient's well-being. Consulting and implementing palliative care guidelines into practice should be part of palliative care training, to keep the physicians' and nurses' knowledge up to date.

Public campaigns should also inform the large population that old age or end of life are not intrinsically linked with pain.

In light of the differences between European countries, health care institutions must pay attention to the nurses' and nursing assistants' palliative care knowledge and attitudes towards symptom assessment, end-of-life medication use[44] and communication in end-of-life[15]. When recycling or retraining courses are organised, these items could be taken into account.

6.4.2.2 Symptom assessment

The use of validated tools to assess pain, amongst other symptoms, and the way how to use them in electronic medical and nursing files, should be instructed in the nurses and physician curriculum. Their implementation and regular use could be considered as a mandatory aspect of quality control in nursing home care. The possibility to assess pain in non-communicative older people with validated, reliable assessment tools deserves special attention as residents with dementia are undertreated for pain symptoms .

6.4.3. Implications for clinical practice

6.4.3.1 Pharmacological treatment of symptoms

The existing difference in medication prescription between cancer and non-cancer patients is a concern for clinical practice, research established that the symptoms at the end of life in

disease other than cancer are remarkably similar to those experienced by cancer patients[45, 46]. For people with advanced, progressive life-limiting illness, a core group of symptoms, including pain, depression, dyspnoea, and fatigue is found as patients approach death in both malignant and non-malignant chronic illnesses[47].

This, again, pleads for early integration of palliative care in nursing homes, as recommended earlier by researchers[25]. The same concerns are reflected in a new world-wide consensus based definition of palliative care which states that palliative care is applicable throughout all health care settings and according with the patient's needs[48].

Palliative care clinicians and, consequently, nursing home clinicians should focus on the symptoms as such, and aim to improve the patients' comfort, regardless of the underlying disease. Symptom relieve is not justified because a patient has cancer, but because he or she is suffering. An emphasis on needs-based care, rather than on diagnosis- or prognosis-based care, has been advocated by many.[49] In any case, palliative care guidelines need to be enlarged or refined for dying from non-cancer diseases and older patients.

The use of opioids for treating dyspnoea in palliative care, and certainly in the terminal phase should be considered more often, especially in chronic respiratory diseases, physicians will have to overcome their fear to use opioids[50].

6.4.3.2 Symptom assessment

In our research, we found that the lack of pain assessment tripled the odds of potential opioid underuse. Symptom prevalence is the onset of symptom treatment and is warranted

in nursing home residents for optimising symptom relief in the dying phase. As supported by previous research: pain[51] and other symptoms should be regularly and systematically assessed in nursing homes[33, 43, 52]. Regular assessment creates awareness of symptom burden and can results in a more compassionate approach in contact and care, even if thorough treatment of the symptom is not, or no longer, possible.

At regular moments, certainly when death is approaching, staff and family carers should reiterate advanced care directives, reconsider goals of care and nursing plans. Family should be informed what to expect normally in the dying process, with regard to the potential symptoms, the burden it (maybe) represents for the resident and the possible treatment and the possibilities of palliative care, provided in the nursing home. Family carers and, if possible, residents should have the opportunity to reaffirm or determine their priorities in evolving situations near end of life.

Staff must be continuously educated in symptom assessment with feasible, validated assessment tools. It is desirable that these educational sessions are repeated regularly in the nursing homes, enabling family caregivers to participate since, in our opinion, symptom assessment is the beginning of mutual dialogue and consideration between residents, family carers and professional staff. As a result, family caregivers' observations can be more effectively integrated in the symptom assessment and treatment. Regular symptom assessment has to be accompanied by standing orders, issued by the physician, in order to respond quickly and effectively in case of symptom burden.

As a result, symptom assessment and treatment could become a negotiated, shared, common goal for residents, family carers and professional staff.

6.5 References chapter 6

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English summary

Taken the demographic evolution into account, nursing homes will continue to be major providers of palliative care for the frail aged in Europe. For the nursing home residents with multiple, complex comorbidities, symptom management remains an essential palliative care need. Symptom management in end-of life in nursing homes in six European countries was the subject of this dissertation. Symptom management is an ongoing cycle of symptom assessment and symptom treatment.

With regard to the pharmacological treatment of symptoms, we compared the prescription of opioids, antipsychotics, and hypnotics in the last three days of life of nursing home residents (chapter 2). We found large differences in the prescription of opioids, antipsychotics, and hypnotics between countries. The resident's country appeared to be the predominant factor associated with opioid, antipsychotic and hypnotic use. Dying from cancer tripled the odds for receiving opioids and doubled the odds for receiving hypnotics in the last days of life.

For opioids, more particularly, we explored possible underuse and searched for associated factors (chapter 3). Potential opioid underuse differed significantly between countries and was more prevalent in residents with dyspnoea then in residents with pain and residents suffering from both symptoms. Odds of opioid underuse lowered to a third when pain was assessed.

With regard to the assessment of symptoms, we described the residents' symptom burden at the end of life and explored differences in the perception of symptoms between professional staff and family carers (chapter 4).

On group level, mean staff scores significantly reflected better comfort than those of family carers for the total symptom burden and for the physical distress and dying symptoms. No significant differences were found for emotional distress and well-being.

Lastly, we developed and validated the SATISFIE tool, an instrument for regular, multiple-symptom assessment in institutionalised elderly (chapter 5). SATISFIE is a tool for self-assessment of then frequently prevalent and potentially burdensome symptoms and offers the possibility to assess three additional symptoms, mentioned by the patient. The SATISFIE-tool was found to be feasible for regular multi-symptom assessment in clinical practice.

Nederlandse samenvatting

In het licht van de demografische evolutie, zullen woonzorgcentra (WZC) in Europa de belangrijkste verstrekkers van palliatieve zorg blijven voor kwetsbare ouderlingen. Voor residenten met complexe, multimorbiditeit zal symptoomcontrole een belangrijke palliatieve-zorgnood blijven. Deze symptoomcontrole aan het levenseinde van zorgresidenten in 6 Europese landen, was het onderwerp van deze doctoraatsstudie. Symptoomcontrole is een voortdurende cyclus van het symptoommeting en symptoombehandeling.

Wat betreft de symptoombehandeling hebben we het voorschrijven van opiaten, antipsychotica en hypnotica in de laatste 3 levensdagen onderzocht (hoofdstuk 2).

We vonden grote verschillen in het gebruik van opiaten, antipsychotica en hypnotica tussen de landen. Het land waarin de resident verbleef was de belangrijkste factor geassocieerd met het gebruik van opiaten, antipsychotica en hypnotica. Sterven aan kanker verdrievoudigde de kans op het gebruik van opiaten en verdubbelde de kans op het gebruik van hypnotica in de laatste levensdagen.

Voor opiaten, meer specifiek, onderzochten we mogelijk ondergebruik en gingen we op zoek naar daarmee geassocieerde factoren (hoofdstuk 3). Het potentieel ondergebruik van opiaten verschilde significant tussen de landen en was frequenter bij residenten met dyspnoe dan bij residenten met pijn en met beide symptomen. De kans op potentieel ondergebruik van opiaten verminderde tot een derde bij residenten waarbij de pijn werd gemeten.

In verband met het meten van symptomen, beschreven we de symptoomlast van residenten en onderzochten we de verschillen in perceptie van de symptoomlast tussen professionele en familiale zorgverleners van de residenten (hoofdstuk4).

Op groepsniveau weerspiegelden de gemiddelde scores van de professionele zorgverleners een beter comfort qua totale symptoomlast en voor fysieke belasting en stervenssymptomen dan de scores van familiale zorgverleners. We vonden geen significant verschil in de perceptie van emotionele belasting en algemeen welzijn.

Tenslotte ontwikkelden en valideerden we de SATISFIE-schaal, een instrument voor regelmatige meting van meerdere symptomen bij geïnstitutionaliseerde ouderen(hoofdstuk5). SATISFIE is een instrument voor zelfrapportage van 10 frequente en potentieel belastende symptomen en geeft de mogelijkheid van zelfrapportage van 3 bijkomende symptomen die door de resident worden genoemd. Het SATISFIE instrument werd als geschikt ervaren en is een aanzet voor regelmatig inschatten van meerdere symptomen in de klinische praktijk.

Curriculum vitae Marc Tanghe

Personal data

Place & date of birth: Gent, 23 mei 1967.

Civil status: married to Christel Geeraerts, father of Fien Tanghe(°1999)

Phone: 032 483 370 617

Mail: marc.tanghe@Ugent.be

Training

1988: Gegradueerde ziekenhuisverpleger, met onderscheiding.
Hoger Instituut voor Paramedische Beroepen, Gent

1991: Licentiaat in de medisch-sociale wetenschappen en het ziekenhuisbeleid, met onderscheiding. Katholieke Universiteit, Leuven.

1993: Geaggregeerde voor het onderwijs in de medisch-sociale wetenschappen.
Katholieke Universiteit, Leuven.

Specific training

1999: Certificaat voor verpleegkundig pijnspecialist.
Centrum voor posthogeschoolopleidingen, KU, Leuven.

2014 Certificat de la formation d'infirmier ayant une expertise particulière en soins

palliatifs. Grande distinction, Henallux, Namur.

2017 Erkenning van beroepsbekwaamheid van verpleegkundige met een bijzondere deskundigheid in de palliatieve zorg. Erkenningsnr NB19036243

Professional experience

07/'91-12/'91: Nurse, palliative care unit Zr Leontine, Sint-Jan, Brussels.

1992: Military service, nurse, burns center, high-care-unit, Neder-Over-Heembeek.

01/'93-03/'93 Nurse, intensive care unit, Sint-Elisabeth, Ukkel.

03/93-08/'94 Nurse, palliative home care, Omega, Brussels

09/'94-12/'94 Nurse, palliative home care, Continuing Care, Brussels

01/'95-03/'97 Nurse, , palliative care unit, 2 Alice, Uccle.

03/'97- 11/'12 Nurse, palliative home care, Omega, Brussels

11/'12 – 02/'14 Head nurse, palliative care unit, CHRPBW, Bois de la Pierre, Wavre.

02/'14 - 05/'15 Head care, nursing home Keymolen, Armonea, Lennik.

06/’15 – 05/’18 PhD student, Ugent, End-of-life care researchgroup.

Present post

08/’18 – now Nurse, half-time, palliative care supporteam, GZA, Antwerp.

03/’20 – now Nurse, half-time, palliative care supporteam, Sint-Jan, Brussels.

Professionally related activities

2003-2007 Guest lecturer postgraduate training palliative care

HUBrussel-Erasmushogeschool-Netwerk BHV.

2005-2013 Member of coordination committee BanaBa palliative care.

HUBrussel-Erasmushogeschool-Netwerk BHV.

2007 – 2013 Guest lecturer BanaBa palliative care.

HUBrussel-Erasmushogeschool-Netwerk BHV.

2011 – 2013 Guest lecturer bijzondere beroepstitel oncologie.

Erasmushogeschool, Jette.

2010 – 201: Member editorial committee Pallialine.be

2010 – 2013 Co-author “pijnbestrijding bij palliatieve patiënten”. Pallialine.be

Cooperator in several palliative care guidelines, pallialine.be

09/2013 Member of the stakeholder-panel KCE-report “Support Onco-Cancer Pain”.

01–09/19 Co-author E-learning program palliative care, HOWEST, Bruges, sponsored by the “Koning Boudewijn” foundation.

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Presentations

Presentations in International congresses

Tanghe M, Van Den Noortgate N, Pivodic L, Deliens L, Onwuteaka-Philipsen B, Szczerbińska K, Finne-Soveri H, Collingridge-Moore D, Gambassi G, Van den Block L, Piers R. **Medication use in the last 3 days of life in nursing homes**; PACE consortium meeting, Treviso; 08/05/2017; oral presentation.

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