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General introduction

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BACKGROUND

Dying is a natural and universal event, socially and culturally embedded around the world.[1] While dying will remain an inevitable consequence of living, the causes leading to death have changed over time (Figure 1).[2,3]

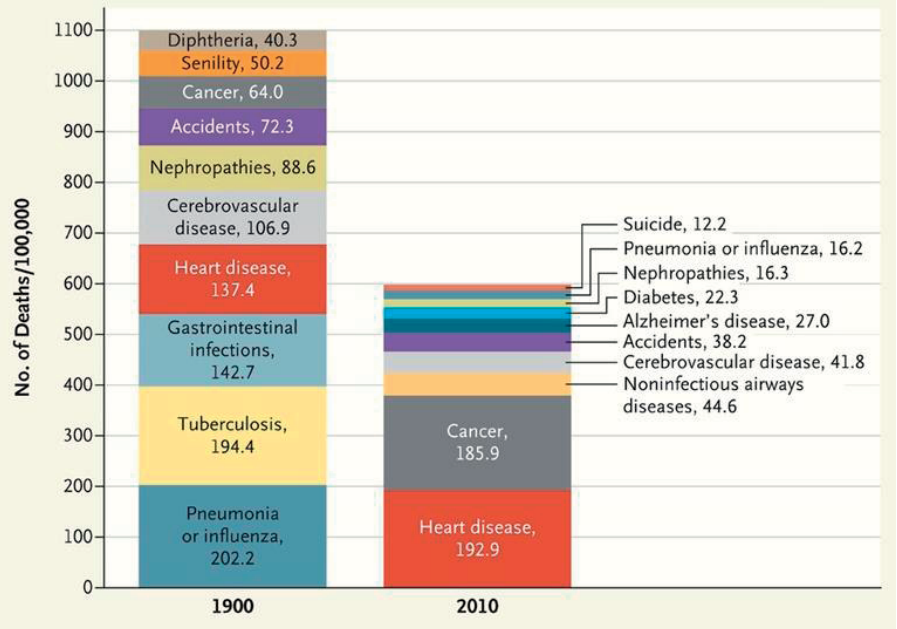

Figure 1. Top 10 causes of death in the United States: 1900 vs. 2010.[3]

In the beginning of the 20th century, death was often caused by communicable and infectious diseases.[4] The course of these diseases was typically short and death occurred without warning and little time to prepare.[2] Nowadays, death is mainly caused by non-communicable diseases, such as cardiovascular diseases or cancers.[4] These diseases tend to have an extended illness trajectory, with a functional decline over months or years that is often disrupted by episodes of acute illness and decompensation.[2] The end of life can now often be anticipated and the process of care planning and medical decision-making allows for incorporating patients' preferences.[2]

Advance care planning can be part of this decision-making process and enables individuals to define their goals and preferences for future medical treatment and care.[5] Discussing personal preferences with clinicians has been associated with greater concordance between patients' preferences and actual care, and increased patient satisfaction with care.[6,7] It has been suggested that the process of defining goals and preferences is influenced by the way patients attend to their disease, the way they deal with it and their personal values concerning everyday quality of life.[8,9]

PATIENTS' WELL-BEING NEAR THE END OF LIFE

Receiving the diagnosis of an advanced, life-limiting disease is confronting for patients, with far-reaching consequences for their well-being.[10,11] Patients with an advanced disease typically experience a reduced quality of life and multiple physical symptoms that gradually worsen and may interfere with their daily activities.[2,12] Next to the physical symptoms, patients face emotional consequences of their illness and its advanced stage.[13-15] Patients with an advanced disease frequently experience symptoms of depression and anxiety.[16,17] Other common symptoms are preparatory grief,[18] death anxiety[19] and psychological distress.[20,21] This distress is also related to the prognostic uncertainty that many patients face, particularly since healthcare professionals hold a justified humility when it comes to prognostication.[11]

Patients' experience of their illness, the way they attend to their illness and the choices they have to make are combined in the term 'lived experiences',[24] which is known to influence the decision-making process.[9] In this thesis, three concepts within the lived experience of suffering from an advanced, life-limiting disease will be characterized, namely illness representations, coping and quality of life. These concepts are unique though interrelated and important in explaining how patients experience their advanced, life-limiting illness.

The process of forming cognitive and emotional representations of a disease is described in the Common Sense Model.[22,23] So-called 'illness representations' are formed in an effort to make sense of and manage the illness.[22,23] To illustrate, the illness representation 'Identity' concerns the extent to which patients attribute experienced symptoms to their disease; 'Personal control' concerns the extent to which patients experience having control over their current situation.[23] Patients' illness representations are influenced by information from healthcare professionals, media, friends or family.[24] They may be in line with the actual situation, but can also be a distorted interpretation of medical facts.[24] Due to the constant process of appraisal and re-appraisal, illness representations are highly modifiable.[25]

Illness representations influence patients' well-being, illness understanding and treatment effects.[23,25,26] Besides, they have been shown to motivate participation in psychosocial support programmes, e.g. women with breast cancer with a higher experienced personal control were more likely to join the programme.[27] Addressing and acknowledging illness representations has been identified to be useful for the adaptation and improvement of information provision, psychological interventions[26] and decision-making.[9]

According to the Common Sense Model, illness representations guide patients' coping efforts.[22,23] Coping is defined as

> *constantly changing cognitive and behavioral efforts to manage specific external and/ or internal demands that are appraised as taxing or exceeding the resources of the person.*[28]

Hence, coping is the reaction towards a (health) threat of one's psychological, physical and social well-being.[29] As opposed to a trait, coping is considered to involve a shifting process.[28] This means that one could rely more heavily on one coping strategy in one particular situation than in another, and engage in a different coping strategy when the situation changes.[28] These shifts in coping strategies are the result of a continuous process of appraisal and re-appraisal of a threat, such as an advanced, life-limiting illness.[28] Coping involves efforts, rather than mastery, since it concerns anything a person thinks or does to address the consequences of an illness, regardless of how 'successful' that strategy is.[28] Coping strategies have a direct impact on a person's well-being,[29, 30] they are dynamic and modifiable and due to these attributes are increasingly incorporated in interventions aiming at improving patients' well-being.[31] Recent clinical guidelines therefore highlight the importance of including coping in healthcare interventions for patients nearing their end of life.[32] However, thorough research on coping strategies within this patient group is lacking: until now research has mainly focused on patients with earlier stages of a disease. For instance, women diagnosed with early stage breast cancer showed a high use of the coping strategy 'Acceptance' and low use of 'Social support'.[30] Conversely, patients newly diagnosed with incurable cancer were using 'Emotional support' to a greater extent, while fewer patients used 'Acceptance', 'Self-blame' or 'Denial'.[33] These studies show the complexity of coping and its highly individual and situational dependency. It is unclear to what extent the findings from previously studied patient populations can be extended towards patients nearing the end of life, since they face unique challenges related to the terminal diagnosis of their disease, among which death anxiety[19] and increased existential distress.[20]

Insufficient knowledge about the coping strategies of patients with an advanced, life-limiting disease can lead to care and treatment failing to adequately address individual coping strategies[34] or to inadequately tailored interventions. Tailored interventions are modeled after the patients' coping strategies, for instance, patients with a problem-focused coping strategy would receive an intervention with problem-solving activities, whereas patients with emotion-focused coping would be offered support for seeking sympathy and social support.[35] These 'matched' interventions have been demonstrated to be more successful than generic, mixed-focused interventions.[35] Not taking patients' coping strategies into account can have detrimental effects on their well-being and can decrease the efficiency of psychological interventions.[34] Particularly patients near the end of life might benefit from coping support, since medical treatment options to prolong life are usually limited and medical treatment of symptoms is not always successful.[36]

The adaptive effect of coping strategies is often reflected in patients' quality of life. Quality of life captures

> *an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health,*

> *psychological state, personal beliefs, social relationships and their relationship to salient features of the environment.*[37]

Quality of life describes and combines patients' own perspective of their health and the subjective impact of treatment. It is linked to the physical, as well as the psychological dimension of the patients' lived experience, among which patients' illness representations and coping strategies.[37] Quality of life can be used as a supplement to and enrichment of objective clinical measures. Consequently, it has become a main outcome measure for the evaluation, monitoring and improvement of healthcare interventions for patients with an advanced, life-limiting disease.[38]

Since the concept of quality of life is widely established and accepted, research efforts are now focusing on the improvement of its measurement. One particular challenge in research and care near the end of life is the vulnerability of the patients, which makes filling in long and often complicated questionnaires burdensome.[39] This can lead to attrition due to drop-out or missing data.[39] The challenge is to construct a measure that is patient-centered and captures the uniqueness of individuals, while simultaneously increasing the efficiency of its measurement abilities.

Illness representations, coping and quality of life each describe a different dimension of patients' lived experience. In order to support patients in their last phase of life and decision-making, the challenge for healthcare professionals lies in understanding this lived experience and translating or 'objectifying' it into medical care options.

PATIENTS' PREFERENCES NEAR THE END OF LIFE

The discussion of medical treatment options typically intensifies nearing the end of life. Goals of care may have to be reconsidered to adequately control patients' symptoms and optimize their quality of life. This may mean that extension of life is not unreservedly appropriate or desired by all patients and that other goals may guide medical decision-making and care. For instance, older patients have been found to be more likely to prioritize care aimed at comfort and quality of life, which may mean a reduced time to live, over aggressive care.[40,41] Younger patients or patients with children on the other hand have been found to prefer aggressive care aimed at prolonging life.[41]

Ideally, patients take part in this decision-making process as much as they prefer. However, the nature and progress of their disease may impair their physical, cognitive or emotional abilities to formulate their preferences.[42,43] A delay in these discussions can thus hinder their involvement in the decision-making process. It may also increase avoidable hospitalizations[44] and lead to late referrals to palliative care or hospices, which may reduce the benefits of these care options, for instance in symptom control.[45,46]

The identification of the right moment and approach to engage in conversations about treatment preferences is one of the main challenges for healthcare professionals.[5] When the conversations occur too early, they might risk to discourage patients or exceed patients' imagination of their preferences and what these preferences might mean.[47] However, having these conversations in moments of crisis is clearly too late and equally undesirable.[47] In an effort to increase the uptake of the conversations about treatment preferences, clinical organizations such as the American Association for Clinical Oncology or the Royal College of Physicians in the United Kingdom endorse early communication about treatment preferences[48,49] and advance care planning.[50,51] Advance care planning is defined as

> *the ability to enable individuals to define goals and preferences for future medical treatment and care, to discuss these goals and preferences with family and health-care providers, and to record and review these preferences if appropriate.*[5]

Advance care planning aims at improving the decision-making process and alignment of patients' preferences with delivered care.[5] It has been suggested that advance care planning has indeed a positive impact on the quality of end of life care.[6] However, most evidence on advance care planning for patients with an advanced, life-limiting disease is based on the evaluation of hypothetical scenarios; evidence on experiences of patients participating in actual interventions is lacking. The same applies to evidence on the attitudes of both patients and healthcare professionals, particularly outside of patient populations in nursing homes and the United States of America. To enrich the body of evidence on the effects and acceptability of advance care planning and in order to make a possible step towards better implementation, systematic gathering and combining existing findings is necessary.

Another unknown factor within advance care planning is the stability of patients' treatment preferences, which is important to identify the time frame in which these conversations should ideally take place to inform medical care meaningfully. So far, evidence on the stability of patients' treatment preferences is equivocal and limited to hypothetical scenarios and/ or various (patient) groups other than patients with an advanced, life-limiting disease nearing their end of life.[52] The direct and general applicability of these findings to patients with an advanced, life-limiting disease who are de facto going through the process of decision-making is thus questionable.

AIMS AND OBJECTIVES

Following the developments in advance care planning for patients with an advanced, life-limiting disease and in an effort to answer some gaps of knowledge, the aim of this thesis is twofold:

In the first part, this thesis characterizes patients' illness representations, coping and quality of life, in an attempt to better understand patients' well-being and lived experience near the end of life. The specific objectives of Part I of this thesis are:

(1) to decompose the complex relationship between illness representations and quality of life of patients with advanced cancer (Chapter 3),

(2) to characterize the prevalence and influencing factors of coping strategies of patients with advanced cancer (Chapter 4),
(3) to investigate an improved way of assessing quality of life of patients with advanced cancer (Chapter 5),

The second part of this thesis focuses on the experiences of both patients and healthcare professionals with advance care planning. It includes an exploration of the stability of patients' treatment preferences. The specific objectives of Part II of this thesis are:

(4) to explore the experiences of patients with a life-threatening or life-limiting illness with advance care planning interventions (Chapter 6),
(5) to summarize preferences and practices of advance care planning for patients with chronic respiratory diseases (Chapter 7),
(6) to examine the stability of treatment preferences of patients with advanced cancer (Chapter 8).

OUTLINE OF THIS THESIS

Chapter 2 includes the study protocol of the international ACTION trial. This cluster randomised clinical trial investigates an advance care planning intervention that is based on the Respecting Choices advance care planning intervention from the United States of America.

Part I: Patients' well-being near the end of life

The first objective is addressed in **chapter 3,** where we use data of a cross-sectional registry on the physical and psychosocial impact of cancer and an innovative statistical methodology to decompose the complex relationship between illness representations, mental health and quality of life. In **chapter 4** we characterize the prevalence of the coping strategies Denial, Acceptance and Problem-focused coping and their associated variables among patients with advanced cancer in six European countries. In **chapter 5** we investigate an improved method to measure quality of life of patients with advanced cancer with increased power.

Part II: Patients' preferences near the end of life

In **chapter 6** and **chapter 7** we systematically review the evidence on advance care planning in different patient groups. **Chapter 6** focuses on the experiences of patients with a life-threatening or life-limiting illness with advance care planning interventions. **Chapter 7** presents an overview of advance care planning programmes in chronic respiratory diseases and the attitudes towards and experiences with advance care planning of both patients and healthcare professionals. In **chapter 8**, we use data from a cohort study in the United States of America to explore the stability of patients' treatment preferences near the end of life.

Chapter 9 contains the general discussion of and reflection on the findings and **Chapter 10** summarizes the findings of this thesis.

METHODS OF THIS THESIS

The aim of this thesis will be investigated through a variety of databases and research methodologies.

The ACTION study

The 'Advance care planning – a multi-centre cluster randomised clinical trial' (ACTION) study investigates the effects of an advance care planning programme on the quality of life of patients with advanced lung or colorectal cancer in six European countries.[53] In this thesis, we used the data to characterize the prevalence and associated variables of coping strategies of patients with advanced cancer and to investigate more efficient ways of measuring quality of life.

The PROFILES database

The 'Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship' (PROFILES) is a registry for the study of the physical and psychosocial impact of cancer and its treatment from a dynamic, growing population-based cohort of both short and long-term survivors.[54] The data and detailed information are available at www.profilesregistry.nl. We used data from adult patients diagnosed with stage IV (non)Hodgkin lymphoma, colorectal cancer or thyroid cancer, without cognitive impairment. The registry included patient characteristics and clinical information. Patients completed measures on illness representations, symptoms of anxiety and depression and quality of life.

Systematic reviews

To review current evidence on practices, experiences and attitudes regarding advance care planning, two systematic reviews were conducted. Several electronic databases were systematically searched for relevant empirical studies. Identified studies underwent full review and data extraction.

Coping with Cancer-2

The Coping with Cancer-2 (CwC-2) study is a National Cancer Institute funded, prospective, multi-institutional cohort study of patients with advanced cancer. It was designed to evaluate end of life communication processes and end of life care. Patients with advanced cancer and a life expectancy of six or fewer months were recruited from nine cancer centers across the United States of America.

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