Chapter 1

General introduction
Definition and history of palliative care

Palliative care finds its origin in the modern hospice movement led by Dame Cicely Saunders.1,2 In 1967 Cicely Saunders founded the first professional hospice, St. Christopher’s Hospice, in London. The hospice was founded on the principles of combining teaching, research and clinical care, seeking a balance between ‘too much’ and ‘too little’ treatment. By listening carefully to patients’ stories of illness, disease and suffering the concept of ‘total pain’ was developed. Cicely Saunders coined the term ‘total pain’ to describe the multidimensional character of the palliative patient’s pain experience including physical, social, emotional and spiritual aspects of suffering. The holistic approach to pain has become a new strategy in the care of dying patients.3 The active total care for patients whose illness is chronic and who are in the last phase of life is nowadays defined as palliative care. Palliative care focuses on the control of pain and physical symptoms in addition to the social, emotional and even spiritual aspects of suffering, and is neither intended to prolong life nor hasten death, but to enhance quality of life.

In 2002, the World Health Organization (WHO) defined palliative care as: … a new 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.5

The need for palliative care

The world’s population is ageing. People are living longer and the proportion of people living to old age is increasing.6,7 In line with increasing life expectancy more and more people die from serious chronic diseases.6,8 Chronic diseases such as cancer, cerebrovascular disease, heart disease and dementia tend to become more common with age. It might be expected that along with an increasing number of people living to older ages more people will live a relatively longer period of life with the effects of decline due to chronic diseases.6,8 Older people reaching the end of life frequently suffer from more than one chronic condition. Multi-morbidity causes a wide range of physical, psychological and social problems, and, consequently, complex needs for care and support towards the end of life. As long-term care facilities such as nursing homes and homes for the elderly are increasingly settings where people live the last period of their life, long-term care facilities will also play an increasing role in the care of frail older people at the end of life. Projections of the ageing population show that more people will die from old age and/or complications due to end-stage chronic diseases emphasizing the importance of the availability of appropriate and effective palliative care to ensure people die with dignity.

Palliative care policy

Following the increasing and complex needs for care for people near the end of life, interest in palliative care has significantly increased in recent decades. An analysis by the Economist Intelligence Unit looked at access to services, quality of care and public awareness in 40 countries and found that the UK has led in terms of its hospice care and statutory involvement in end-of-life care. Other European countries including Denmark, Finland and Italy were found to lag a long way behind as the quality and availability of care is often poor and there is a lack of policy co-ordinations in these countries. In 2003, the European council approved a recommendation on palliative care that was adopted by the ministers of health in all 45 of the member countries; however, policy-making is mainly the responsibility of national governments in Europe.9

In the Netherlands, palliative care has become an important topic in the political agenda.10 Several incentive programmes have been developed to improve palliative care, and to encourage education and training in palliative and end-of-life care.11,12 An important step in the development of palliative care in the Netherlands was the policy programme ‘Palliative care in the terminal phase’ that the Ministry of Public Health assigned to ‘ZorgOnderzoek Nederland’ (ZON; in English: ‘Health Research and Development Council’).13,14 This programme started in 1997 and aimed to develop palliative care in the context of already-existing institutions such as home care services, nursing homes and hospitals. Following on from the programme ‘Centers for the development of palliative care’ (COPZ’s) were established which have significantly contributed to the expertise and increase in research activities in palliative care. Currently, palliative care is firmly on the public agenda and has become even more important for policy makers who organise and provide care. The state secretary for Health Well-being and Sports described palliative care as essential to the quality of life in the last phase of life and to ensure a dignified death.15 As policy makers and health care professionals need to be provided with knowledge to develop policy and improve clinical practice, palliative care research is of great importance. The volume of research on end-of-life care, death and dying has grown considerably in recent decades and much progress has been made. However, end-of-life care research is still relatively new and faces many challenges.

Conceptual challenges in palliative care research

Conceptual clarity is a challenging factor in all research but particularly in a young and evolving research field such as palliative care. A great variety of operational definitions are found in research on this phase of life.16,17 A disparity exists between conceptual and operational concepts of terminal illness and dying, and it is unclear what time period is meant by the end of life. Palliative care populations have been defined in various ways by researchers and policy makers.17,18 Defining the scope of palliative care is of significant importance for research in this field, especially to enable the comparison of results across studies and countries. Borgstedt et al describe the lack of clear population criteria as a consequence of the WHO-definition of palliative care which focuses on the goals of palliative care but is rather vague in describing the eligible population.18 Palliative care is most commonly associated with people facing life-threatening illness and, consequently, much research on palliative care focuses on people with cancer. However, palliative care can also be applied to those with other chronic diseases such as heart failure, renal disease or neurodegenerative diseases such as multiple sclerosis or amyotrophic lateral sclerosis. Palliative care populations can be defined by the type of care provided in different health care settings e.g. hospice or palliative care unit. Patients can also be categorized as palliative care patients when receiving treatment that is not directed at cure or prolongation of life or when death is expected in the near future. In several randomized clinical trials investigators rely on the physician’s prognosis about the last phase of life.16,20,21 Conceptual differences as described above can be highly limiting with regard to generalizability, cross-study comparisons, research design and the selection of measurement instruments.17
Ethical challenges in palliative care research

In addition to conceptual challenges, end-of-life research creates some ethical challenges. Firstly, ethical questions arise when defining the risks and benefits of participation in a study.23 This may become even more difficult as a patient's needs for care change substantially as they near the end of life.23 In particular, randomizing terminally ill patients into two groups, one receiving a new intervention or therapy and the other receiving 'no treatment', standard therapy, or perhaps placebo, raises ethical difficulties.24-25 This may become even more difficult as care needs change substantially towards the end of life. Second, research involves extensive and increased frequency of testing compared with standard clinical care while the goal of palliative care is to relieve suffering and improve comfort for patients and their families. Third, ethical concerns can be raised by the fact that the competence of patients near the end of life may be impaired. People can only give consent to participate in study if they are capable of understanding the information given by researchers. In addition, study participants must be competent to be able to decide at any time to withdraw from a study.24-26 Especially for people facing a life threatening illness voluntary informed consent to participate in a research study may be difficult. These patients may be willing to try any treatment that might offer relief and may feel dependent on a research institute or investigator for their care. The vulnerability of patients near the end of life may influence their decision to participate in research projects.27,28 A care provider's decision to ask a patient to participate in a research study may also be influenced by a patient's health condition. Care providers may believe that participating in a study may harm the patient. However, patients may be quite willing to participate and may see the benefit of interaction with a researcher or therapist, of making a contribution and of telling their story.29

Practical and methodological challenges in palliative care research

Research on end-of-life or palliative care is also characterized by several practical problems. A major practical issue in conducting prospective studies in general may be the characteristics and condition of the study population. The prospect of attrition due to early death is inevitable in end-of-life care studies, in addition to functional attrition, referring to the fact that palliative care patients are often unable to complete questionnaires or participate in interviews due to weakness, exhaustion or cognitive impairment.17 However, randomized controlled trials have been considered as the gold standard for establishing robust evidence of the effects of a particular treatment or intervention as selection bias and confounding are avoided using this study design.30-32 In general, because a patient's condition and evaluations can be followed over time or until the point of death, to study the process or trajectories of dying, prospective study designs are preferred over retrospective designs.32-35 A challenge may be recruiting sufficient patients in the last phase of life to create a sample that is large enough. Recruitment often takes much more time than investigators have estimated. Lasagna's law described this phenomenon: at the time patient recruitment starts, the number of eligible patients becomes a fraction of what it was assumed to be before recruitment began. Investigators frequently depend on general practitioners (GPs) or other physicians to enrol patients into their study. However, GPs may tend to forget about the study or become less aware, due perhaps to the low prevalence of eligible patients or to time constraints.34-35 Other reasons that eligible patients will not be recruited may be an unexpected rapid physical deterioration in the patient, a lack of skill and confidence in the physician or researcher in inviting them to take part, or the view that involvement would be too burdensome for the patient.36 Moreover, at the time recruitment for end-of-life care studies starts, patients, especially those treated or residing in academic settings, may already be taking part in other research studies. In addition to the fact that terminally ill patients are rarely stable, the clinical heterogeneity regarding type of intervention, dose and duration of treatment, may limit end-of-life research and make any comparison and generalization extremely complicated. Another important methodological challenge includes the difficulty of determining appropriate outcomes and identifying measurement instruments to adequately assess those outcomes.

Palliative care research has frequently been associated with cancer patients and, consequently, not much research has investigated palliative care in long-term care facilities. However, palliative care can make an important contribution to improving the quality of life of older patients who suffer from multiple chronic diseases rather than cancer, though this may involve more challenges as there is a higher prevalence of cognitive impairment among older patients. As long-term care facilities are becoming more important in the provision of palliative care for those older people with multiple chronic diseases, part I of this thesis specifically focuses on the state of the art and the methodological rigour in palliative care research in long-term care facilities.

Measuring quality of life in palliative care

Over the past few decades, there has been a growing interest in the impact of health and health care on the quality of human life.36 Not quantity of life but the improvement of quality of life has been increasingly used as an outcome in health care research. Currently, in numerous scientific studies outcome measurement plays an important role in order to observe changes in patients' subjective health status or to demonstrate improvement in quality of life which can be attributed to the effects of a specific intervention.37 The European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group developed one of the most widely used outcomes measures to assess health-related quality of life.38 This questionnaire, the EORTC QLQ-C30, has been developed to assess physical and psychosocial symptoms and functioning in cancer patients. Several supplementary questionnaire modules have been developed to assess more specific issues relevant to particular types of cancer such as colorectal cancer, lung cancer and breast cancer. In addition, a shortened version of the EORTC QLQ-C30 was developed for use in palliative care patients, EORTC QLQ-C15-PAL.39 Quality-of-life measurement is a fundamental aspect of palliative care because achieving the best quality of life for the patient and his or her family is the main purpose of palliative care. Most researchers and clinicians agree that quality of life is a multi-dimensional construct referring to a state of subjective wellbeing. However, the understanding of quality of life may be affected by several factors, such as the patient population, the setting, culture and whether the concept is used in research or clinical practice.40 A consequence might be that quality of life has been approached in many different ways and that a great variety of measurement instruments has been developed and used in the last few decades. In addition, patients receiving palliative care are frequently not able to complete a questionnaire themselves and a proxy or health care professional will need to rate or assess the patient’s quality of life.

Results obtained by instruments are used by researchers, health care professionals and policy-makers in order to develop further research, guidelines, evidence-based care and
policy. Therefore the use of good or high-quality measurement instruments is of significant importance as these are able to provide more trustworthy results. First of all, in selecting a measurement instrument, a good content validity is one of the most important measurement properties of an outcome measure. Content validity refers to the degree to which the content of a measurement instrument is an adequate reflection of the construct to be measured.\textsuperscript{11} Does a questionnaire developed to assess quality of life in terminally ill patients include all aspects relevant to these patients and are the aspects appropriate and sufficiently covered? In addition to a good content validity, a high-quality measurement instrument should measure what it is intended to measure, and all items in an instrument’s scale or sub-scale should be internally consistent or, in other words, measure the same construct. The instrument should also be able to provide similar results on repeated measurements, and to detect changes over time.\textsuperscript{41-44} A measurement instrument that meets all the aforementioned criteria can be considered as a high-quality instrument. Additionally, a measurement instrument needs to be appropriate and practically feasible for use in a particular study and setting.

Therefore, part II of this thesis aims to identify any existing instruments that might be able to assess quality of life in palliative care patients and to assess the content and clinimetric quality of these instruments.

**Measuring dignity at the end of life**

Palliative care is of great societal importance and growing attention has been paid to the perspective of the patient. Patients considering the end of life frequently mention the importance of preserving dignity. Dignity has been increasingly considered as a central goal in palliative care.

Dignity can be defined as the quality of being worthy of esteem or respect. A distinction can be made between two types of dignity: basic dignity and personal dignity. Basic dignity is the inherent dignity of every human being, which nothing can take away, and personal dignity refers to a personal sense of worth, associated with personal goals and social circumstances. It is related to a person’s self-esteem and perception of being respected by others, and consequently it can be taken away or enhanced.\textsuperscript{45,46} In this thesis we focus on personal dignity at the end of life.

The preservation of their dignity is mentioned frequently by patients when considering the end of life. Dignity is important to 92 per cent of the Dutch general public when asked what they consider important in their dying phase.\textsuperscript{47} Disease and disabilities often elicit concerns about loss of dignity. In addition, loss of dignity is one of the most important reasons to formulate an advance directive in the Netherlands,\textsuperscript{48} and one of the most common reasons for requesting euthanasia or physician-assisted suicide.\textsuperscript{5,12} The law in Oregon concerning physician-assisted suicide is called ‘the Oregon Death with Dignity Act’.\textsuperscript{13} Understanding the causes of dignity-related distress could help to improve palliative care and research in palliative care. However, in order to make a concept measurable the concept first needs to be given theoretical meaning. In other words, to identify aspects that cause dignity-related distress at the end of life, conceptualization and operationalization of the concept of dignity is required. Dignity-related distress refers to suffering that can be caused by physical, psychosocial, spiritual, or existential issues, or as is often the case in terminally ill patients, some combination thereof.\textsuperscript{13} Chochinov and colleagues developed an empirical model of dignity from a qualitative study to understand how dying cancer patients understand and define dignity.\textsuperscript{54} As research involves empirically studying variables in order to describe and test hypotheses about the concept of interest, Chochinov and colleagues developed items from the themes and sub-themes in the model.\textsuperscript{13} Subsequently, terminally ill cancer patients were asked how much they thought that these items could influence their sense of dignity. In this way the dignity model was validated and the Patient Dignity Inventory, a measurement instrument to detect end-of-life dignity-related distress, was developed.\textsuperscript{55}

Dignity is comparable to the concept of quality of life with regard to breadth and level of abstraction. Compared to the number of studies that investigated quality of life, far fewer investigated the concept of dignity or used dignity as an outcome. Personal dignity goes beyond the assessment of physical and psychosocial health status and also includes perceptions of personal worthiness as well as worthiness in relation to others. In addition to quality of life, dignity can contribute importantly to palliative care research. Therefore, part III of this thesis focuses on further exploring the construct of personal dignity at the end of life as personal dignity.

**Objectives and research questions of this thesis**

This thesis consists of three parts, each with a different objective and different research questions.

The general objective of the first part is to provide insight into the research methodology in palliative care research in long-term care facilities. Most scientific studies on palliative care have been conducted with cancer patients; however, long-term care facilities are becoming more important in the provision of palliative care for older people. Therefore, part I specifically focuses on palliative care research in long-term care facilities. Accordingly, the research question addressed in Part I is as follows:

1. What is the methodological rigour of palliative care research in long-term care facilities in Europe?

The objective of the second part of this thesis is to explore the concept of quality of life in terminally ill patients and to evaluate quality-of-life measures suitable for use in palliative care. The main goal of palliative care is to improve the quality of life of the terminally ill patient, and therefore the measurement of quality of life plays an essential role in research in palliative care. Spiritual support is associated with better quality-of-life but the concept of spirituality is not well defined.\textsuperscript{56} Therefore, another objective of part II is to investigate whether and how spirituality is operationalized in the quality-of-life instruments. The following research questions are addressed in part II of this thesis:

2. What are the most important quality-of-life-domains for palliative care patients?

3. What is the content of and what are the domains measured by quality-of-life instruments that are suitable for use in palliative care?

4. How is the domain of spirituality operationalized in the quality-of-life instruments?
5. What is the feasibility and clinimetric quality of quality-of-life measures for use in palliative care?

The third part of this thesis focuses on personal dignity at the end of life. Dignity is increasingly considered as a goal of palliative care. The general objective of part III is to gain insight into the construct of personal dignity at the end of life, and to explore personal dignity as an outcome assessed by the Patient Dignity Inventory. The Patient Dignity Inventory is a measurement instrument that was originally developed to detect end-of-life dignity-related distress in terminally ill cancer patients. The research questions addressed in Part III are:

6. What is the meaning of personal dignity at the end of life and can this be adequately measured with the Patient Dignity Inventory?

7. Does health status affect perceptions of factors influencing dignity at the end of life?

8. What are the perceptions of caregivers on factors influencing personal dignity in the terminally ill?

Methods
In order to answer the research questions different studies were performed. This section presents the main characteristics of these studies. The methods are described in more detail in the separate chapters of this thesis.

Systematic literature review on research methodology in palliative care research in long-term care facilities
In order to answer the first research question a systematic literature review was performed to find out what types of studies have been done with respect to the patient populations, study design and patient outcome measures on palliative care in long-term care facilities in Europe. PubMed, Embase and PsychINFO databases were searched from 2000 up to May 2010 by use of a search strategy including search terms related to ‘palliative care’ and ‘end-of-life care’ combined with search terms related to ‘long-term care’. The search strategy yielded a total of 2825 hits of which 14 articles were included because they reported on patient outcome data of palliative care populations residing in a long-term care facility in Europe.

Literature reviews on quality of life
Two other literature reviews were conducted in order to answer research question 2 to 5. One to identify the domains that are most important for the quality of life of incurably ill patients and, one to identify instruments that can be used to measure these quality-of-life domains. For the first review, a nonsystematic search was performed in PubMed to find conceptual frameworks, indicators that are relevant for the evaluation of quality of life, and aspects that are important for the quality of life of palliative care patients. From the relevant studies that were found a framework that included the quality-of-life domains most important for incurable patients was developed. The other review was a systematic literature search in PubMed, Embase, CINAHL and PsycINFO databases to identify instruments measuring (at least one domain of) quality of life. This search yielded a total of 2015 hits.

Finally, a total of 36 studies that described the development or validation of 29 instruments in a population of patients with no curative treatment options were included in the review. A checklist was used to describe the instruments’ characteristics and, a rating list was used to evaluate the clinimetric quality of the instruments.

Survey study on dignity within the framework of a cohort study
The data used to answer research question 6 and 7 were collected within the framework of an advance directives cohort study. This cohort study is a major ongoing longitudinal study aiming to get insight into how advance directives are involved in end-of-life decisions in the Netherlands. The data were collected by a structured questionnaire that was completed by 3812 participant of the cohort in the Spring of 2007. One half of the participants of the cohort completed the 22 items of the Patient Dignity Inventory by indicating the extent to which they thought the items could influence their sense of dignity during the last phase of life. The other half of the cohort responded to an open-ended question on their definition of dignity and what issues would influence their sense of dignity during the last phase of life. The responses to the open-ended question were used to define the construct of dignity. The content validity of Patient Dignity Inventory was evaluated by assessing the relevance and comprehensiveness of the items of Patient Dignity Inventory by use of the COSMIN checklist (Consensus-based Standards for the selection of health status Measurement Instruments). The data collected from the subsample of the advance directives cohort study that completed the Patient Dignity Inventory (n=2282) were used to study the effect of health status on the perceptions of factors influencing dignity at the end of life. This study sample was divided in three different health status groups (good, moderate, poor) based on a question on whether they had an illness and scores on the Euroqol-5D (EQ-5D) items. Descriptive statistics and logistic regression analyses were used to investigate the effect of health status on the perceptions of factors influencing personal dignity at the end of life, and the relationship between those perceptions and socio-demographic characteristics.

Survey study on dignity among caregivers
In order to answer the last research question another survey study was performed. Trained volunteers and end-of-life consultants (SCEN-physicians) were asked to indicate the extent to which they consider the items of the Patient Dignity Inventory can influence personal dignity in the last phase of life, and can make it problematic in practice to maintain personal dignity in the last phase of life. From the Fall of 2006 to January 2007 the survey questionnaire was completed by 236 volunteers and 427 physicians.

Outline of this thesis
The chapters of this thesis are based on articles that have been published in or submitted to a peer-reviewed scientific journal, and can be read independently.

Chapter 2 describes what types of studies on palliative care in long-term care facilities in Europe have been performed between the year 2000 and 2010.

Chapter 3 presents a quality-of-life framework and describes the content of and domains measured by quality-of-life instruments that are suitable for use in palliative care. In particular, there is a focus on how the domain of spirituality is operationalized in the instruments.
Chapter 4 provides an overview of the feasibility and clinimetric quality of all the quality-of-life instruments appropriate for use in palliative care is given.

Chapter 5 evaluates the construct of dignity and the content validity of the Patient Dignity Inventory in people with an advance directive in the Netherlands.

Chapter 6 describes how the perceptions of personal dignity at the end of life are related to health status, and other demographic factors.

Chapter 7 examines and compares how two different groups of care givers understand personal dignity in terminally ill patients.

Chapter 8 will discuss the main findings. In addition to some methodological considerations, implication for research policy and suggestions for further research will be considered in the final chapter of this thesis.

References
