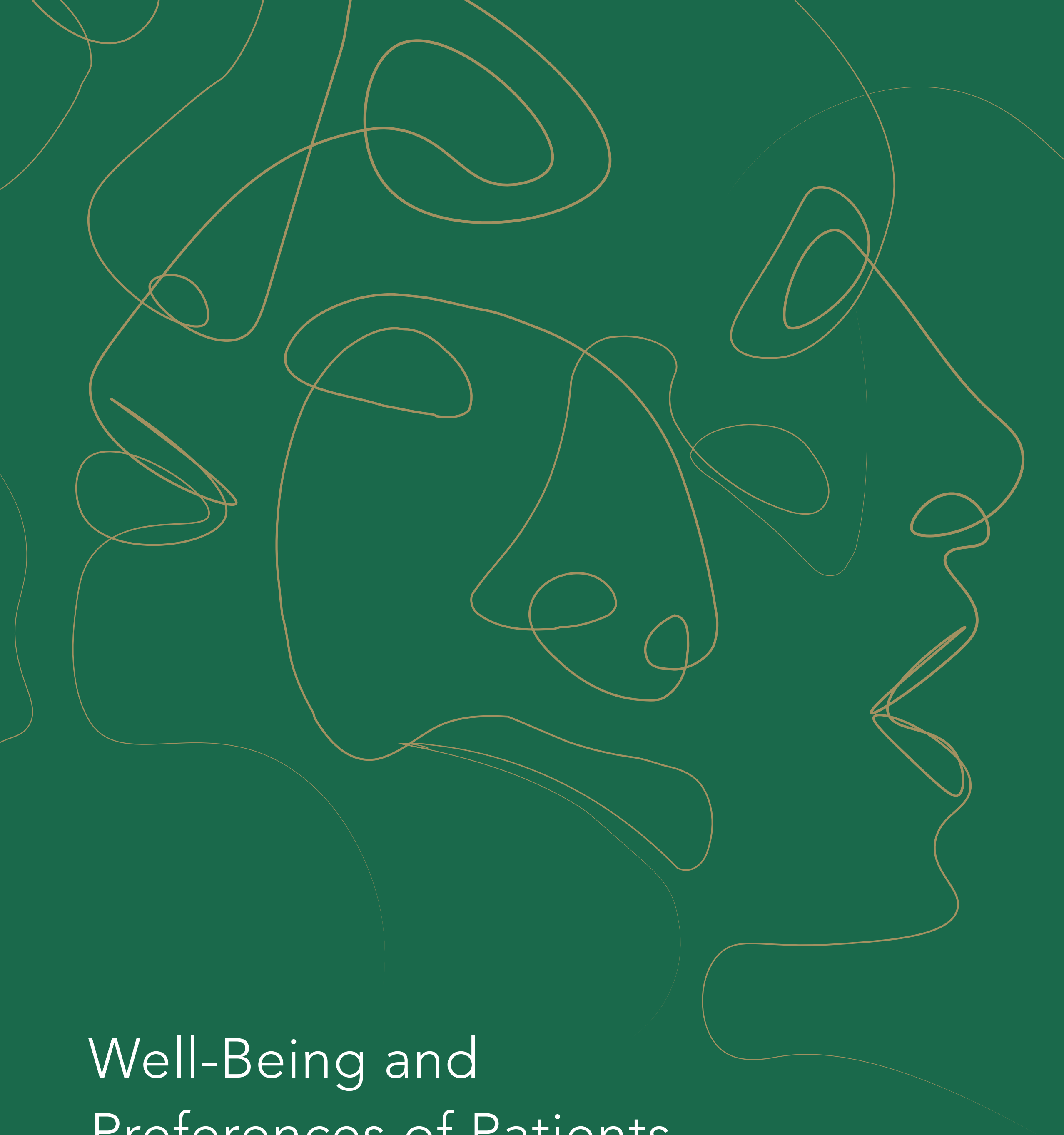

Well-Being and Preferences of Patients Near the End of Life

Towards better care through better communication

Lea Jabbarian

Well-Being and Preferences of Patients Near the End of Life:

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Welzijn en voorkeuren van patiënten rond het levenseinde:

Op weg naar betere zorg door betere communicatie

Lea Jasmina Jabbarian

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Towards better care through better communication
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Copromotoren:	Dr. I.J. Korfage Dr. J.A.C. Rietjens

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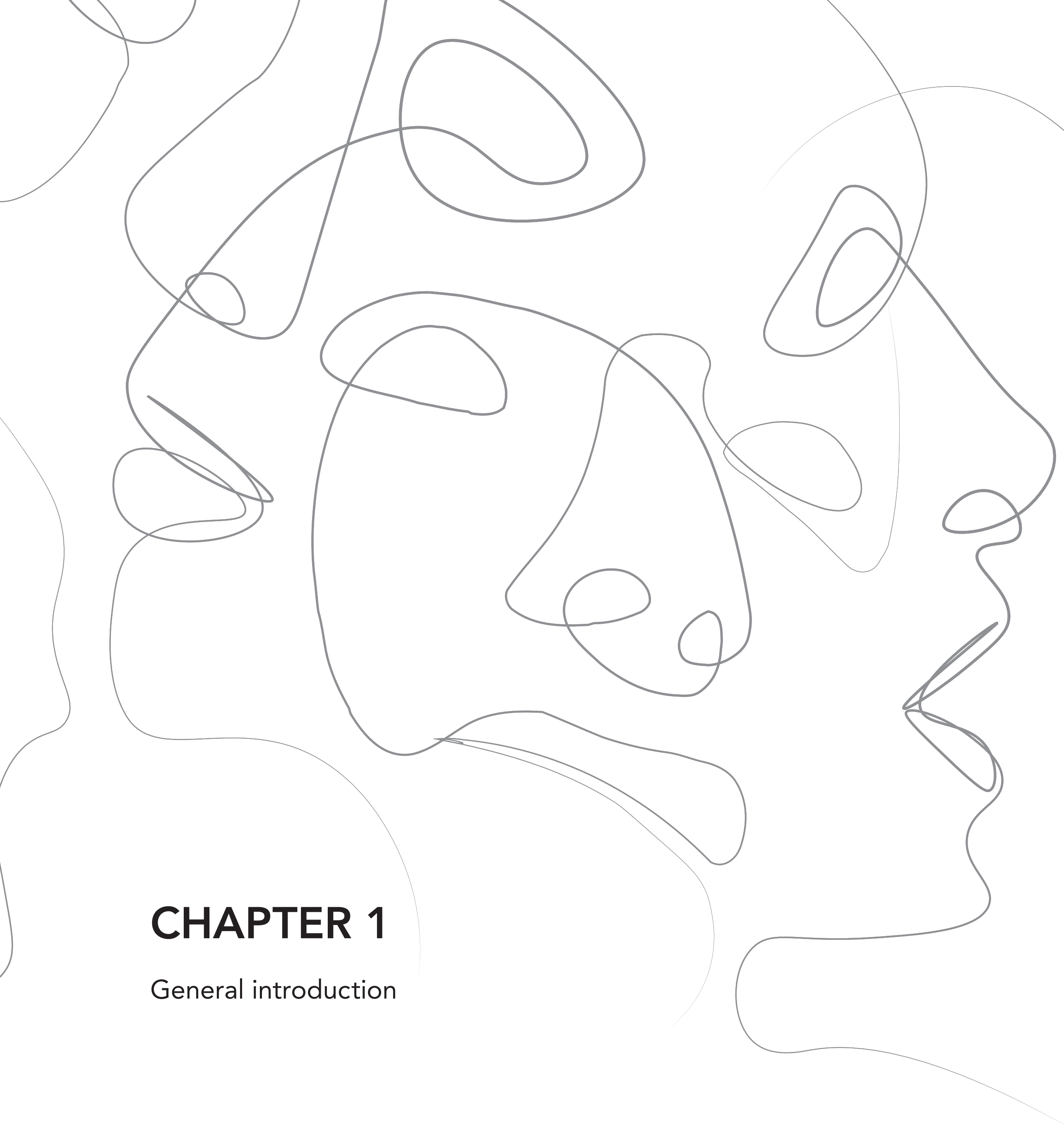

CHAPTER 1

General introduction

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]

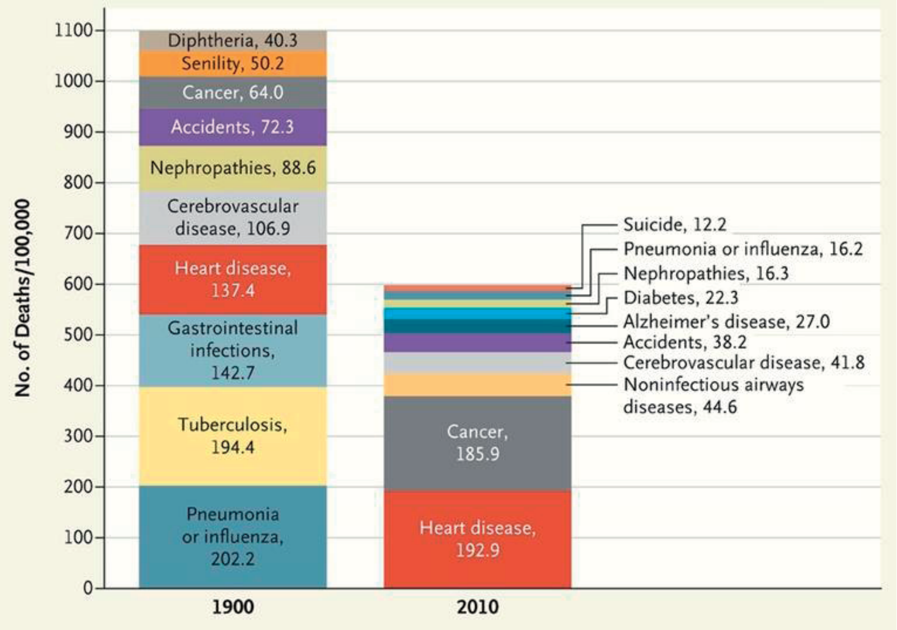

Figure 1. Top 10 causes of death in the United States: 1900 vs. 2010.[3]

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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CHAPTER 2

Advance care planning – a multi-centre cluster randomised clinical trial: the research protocol of the ACTION study

Rietjens JA*, Korfage IJ*, Dunleavy L, Preston NJ, Jabbarian LJ, Christensen CA, de Brito M, Bulli F, Caswell G, Červ B, van Delden J, Deliens L, Gorini G, Groenvold M, Houttekier D, Ingravallo F, Kars MC, Lunder U, Miccinesi G, Mimić A, Paci E, Payne S, Polinder S, Pollock K, Seymour J, Simonič A, Johnsen AT, Verkissen MN, de Vries E, Wilcock A, Zwakman M, van der Heide A

**Equal contributors*

BMC Cancer. 2016;16:264

ABSTRACT

Background

Awareness of preferences regarding medical care should be a central component of the care of patients with advanced cancer. Open communication can facilitate this but can occur in an ad hoc or variable manner. Advance care planning (ACP) is a formalized process of communication between patients, relatives and professional caregivers about patients' values and care preferences. It raises awareness of the need to anticipate possible future deterioration of health. ACP has the potential to improve current and future healthcare decision-making, provide patients with a sense of control, and improve their quality of life.

Methods/Design

We will study the effects of the ACP program Respecting Choices on the quality of life of patients with advanced lung or colorectal cancer. In a phase III multicenter cluster randomised controlled trial, 22 hospitals in 6 countries will be randomised. In the intervention sites, patients will be offered interviews with a trained facilitator. In the control sites, patients will receive care as usual. In total, 1360 patients will be included. All participating patients will be asked to complete questionnaires at inclusion, and again after 2.5 and 4.5 months. If a patient dies within a year after inclusion, a relative will be asked to complete a questionnaire on end-of-life care. Use of medical care will be assessed by checking medical files. The primary endpoint is patients' quality of life at 2.5 months post-inclusion. Secondary endpoints are the extent to which care as received is aligned with patients' preferences, patients' evaluation of decision-making processes, quality of end-of-life care and cost-effectiveness of the intervention. A complementary qualitative study will be carried out to explore the lived experience of engagement with the Respecting Choices program from the perspectives of patients, their Personal Representatives, healthcare providers and facilitators.

Discussion

Transferring the concept of ACP from care of the elderly to patients with advanced cancer, who on average are younger and retain their mental capacity for a larger part of their disease trajectory, is an important next step in an era of increased focus on patient centered healthcare and shared decision-making.

BACKGROUND

Despite progress in diagnosis and treatment, cancer remains a major life limiting disease, with 14.1 million new cases and 8.2 million deaths worldwide in 2012.[1] Patients with advanced cancer typically suffer from a reduced quality of life and multiple symptoms, such as pain, fatigue, and dyspnoea, due to their illness and/or its treatment.[2] A diagnosis of advanced cancer often has a tremendous impact on patients' emotional well-being and may result in depression, anxiety and a feeling of loss of control.[3,4] Ideally, these patients receive patient-centered care, addressing their needs concerning symptom control, psychosocial support, spiritual support, and practical issues. Patients' preferences regarding care and their wishes concerning their place of residence at the end of life should be central in the decision-making. Currently, treatment aimed at prolonging life has been found to often prevail over care aimed at relieving patients' suffering and enhancing their quality of life, which may not always be in accordance with patients' needs and preferences.[5]

Timely and efficient communication is an important prerequisite for care that adequately addresses patients' needs and preferences.[6] However, research findings consistently demonstrate that communication between physicians, patients with advanced cancer and their relatives is complex. Physicians tend to focus on treatment,[7] patients may be overwhelmed and unaware of the possibility to opt for treatment aimed at relieving suffering, and relatives may feel stressed and uncertain to be involved in medical decisions without being aware of their beloved one's preferences.[8]

Advance care planning has moved from being a process which aims to elicit specific instructions about medical treatment at the end of life, to being recognized as an opportunity to help patients and their families to prepare, in their own terms, for the changes wrought by serious progressive illness and work with them to plan nursing, social and medical care so that it better fits their needs, hopes and aspirations.[9] ACP is a formalized process of communication between patients, relatives and professional caregivers. It has been defined as "a voluntary process of discussion about future care between an individual and their care providers, irrespective of discipline. […] It is recommended that with the individual's agreement this discussion is documented, regularly reviewed, and communicated to key persons involved in their care".[10] ACP promotes discussion of preferences and communication of these preferences to family, friends and healthcare professionals. Patients are encouraged to document their preferences in an advance directive and to review these preferences as circumstances change. Patients are also encouraged to appoint a personal representative, who can express their preferences if they are unable to do so themselves. However, the legal status of advance directives and personal representatives differs across countries. A review of the literature[11] shows that ACP programs have the potential to improve communication between patients and healthcare professionals, increase the quality of life and well-being of patients and their relatives, reduce the use of futile treatments and unnecessary hospitalisations, enhance provision of care that is consistent with patient goals, and increase patients' satisfaction with care. Other studies have shown that ACP can reduce healthcare costs.[12-14] The Respecting Choices program is one of the most promising ACP programs. This program was developed in the US and successfully trialed in a geriatric setting in Australia, showing that patients' end of life care wishes were much more likely to be known and followed in the intervention group (86%) compared to the control group (30%).

Most ACP studies have been performed in the US, amongst nursing home patients with the main aim of establishing patients' preferences before they lose their competence. We will conduct our study in a European context and hypothesize that ACP can also be effective in improving the quality of life of patients with cancer who often remain competent until death or very close to death. ACP may support them in timely recognizing and continuously expressing their core values and preferences, and to communicate these with their loved ones and professional care givers, which will enable strategic and effective planning of care and decision-making. As a result, care may more adequately address patients' values and preferences, which may result in improved quality of life and more adequate symptom control, while patients feel more in control and receive less unwanted or futile interventions.

The overall hypothesis that will be studied in the ACTION project is that a formalized ACP program such as Respecting Choices significantly improves the quality of life and reduces the symptom burden of patients with advanced lung or colorectal cancer.

The primary objective is to assess the effect of the Respecting Choices ACP program on the quality of life and symptoms of patients with advanced lung or colorectal cancer.

The secondary objectives are:

1. To assess the effect of the Respecting Choices ACP program on the quality of life and symptoms of patients with advanced cancer in different subgroups (gender, age, education, ethnicity, country and type of cancer).
2. To assess the effect of the Respecting Choices ACP program on the extent to which care as received is in line with patients' documented preferences, on patients' evaluation of the quality of the decision-making process, and on how they cope with their illness.
3. To assess patient satisfaction with the Respecting Choices ACP program.
4. To assess the effect of the Respecting Choices ACP program on the quality of end of life care of patients with advanced cancer from the bereaved carers' perspective, and on the wellbeing of these carers.
5. To assess the cost effectiveness of the Respecting Choices ACP program.
6. To gain insight into how patients, patients' relatives and professional caregivers experience and respond to facilitated ACP.

METHODS/ DESIGN

Study design and setting

We will perform a multicenter cluster-randomised clinical trial in 22 hospitals in six European countries (Belgium, Denmark, Italy, the Netherlands, Slovenia and the United Kingdom). Per country pairs of comparable hospitals (academic/non-academic) will be randomised to provide either 'care as usual' supplemented with ACP or 'care as usual'. Cluster-randomisation prevents healthcare providers from giving patients in the control group ('care as usual') more opportunity to discuss their preferences than usual due to their experience with providing the intervention in the intervention group ('care as usual' supplemented with ACP). The nature of the intervention makes blinding, for both healthcare professionals and patients and their relatives, impossible.

Study population

In total, 1,360 patients with advanced lung (*N* = 680) or colorectal cancer (*N* = 680) will be included. Lung and colorectal cancer patients are selected for this study because both types of cancer have high incidence and mortality rates in Europe and affect both sexes; see Table 1 for in- and exclusion criteria. At inclusion, the average life expectancy of these patients is about one year; their minimum estimated life expectancy to be eligible for the study is three months.

Table 1. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Histologically confirmed diagnosis of:	Age < 18 years
- Lung cancer	Unable to provide consent
- small cell - extensive disease/ Stage III or IV*	Unable to complete questionnaire in country's language
- non-small cell - stage III or IV*	Less than 3 months anticipated life expectancy
- Colorectal cancer, stage IV or metachronous metastases*	Taking part in a research study that is evaluating palliative care services or communication strategies.
Written informed consent to participate	
WHO performance status of 0-3.	

*according to 7th edition of TNM classification and staging system

Intervention

In this study, we will evaluate the ACP Respecting Choices program. It involves trained healthcare professionals ("facilitators", mostly nurses) who assist patients and their relatives in reflecting on the patient's goals, values and beliefs and in discussing their healthcare wishes.[12,15] The program also supports people to identify specific activities and experiences that may contribute to, or detract from, their quality of life. Patients are encouraged to appoint a patient representative who preferably also attends the Respecting Choices sessions, and to document their preferences for (future) medical treatment and care in an advance directive; the so-called My Preferences form. These wishes can e.g. concern the (non-)use of potentially burdensome life-prolonging interventions such as hospitalisations or cardio-pulmonary resuscitation. Patients are encouraged to discuss their preferences and questions they may encounter with their physician. The content of the communication during these meetings will be structured by the use of interview guides.

Study procedures

For each participating hospital, baseline background data will be collected, such as number of cancer patients attending annually, academic/nonacademic setting, number of beds and palliative care services, and a description of common practices regarding ACP and decision-making at the end-of-life. In addition, background reports for each of the six participating countries will be created summarizing baseline national and local policies related to the provision of palliative care and ACP.

We will carefully translate the Respecting Choices program into the required European languages and adapt its content, in close collaboration with the US developers, to the specific legal, clinical, ethical, and cultural contexts of the participating European countries. To test the intervention and the process for acceptability and efficiency, a feasibility study will be conducted with five patients and potentially their family caregiver in each country. The patients will be offered the ACP program and will subsequently be interviewed. We will also test the questionnaires and have conversations with their healthcare providers.

Extensive training of the ACP facilitators is essential in this project. We will use the well-established structure of the training and implementation of the Respecting Choices program and will adopt a two-step education process. First, one representative per country will be trained in La Crosse, Wisconsin (USA) by the instructors of the Respecting Choices program. Subsequently, the country representative will train the local facilitators, who will be --where possible- selected among the healthcare workers of the hospitals, e.g. nurses. All together about 40 facilitators will be trained in the project.

Patients will be followed until one year after inclusion. During the inclusion period eligible patients in both intervention and control hospitals, will be approached for written informed consent. The information provided in the consent form for the intervention group and the control group will be as similar as possible to avoid selection bias with respect to interest in ACP. However, to minimize contamination, patients will be informed that the project aims at investigating the experiences of patients with different approaches towards medical decision-making in advanced stages of cancer, but no or limited details of the Respecting Choices program will be revealed in the control group. Patients will be given ample time to consider participation and they are free to withdraw from participating in the study without any effect on their care.

Patients in the intervention group will be offered the Respecting Choices program in addition to their usual care. Depending on the health status of the patient and the content of the conversations, a facilitated interview will last 45–60 min on average. We plan to have one or two sessions per patient. The facilitator will assist the patient in documenting preferences, including the assignment of a personal representative. For quality assurance, the interviews will be audio recorded by the facilitator.

By a standardized checklist a proportion of the interviews will be rated for intervention fidelity.[16]

Ethical committee procedures have been followed in all countries and institutions involved, and approval has been provided. The names of the main IRB's are:

The Netherlands: Medische Ethische Toetsings Commissie (METC) ErasmusMC;
Belgium: Universitair Ziekenhuis Brussel Commissie Medische Ethiek;
United Kingdom: NRES Committee North West - Liverpool East;
Italy: Comitato Etico Area Vasta Centro, Regione Toscana;
Denmark: De Videnskabsetiske Komiteer for Region Hovedstaden;
Slovenia: Komisija Republike Slovenije za medicinsko etiko (KME).

Approval was also obtained from the IRB's of all the remaining institutions.

The trial is registered in the International Standard Randomised Controlled Trial Number (ISRCTN63110516). A Data Steering Monitoring Board (DSMB) will be established.

Measurements

In ACTION, the following measurements will be performed (see Table 2):

a) Questionnaire study. Patients will be asked to complete a written questionnaire about quality of life, symptoms, the decision-making process, patient activation, coping, and satisfaction with care (and the intervention) at baseline (i.e., the moment of inclusion, before the ACP program is delivered in the intervention group), and at 2.5 and 4.5 months after inclusion. If a patient dies during follow up (i.e., within one year after inclusion), a relative identified by the patient as next of kin will receive a questionnaire to assess the patient's quality of end-of-life care and the relative's own wellbeing.
b) Medical file study. Data on patients' survival will be collected, as well as preferences as documented and care as received to assess whether patients' preferred care was congruent with received care. Data on care as received will also be used in the cost-effectiveness analysis. These medical files will be studied one year post-inclusion with a checklist.
c) Study of recorded ACP sessions. Data will be obtained from audio recorded facilitated interview sessions. Compliance with the intervention will be systematically evaluated with a predefined checklist.

Data management

Our data collection tool GemsTracker will be used to safely store data of all participating patients across hospitals and countries. GemsTracker enables restricted access to selected parts of its

Table 2. Patient and bereaved carer endpoints of the project

I. Measured by questionnaire	Measure
Primary endpoints	
- Quality of life	EORTC QLQ-C30 4-item emotional functioning scale[24] EORTC emotional functioning short-form based on CAT item bank
- Symptoms	EORTC QLQ-C15-PAL[25]
Secondary endpoints:	
- Shared decision-making	APECC[26]
- Patient involvement	Self-constructed questions
- Satisfaction with care	EORTC IN–PATSAT32[27]
- Coping with illness	COPE[28-30]
- Satisfaction with intervention	Self-constructed questions
- Socio demographic measures	Self-constructed questions
- Quality of end-of-life care	VOICES-SF[31]*
- Bereaved carer wellbeing	HADS[32]; IES[33]*
II. Obtained from medical files	
- Survival; date and place of death (if applicable)	
- Completion and content of advance directives; preferences for care; assignment of proxy decision-maker; physician orders	
- Diagnostic procedures and treatments received by the patient, hospitalisations and specialist palliative care input.	
III. Obtained from intervention sessions and qualitative interviews	
Systematic cross-cultural comparison of patient experiences, responses and concerns.	

* These endpoints are measured by the bereaved carer questionnaire and not by the patient questionnaire

content. Legislation in the participating countries for research on humans, not involving medical products, will be taken into account.[17–22]

Power calculation, sample size and feasibility of recruitment

With at least 11 intervention and 11 control hospitals each recruiting 34 lung cancer patients and 34 colorectal cancer patients (of which 25 in each tumour type group are expected to remain in the study until at least month 2.5), this multicentre cluster-randomised clinical trial has an overall power of 90% to identify a minimum difference between intervention and control groups of half a standard deviation on the emotional functioning scale of the QLQ-C30 scale, assuming an intra-class correlation (ICC) of 0.1. On country level, these numbers give a power of 50% to show such a difference (assuming an ICC of 0.05).

The main outcomes are measured at 2.5 months post-inclusion. Although included patients have an average life expectancy of at least 3 months, we expect that a number of them will die within 2.5 months after inclusion. Based on Dutch colorectal and lung cancer survival statistics,[23] we conservatively assume that this will be the case for 15% of included patients. Furthermore, we anticipate that around 10% of included patients may drop out of the study for other reasons, resulting in a total attrition rate of 25%. Based on this attrition rate and an estimated willingness of patients to participate of 33%, the total number of eligible patients per hospital per cancer type needs to be 101 in a 2-year period, which is feasible in the participating hospitals.

Analyses

Analyses of the primary and secondary endpoints will be performed following the intention-to-treat principle. Descriptive statistics will be used to summarize characteristics of countries, hospitals and patients. Patient characteristics (age, gender, socio-economic class, educational level) will be compared at baseline between the intervention and control group. A multilevel modelling approach will be used to examine differences in the endpoints between the intervention and control groups, taking account of clustering effects at both hospital and country-level. All statistical tests will be two-sided and considered significant if $p < 0.05$. Repeated-measures analyses of variance will be conducted to assess the development of endpoints over time.

Subgroup analysis will be conducted by means of formal interaction tests for intervention and those variables which are more likely to influence the effect of the intervention itself: gender, age class (<65, 65–74, 75+), educational status, and country.

Those conducting the data analysis will be blinded as to whether the patient was included in the intervention group or in the control group.

Qualitative study

A complementary qualitative study will be carried out in at least 3 of the 6 countries, to qualitatively explore the lived experience of engagement with the Respecting Choices intervention from the perspectives of patients, their Personal Representatives, healthcare providers and Respecting Choices facilitators. The patient and Personal Representative will undertake a facilitated advance care planning (ACP) conversation following the Respecting Choices program. Within two weeks of completing the ACP program they will be invited to take part in a baseline qualitative interview about their experiences. A follow up interview will occur 10–14 weeks after the initial intervention. At this second interview the patient will be asked whether he or she has discussed the Respecting Choices intervention with anyone from the healthcare team and for consent to contact this person. If the patient dies before the second interview, the Personal Representative will be contacted and invited for a qualitative interview. This will not be arranged until a minimum of six weeks after the patient’s death. Healthcare professionals identified by the patient as being closely involved in the care will be invited to participate in a single face to face, Skype or telephone interview. Respecting Choices facilitators will be invited to participate in a single focus group discussion. In each of the participating countries, the qualitative study will involve between 6–10 cases including a patient and where appropriate a Personal Representative and healthcare professionals. All interviews and focus groups will be recorded and transcribed verbatim. Data will be thematically analysed using a pre-defined coding framework which will be developed through an iterative process of discussion and consensus among the research team.

Cost-effectiveness study

The economic evaluation will be performed from a healthcare perspective, for a period of one year post-inclusion per patient. Data on total in-hospital medical care will be obtained from medical files, using a standardized and piloted data extraction form. Medical costs will be calculated by multiplying the volumes of healthcare use with the corresponding unit prices. Unit prices will be calculated for all six countries separately. Costs for inpatient days in hospital will be estimated as real, basic costs per day using detailed administrative information. For other cost prices we will use charges. The unit price of the ACP intervention will be determined with the micro-costing method, which is based on a detailed assessment of all resources used. To compare the relative costs and outcomes of ACP versus 'care as usual' we will calculate the Incremental Cost Effectiveness Ratio (ICER); the average additional costs of ACP divided by the average change in emotional functioning measured with the EORTC-QLQ-C30 emotional functioning subscale (4 items). A sensitivity analysis will be performed to assess the stability of the results to changes in costs and effectiveness parameters (EORTC QLQ-C15-PAL quality of life subscale), and differences in healthcare systems between the European countries.

Dissemination

We have set up an Advisory Board of future international policy users of the project results. The role of the Advisory Board will be to provide a critical perspective throughout the life of the project. The project results will be disseminated through publications in scientific journals and conferences. To disseminate the knowledge to all stakeholders we will use the project website (www.action-acp.eu). A link of ACTION to the websites of the consortium and Advisory Board members will be featured.

DISCUSSION

This project aims to study the effects of the Respecting Choices program on quality of life and symptoms of patients with advanced lung or colorectal cancer. This study has several strengths. First, studies about Advance Care Planning have mainly been performed with older nursing home patients. Transferring the concept of ACP from care of the elderly to patients with advanced cancer, who on average are younger and remain competent for a larger part of their disease trajectory, is a highly relevant next step in an era of increasing focus on patient centered healthcare and shared decision-making. Second, a randomised controlled trial design will enable us to draw conclusions about the causal relations between ACP and the outcomes under study. The clustered design of this project prevents contamination between the control and intervention group. Third, the unique combination of quantitative and qualitative methods in this project will result in profound insights into the underlying working mechanisms of ACP.

In ACTION, we expect to encounter some challenges and possible limitations. First, patients may decline participation for different reasons. They may feel overwhelmed by the topics raised in the

ACP intervention sessions and may not (yet) feel prepared to talk about these issues. We will use a patient-centered approach to facilitate study participation. Patients will receive information about the project through their treating specialist. Since patients may refuse because they do not want to engage in ACP conversations, non-response bias cannot be ruled out. Also selection bias cannot be ruled out, e.g. in intervention hospitals' where including physicians may be more likely to ask patients who they think are more 'open' to ACP to participate in the study. If such 'gatekeeping' comes into play, the effect of the intervention may be overestimated. However, our approach to systematically assess all lung and colorectal cancer patients for eligibility, and subsequently invite all who are eligible to participate in the study may reduce this risk. Attrition is another potential limitation to this project. Attrition may occur because the condition of the patient might worsen such that further participation becomes impossible, or patients might die during follow-up. We try to limit attrition by adding the inclusion criterion of a minimal anticipated life-expectancy of three months and to measure our main outcome measure at 2.5 months. Third, the international character of this project might be a challenge, as a balance needs to be found between on the one hand testing a uniform intervention in the six countries, that on the other hand is tailored to the specific cultural, ethical and legal context of each country. Fourth, the extent to which actual care will be reflected in medical files can be questioned. Potentially, not all treatments that patients receive will be documented in the hospital medical files.

Conclusion

Advanced cancer typically involves multiple symptoms and seriously affects patients' quality of life. Focusing care at patients' preferences and open and respectful communication are important values in end-of-life care, yet these have been found to be a challenge for healthcare professionals as well as for patients and relatives. Little is known about the outcomes of formal ACP, the effects of formal ACP on medical care and medical decision-making, costs and cost-effectiveness of formal ACP and country-specific factors that might influence ACP. Our project will fill these gaps in knowledge, based on an international multicenter cluster-randomised clinical trial to test the outcomes and effects of a formal ACP program, which is enriched by a qualitative study and a cost-effectiveness study.

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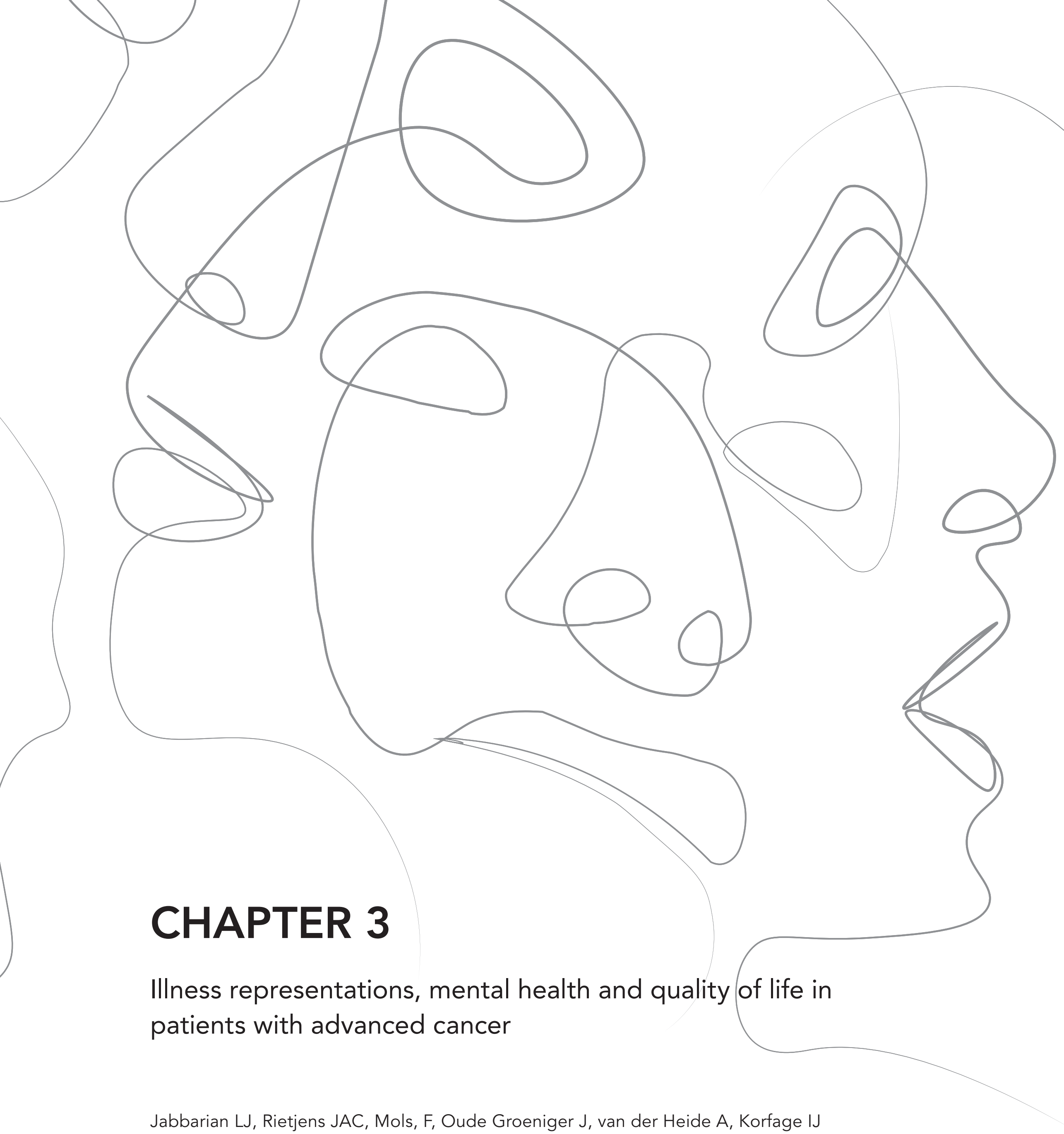

CHAPTER 3

Illness representations, mental health and quality of life in patients with advanced cancer

Jabbarian LJ, Rietjens JAC, Mols, F, Oude Groeniger J, van der Heide A, Korfage IJ

Submitted

ABSTRACT

Objective

Quality of life (QoL) is an important yet complex outcome of care in patients with advanced cancer. QoL is associated with physical and psychosocial symptoms, and with patients' illness representations. Illness representations are modifiable cognitive constructs, developed to make sense of one's illness. Better understanding which factors contribute to patients' QoL and how is essential for delivering high quality care. We therefore investigated the mediating role of anxiety and depression in the association of illness representations with QoL.

Methods

Data from 377 patients with advanced cancer were used from PROFILES registry. Patients completed measures on illness representations (BIPQ), QoL (EORTC QLQ-C30) and symptoms of anxiety and depression (HADS). Causal mediation analyses were conducted to decompose the total effect of illness representations on QoL into a direct effect and an indirect effect.

Results

All illness representations but one ("Comprehensibility") were negatively associated with QoL ($p<0.05$); patients with more negative illness representations tended to have worse QoL. The effect was the strongest for patients who felt that their illness affected their life more severely (illness representation "Consequences"), patients who were more concerned about their illness ("Concern"), and patients who thought that their illness strongly affected them emotionally ("Emotions"). Anxiety mediated 41-87% and depression mediated 39-69% of the total effect of patients' illness representations on QoL.

Conclusions

Anxiety and depression mediate the association between illness representations and QoL. Modifying illness representations has the potential to reduce symptoms of anxiety and depression and thereby to improve QoL of patients with advanced cancer.

INTRODUCTION

Patients with advanced, incurable cancer experience impaired quality of life (QoL).[1] Their QoL is affected in a complex way by, among others, physical symptoms and psychological challenges,[2] such as the confrontation with the approaching death[3] and symptoms of anxiety and depression.[4,5] Whereas QoL is an important outcome of care, QoL is by definition multidimensional and subjective[2] and cannot be assessed by others, such as clinicians. Understanding which factors contribute to patients' QoL is therefore of utmost importance for the delivery of high quality care to patients with advanced cancer.[6]

The so-called self-regulation model conceptualizes illness representations as important and well-established determinants of QoL.[7,8] Illness representations are defined as cognitive constructs, developed by patients to make sense of and manage their illness experience.[9,10] Patients can adjust their illness representations after receiving new information, e.g. regarding the progression of the disease, from healthcare providers, the media, friends or family.[11,12] Illness representations can be in line with patients' actual medical situation, but they can also involve a distorted interpretation of medical facts.[11] A study among patients nearing death, including patients with advanced cancer, found a great variability in illness representations, indicating how differently patients perceive their illness.[13] Due to their modifiable nature, illness representations are a potential target for interventions aimed at improving patients' experiences of their illness and thereby their QoL.[8, 14, 15]

While the effects of illness representations on QoL have been described and are recognized,[8, 14, 15] there is little insight into the mechanisms underlying this relationship. Understanding these mechanisms can inform future interventions to improve patients' QoL. Previous research hypothesized a mediating role of anxiety and depression, since these are associated with both illness representations and QoL,[16, 17] and are particularly common in patients with advanced cancer.[18, 19] We therefore performed a study to clarify the relationship between illness representations and QoL, with symptoms of anxiety and depression as potential mediators, in patients with advanced cancer, accounting for interaction effects between the illness representations and the mediators.

MATERIALS AND METHODS

Participants and data collection

The data were derived from the 'Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship' (PROFILES) registry. This registry includes data to study the physical and psychosocial impact of cancer and its treatment. The rationale and design of PROFILES have been described elsewhere,[20] data and detailed information can be found at www.profilesregistry.nl. Ethical approval for the data collection was obtained from local certified Medical Ethics Committees of the Maxima Medical Centre Veldhoven, the Netherlands (colorectal cancer, approval number

0822), the certified Medical Ethics Committee of the Maxima Medical Centre, the Netherlands ((non)Hodgkin lymphoma) and deemed exempt from full review and approval by the Research Ethics Committee Maxima Medical Centre, Veldhoven, the Netherlands (thyroid cancer). Informed consent was obtained from all individual participants included in the study. We used data from adult patients diagnosed with stage IV (non)Hodgkin lymphoma, colorectal cancer, or thyroid cancer, without cognitive impairments (n=377).

Measures

Sociodemographic and clinical characteristics

The PROFILES registry includes the patient sociodemographic characteristics gender, age at the time of survey and at the time of diagnosis (≤40 or >40 years), and time passed since the diagnosis (<2 or ≥2 years). The socioeconomic status was assessed using an indicator developed by Statistics Netherlands, based on the postal code of the residential address of the patient.[21] The registry includes the clinical characteristic tumor subtype. Patients completed the Self-administered Comorbidity Questionnaire.[22]

Illness representations

The Brief Illness Perception Questionnaire (BIPQ)[23] is frequently used in cancer populations[24] and has good psychometric properties.[25] The BIPQ consists of eight items, each addressing a specific illness representation that is scored on a ten-point scale:[23]

Consequences: “How much does your illness affect your life?”
(0-“No affect at all” to 10-“Severely affects my life”)
Timeline: “How long do you think your illness will continue?”
(0-“A very short time” to 10-“Forever”)
Personal control: “How much control do you feel you have over your illness”?
(0-“Absolutely no control” to 10-“Extreme amount of control”)
Treatment control: “How much do you think your treatment can help your illness?”
(0- “Not at all” to 10-“Extremely helpful”)
Identity: “How much symptoms do you experience from your illness?”
(0-“No symptoms at all” to 10-“Many severe symptoms”)
Concerns: “How concerned are you about your illness?”
(0-“Not at all concerned” to 10-“Extremely concerned”)
Emotions: “How much does your illness affect you emotionally?”
(0-“Not at all affected emotionally” to 10-“Extremely affected emotionally”)
Comprehensibility: “How well do you understand your illness?”
(0-“Don’t understand at all” to 10-“Understand very clearly”)

For the statistical analyses, we recoded the responses of three items (personal control, treatment control, and comprehensibility) to be in the same direction as the other items. Higher scores imply more negative illness representations (e.g. experiencing more symptoms due to the illness or being more concerned about the illness).

Health-related quality of life

The European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30; version 3.0) is an often used, validated 30-item self-reported questionnaire that contains five functional scales, three symptom scales, and six single items.[26] We calculated the recently developed QLQ-C30 summary score (range 0-100).[27] A higher score indicates better QoL.

Symptoms of anxiety and depression

The Hospital Anxiety and Depression Scale (HADS) is a widely used self-reported questionnaire that measures levels of anxiety (HADS-A: seven items) and depression (HADS-D: seven items) of patients during the past week.[28] The HADS has shown good psychometric properties in various samples and settings.[29] The items are scored on a four-point Likert-scale (range total score for each subscale 0-21). A score of 8 or higher on the subscales (HADS-A and HADS-D) indicates mild to severe symptoms of anxiety or depression.[29]

Statistical analyses

Pearson correlation analyses were used to examine bivariate associations of illness representations, with anxiety and depression and QoL. From the original PROFILES registry, we selected the 377 patients who were diagnosed with advanced cancer. We conducted the mediation analyses with complete cases. Missing data varied from 0% for gender to 28% for comorbid conditions (Table 1 and 2). Among the 377 patients in the total sample, 216 (57%) to 224 (59%), depending on the exposure, provided full information on the exposure, mediator, outcome variables, and confounders.

The aim of this study was to estimate how much of the observed associations of illness representations (exposure variables) with QoL (outcome variable) could be explained by anxiety or depression (mediators, Figure 1a and b). The analyses were controlled for patient characteristics that, based on literature[30] and a priori assumptions, were suspected to have an impact on illness representations and QoL: tumor subtype, gender, age at time of diagnosis (≤40 or >40 years), time passed since diagnosis (<2 or ≥2 years), socioeconomic status (low, medium, high, living in care institutions), and the number of comorbidities (none, 1, ≥2). We found interaction effects between half of the illness representations and anxiety and depression on QoL. In the presence of interaction effects between exposure and mediator, traditional mediation methods such as the commonly used Baron and Kenny method, will generate invalid mediation effects.[31, 32] We therefore used a novel approach as described by Valeri and VanderWeele (2013), which allows for exposure-mediator interactions.[32] Using the counterfactual framework, the Valeri and VanderWeele method is able to decompose the estimated total effect of an exposure on an outcome into a natural direct effect (i.e. the effect of illness representations on QoL that occurs without mediation) and a natural indirect effect (i.e. the effect of illness representations on QoL that is mediated by symptoms of anxiety and depression). The percentage of the estimated total effect mediated was calculated by dividing the natural indirect effect by the total effect.

In the mediation analyses, the illness representation scores were standardized and natural direct and natural indirect effects were calculated by comparing the mean level of an illness representation score to the mean + 1 standard deviation [SD]. The estimated total effect thus expresses the change in QoL if an illness representation score increases from the mean to the mean + 1 SD. The natural direct effect expresses the change in QoL if an illness representation score increases from the mean to the mean + 1 SD, while the mediator, anxiety or depression, is kept at the level it would have at the mean level of the illness representation. The natural indirect effect expresses the change in QoL if an illness representation score is kept stable at mean + 1 SD, while the mediator score changes from the level it would take at the mean level of the illness representation to the level it would take at the mean + 1 SD level of the illness representation.

Analyses were performed using SPSS version 21. The mediation analyses were performed using Stata version 13 with the package 'Paramed'. *P*-values <0.05 were considered to indicate statistically significant associations. 95% confidence intervals were automatically generated by the package 'Paramed' (based on the delta method) around the estimated total effect, natural direct effect and natural indirect effect.

RESULTS

Patient sample

The majority of patients in our sample (n=377) were male (60%), older than 40 years at diagnosis (92%), and diagnosed with cancer two or more years prior to participation in the study (80%, Table 1). Two or more comorbid conditions were reported by 36% of patients.

Table 1. Sociodemographic and clinical characteristics (n=377)

	No. (%)
Gender	
Male	227 (60.2)
Female	150 (39.8)
Age at time of survey	
≤ 40 years	16 (4.6)
> 40 years	334 (95.4)
Tumor subtype	
Non-Hodgkin lymphoma	52 (13.8)
Hodgkin lymphoma	192 (50.9)
Colorectal cancer	114 (30.2)
Thyroid cancer	19 (5.0)
Age at time of diagnosis	
≤ 40 years	29 (8.3)
> 40 years	322 (91.7)

Table 1. Sociodemographic and clinical characteristics (n=377) (continued)

	No. (%)
Years since diagnosis	
< 2 years	77 (20.5)
≥ 2 years	299 (79.5)
Comorbid conditions	
0	95 (35.2)
1	78 (28.9)
≥2	97 (35.9)
Socioeconomic status	
Low	86 (25.1)
Middle	131 (38.2)
High	123 (35.9)
Living in a care institution	3 (0.9)

Missings: Age at survey n=27, Age at diagnosis n=26, Years since diagnosis n=1, Comorbidity n=107, Socioeconomic status n=34

The mean summary score of the QLQ-C30 was 83.1 (SD 15.7, Table 2). Mean scores on the BIPQ are presented in Table 2. Mild to severe symptoms of anxiety were reported by 26% of patients and 25% of patients reported mild to severe symptoms of depression. All but one ("Comprehensibility") of the illness representations were negatively and significantly associated with QoL ($p<0.05$), indicating that negative illness representations were associated with worse QoL (Table 2).

Table 2. Quality of life, illness representations, anxiety and depression: Summary scores and correlations

	Mean (SD)	Pearson Correlation Coefficients
Quality of life (EORTC QLQ-C30)		
Quality of life	83.11 (15.70)	1.00
Illness representations (BIPQ)		
Consequences	4.97 (2.64)	-.49 *
Timeline	6.94 (3.41)	-.17 **
Personal control	5.82 (3.13)	-.21 **
Treatment control	3.77 (2.61)	-.34 **
Identity	4.47 (2.70)	-.55 **
Concerns	4.97 (2.76)	-.17 **
Emotions	4.21 (2.59)	-.46 **
Comprehensibility	3.89 (2.71)	-.05
Anxiety and Depression (HADS)		
Anxiety	5.10 (4.07)	-.63 **
Depression	4.86 (3.98)	-.68 **

Missings: Quality of life n=8, Consequences n=62, Timeline n=54, Personal control n=46, Treatment n=51, Identity n=45, Concerns n=41, Emotions n=43, Comprehensibility n=40, Anxiety n=10, Depression n=11

Abbreviations: SD, standard deviation; EORTC, European Organisation for Research and Treatment, QLQ-C30, Quality of Life Questionnaire Core 30; BIPQ, Brief Illness Perception Questionnaire; HADS, Hospital Anxiety and Depression Scale

* $p<0.05$, ** $p<0.01$

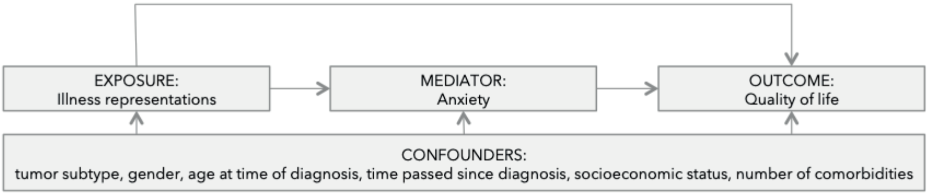

Figure 1a. Mediation model depicting the association of illness representations with quality of life, mediated by anxiety.

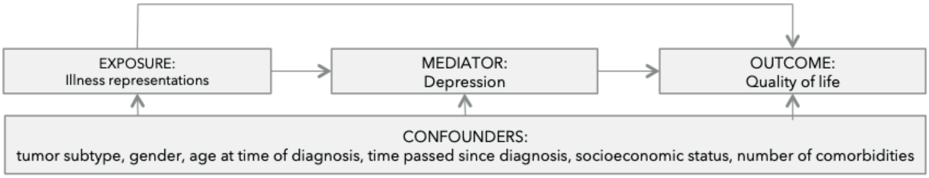

Figure 1b. Mediation model depicting the association of illness representations with quality of life, mediated by depression.

Mediation analyses

Anxiety as a mediator of the association of illness representations with quality of life

Having more negative illness representations was associated with more symptoms of anxiety and having more symptoms of anxiety was associated with worse QoL. The estimated total effect of the different illness representations on QoL was partly mediated by anxiety (Table 3). The total effect on QoL was largest for the illness representations “Consequences” (perceived effects and outcome of the illness on a patient’s life), “Identity” (experience of symptoms due to the illness), “Concerns” (extent to which the patient is concerned about the illness) and “Emotions” (emotional impact of the illness). 41% to 87% of the total effect of illness representations was mediated by anxiety: The mediating effect of anxiety was strongest for the illness representation “Emotions”. The total effect of the illness representation “Timeline” (how long the patient believes that the illness will last) on QoL, which was limited, was to a relatively large extent (84%) mediated by anxiety.

Depression as a mediator of the association of illness representations with quality of life

Having more negative illness representations was associated with more symptoms of depression, which, in turn, was associated with worse QoL. Depression mediated 39% to 69% of the effect of illness representations on QoL (Table 4). The mediating effects of depression were strongest for the illness representations “Emotions”, “Concerns”, and “Consequences”. The limited total effect of the illness representation “Timeline” on QoL was to relatively large extent (69%) mediated by depression. In general, the mediating effects of depression were somewhat weaker than the mediating effects of anxiety.

Table 3. Illness representations and quality of life: Natural direct effect and indirect effect mediated by anxiety

	Total effect			Natural direct effect			Natural indirect effect			Percentage of the total effect that was mediated
	Estimate	95%CI	*p*	Estimate	95%CI	*p*	Estimate	95%CI	*p*	%
Illness representations										
(1) Consequences (n=216)	-8.65	-1.74, -6.57	.000	-4.60	-6.44, -2.76	.000	-4.05	-5.52, -2.59	.000	47%
(2) Timeline (n=216)	-1.80	-3.87, .27	.088	-.28	-2.01, 1.44	.747	-1.52	-2.66, -.37	.009	84%
(3) Personal control (n=223)	-3.12	-5.18, -1.05	.003	-1.04	-2.73, .65	.228	-2.08	-3.32, -.83	.001	67%
(4) Treatment control (n=219)	-5.48	-7.53, -3.43	.000	-2.91	-4.63, -1.2	.001	-2.56	-3.89, -1.24	.000	47%
(5) Identity (n=220)	-7.81	-9.71, -5.92	.000	-4.61	-6.32, -2.89	.000	-3.21	-4.48, -1.94	.000	41%
(6) Concerns (n=223)	-7.03	-9.1, -4.96	.000	-1.95	-4, .09	.062	-5.08	-6.73, -3.44	.000	72%
(7) Emotions (n=224)	-6.43	-8.29, -4.57	.000	-.86	-3.09, 1.36	.446	-5.57	-7.34, -3.79	.000	87%
(8) Comprehensibility[†] (n=222)	-.37	-2.32, 1.58	.708	.80	-.85, 2.44	.344	-1.17	-2.3, -.04	.042	

[†] Comprehensibility affects quality of life via opposing direct and indirect effects. This makes calculating the mediated effect impossible.

Table 4. Illness representations and quality of life: Natural direct effect and indirect effect mediated by depression

	Total effect			Natural direct effect			Natural indirect effect			Percentage of the total effect that was mediated
	Estimate	95%CI	*p*	Estimate	95%CI	*p*	Estimate	95%CI	*p*	%
Illness representations										
(1) Consequences (n=216)	-8.02	-1.01, -6.04	.000	-4.19	-5.95, -2.43	.000	-3.83	-5.25, -2.41	.000	48%
(2) Timeline (n=216)	-2.08	-4.16, .01	.051	-.64	-2.29, 1.01	.447	-1.44	-2.71, -.16	.028	69%
(3) Personal control (n=223)	-2.98	-4.98, -.98	.003	-1.27	-2.86, .33	.119	-1.71	-2.97, -.46	.007	57%
(4) Treatment control (n=219)	-5.45	-7.48, -3.41	.000	-2.68	-4.35, -1.01	.002	-2.77	-4.14, -1.39	.000	51%
(5) Identity (n=220)	-7.70	-9.59, -5.81	.000	-4.71	-6.31, -3.11	.000	-2.99	-4.28, -1.71	.000	39%
(6) Concerns (n=223)	-6.81	-8.8, -4.81	.000	-2.88	-4.63, -1.13	.001	-3.93	-5.36, -2.49	.000	58%
(7) Emotions (n=224)	-6.72	-8.62, -4.83	.000	-2.79	-4.48, -1.1	.001	-3.94	-5.33, -2.54	.000	59%
(8) Comprehensibility[†] (n=222)	-.35	-2.28, 1.58	.723	.97	-.63, 2.56	.235	-1.32	-2.49, -.14	.028	

[†] Comprehensibility effects quality of life via opposing direct and indirect effects. This makes calculating the mediated effect impossible.

DISCUSSION

This study explored the mediating role of anxiety and depression in the association of illness representations with QoL in a large sample of patients with advanced cancer. We were able to confirm prior findings that having more negative illness representations (e.g. experiencing more symptoms due to the illness, being more concerned about the illness) is associated with worse QoL. Our study adds that this association is substantially mediated by symptoms of anxiety or depression.

It is not surprising that the total effect of the illness representation "Emotions" (emotional impact of the illness) on QoL was the largest and was to a relatively large extent mediated by symptoms of anxiety and depression, considering that this item measures the emotional impact of the illness on the patient. In accordance with previous research among patients treated for breast cancer,[33] we found that patients who feel that their illness affects their life more severly ("Consequences") and who experience many symptoms from their illness ("Identity") have a considerable worse QoL. Our findings add that nearly half of that association was mediated by symptoms of anxiety or depression. Patients scoring high on "Identity" tend to attribute commonly occurring symptoms (such as a headache) to their illness, even if no such association exists.[34] This applies in particular to patients with advanced cancer who have to deal with uncertainty about the extent to which their limited life expectancy and who tend to interpret symptoms as signs of potential progression of their illness.[35, 36] Over-interpretation of symptoms can thus lead to symptoms of anxiety and depression, which in turn impairs QoL.

Patients had the highest average score on the illness representation "Timeline", meaning that they believed that their illness would last "forever". Previous research has shown that "Timeline" scores were skewed towards the upper extreme in patients with advanced cancer, which suggests awareness of the incurable nature of their illness.[13] "Timeline" scores were only to a limited extent associated with QoL. This association however was to a large extent mediated by symptoms of anxiety and depression, meaning that being aware of the limited life expectancy does not have a strong direct effect on QoL itself, but mainly impacts QoL negatively through the strong experience of symptoms of anxiety and depression.

Addressing illness representations is a promising approach when supporting patients with symptoms of anxiety or depression, and can thus be a way of improving the QoL of patient with advanced cancer. Since the prevalence of symptoms of anxiety and depression is higher in patients with advanced cancer than in colorectal cancer survivors, and even higher in comparison to the normative population,[37] patients are in clear need of support. Our findings emphasize the importance of raising awareness for patients' illness representations,[38] especially since previous research found that healthcare providers' understanding of the illness representations of their patients was relatively poor,[39] also with regard to important topics such as prognosis.[40] The recent consensus guideline of the American Society of Clinical Oncology on patient-clinician communication highlights the importance of (improved) health care communication and its positive impact on many objective and subjective health outcomes.[38] Our results suggest that illness representations can play an important role in patient-clinician communication and in meeting patients' information needs.[30] Additionally, previous research indicated the usefulness of targeting illness representations as a way to improve health outcomes.[41] Patients who were recovering from a myocardial infarction found a brief intervention on altering illness representations to be effective in improving functional outcomes.[41] Further research on how to adapt negative illness representations of patients with advanced cancer is needed.

The main strengths of this study lie in the use of a relatively large dataset of patients with advanced cancer, a unique and vulnerable group of patients that is rarely investigated, and the use of recently developed mediation analysis techniques that allow for the decomposition of total effects into natural direct and indirect effects, while accounting for exposure-mediator interactions.

Some limitations need to be considered when interpreting the findings. Although previous research and theoretical models suggest a strong temporal sequence, with illness representations preceding symptoms of anxiety and depression,[17] this study cannot draw causal conclusions due to its cross-sectional study design. Second, to interpret the observed direct and indirect effects, one needs to assume that there are no unmeasured confounders of the exposure-mediator relationship, the mediator-outcome relationship and the exposure-outcome relationship.[32] Although we did adjust for several potential confounders, we cannot exclude the possibility that unmeasured confounders may have impacted the results. Third, we performed a complete case analysis on the subset of patients with full information on the exposure, mediator, outcome variables and confounders. While this method is widely applied to treat missing data, it may lead to biased results if the data are not missing completely at random.[42]

In conclusion, our study indicates that negative illness representations are associated with worse QoL in patients with advanced cancer. Symptoms of anxiety and depression substantially mediate this association. Further prospective research is needed to confirm these findings. QoL and symptoms of anxiety and depression in patients with advanced cancer may be improved by addressing illness representations during medical consultations.

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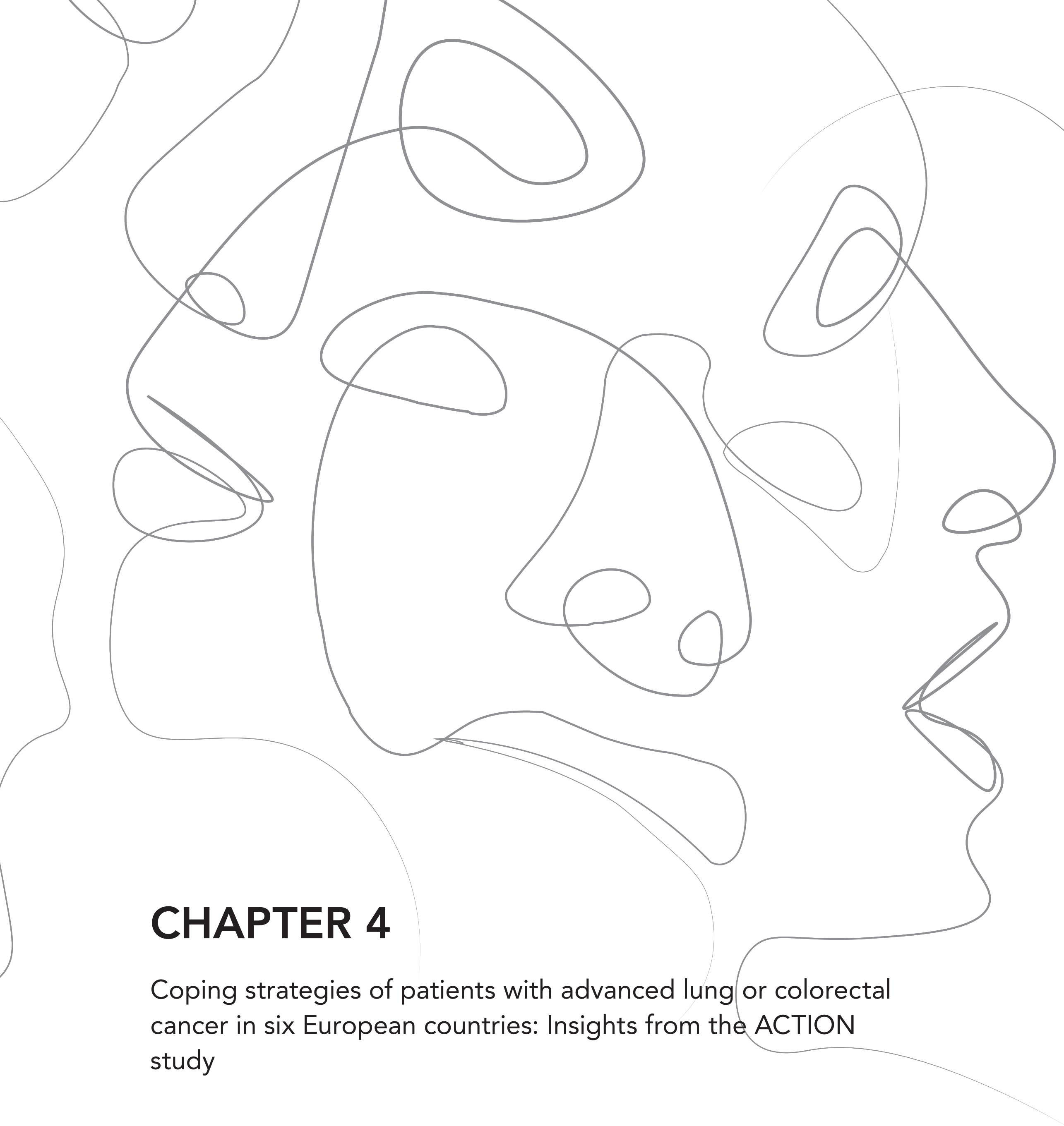

CHAPTER 4

Coping strategies of patients with advanced lung or colorectal cancer in six European countries: Insights from the ACTION study

Jabbarian LJ, Korfage IJ, Červ B, van Delden JJM, Deliens L, Miccinesi G, Payne S, Thit Johnsen A, Verkissen MN, Wilcock A, van der Heide A, Rietjens JAC, on behalf of the ACTION consortium

Under review

ABSTRACT

Objective

Physical symptoms and psychological distress are common in patients with advanced cancer. Even when medical treatments are limited, supporting patients' adaptive coping strategies could potentially improve their quality of life. Developing such support would be aided by a greater understanding of patients' coping strategies and influencing factors. Thus, we examined the prevalence of various coping strategies and associated sociodemographic and clinical variables.

Methods

We used sociodemographic and baseline data from the ACTION trial, including measures of Denial, Acceptance and Problem-focused coping (COPE and Brief COPE inventory), of patients with advanced cancer from six European countries. Healthcare professionals provided clinical background characteristics. Multilevel analyses were performed.

Results

Data from 675 patients with stage III/ IV lung (342, 51%) or stage IV colorectal (333, 49%) cancer were used; mean age 66 (10 SD) years, 60% male. Overall, patients scored low on Denial and high on Acceptance and Problem-focused coping. Multivariate analysis showed that older patients scored higher on Denial than younger patients (β=0.05; 95% CI 0.2 to 0.7), and patients from Italy (β=1.57; 95% CI 0.76 to 2.39) and Denmark (β=1.81; 95% CI 0.88 to 2.75) scored higher than patients in other countries. Higher educated patients scored higher on Acceptance than lower educated patients (β=0.05; 95% CI 0.005 to 0.100). Patients with a WHO performance status of 1 (β=-0.75; 95% CI -1.27 to -0.23) or 2 (β=-1.33; 95% CI -2.33 to -0.34) scored higher on Problem-focused coping than patients with a WHO status of 0.

Conclusion

Coping strategies of patients with advanced cancer appear to vary between subpopulations. We recommend taking these factors into account when developing tailored interventions to support patients' coping strategies.

BACKGROUND

Being diagnosed with advanced, incurable cancer often disrupts patients' lives in diverse ways.[1] Patients can experience multiple physical symptoms and psychological distress.[2,3] When the disease has progressed to a point where curative treatments are unavailable, patients could particularly benefit from interventions aimed at improving their quality of life.[4]

One way of assisting patients in the last phase of their life is to support adaptive coping strategies. Coping strategies are defined as distinct, constantly changing cognitive, emotional and behavioral efforts to manage a (health) threat.[5] Patients can use a variety of coping strategies.[6] For instance, when using Denial, patients reduce the impact of their advanced disease by thinking that it is not real.[6] Acceptance, on the other hand, includes actively dealing with the advanced disease by accepting its reality[7] and managing feelings of distress.[5] Problem-focused coping extends this towards a behavioral approach, for example through taking actions to improve their way of living with their advanced disease.[6] The use of coping strategies can vary between patients, situations and over time.[6] Different coping strategies may be used simultaneously or alternately.[8] Whether a certain coping strategy is beneficial or not is highly dependent on the individual patient and situational context.[6, 7, 9]

Evidently, the way patients cope with their advanced disease has an impact on their physical and psychological well-being.[10] Since coping strategies are modifiable,[6] supporting and encouraging adaptive coping strategies can contribute to the well-being of patients, also when their disease has reached an advanced, incurable stage.[11] Therefore, coping support is increasingly incorporated into interventions for patients with advanced cancer.[12-14] Coping strategies can also be used to tailor interventions. For instance, a pain management program for community dwelling older people was more successful in reducing pain and symptoms of anxiety when the intervention was tailored to the patients' specific coping strategy, as compared to generic and untailored interventions.[15]

The relevance of assessing and responding to coping needs throughout the disease trajectory of patients has been confirmed and recognized by numerous professional organizations, such as the American Society of Clinical Oncology[16] and the National Institute for Clinical Excellence in the United Kingdom.[17] Research in this area has mainly focused on patients in earlier stages of cancer.[18-20] It is unclear if the findings in these patients are generalizable to patients with advanced cancer who face specific challenges, such as preparatory grief,[21] death anxiety[22] and increased existential distress.[23] Given the importance of the sociocultural context for the appraisal of a (health) threat, it is not surprising that coping strategies have been found to differ across age groups,[24] diseases,[8] and cultures.[25,26] It is however unknown to what extent sociodemographic and clinical variables influence the coping strategies of patients with advanced cancer. Detailed insights into coping strategies of patients with advanced cancer can inform the design of interventions delivering coping support, and the evaluation and improvement of existing interventions by tailoring them to patients' individual coping strategies. We aimed to (1) characterize the prevalence of the coping strategies Denial, Acceptance and Problem-focused coping among patients with advanced lung or colorectal cancer and (2) identify sociodemographic and clinical characteristics associated with the use of these coping strategies, including a comparison between countries.

METHODS

Participants

We used the sociodemographic and baseline data of patients included in the care-as-usual arm of the international ACTION trial, a cluster randomized trial investigating the effects of an advance care planning intervention as compared to care as usual. The patients were recruited in outpatient pulmonology and oncology departments in academic and non-academic hospitals in Belgium, Denmark, Italy, the Netherlands, Slovenia and the United Kingdom, between June 2015 and May 2017 (see Box 1 for the inclusion and exclusion criteria). The ACTION study has been described in more detail elsewhere.[27] Written informed consent was obtained. Research ethics committees of the participating countries approved the trial. The trial is registered in the 'international standard randomised controlled trial number' registry (ISRCTN63110516).

Box 1. Inclusion and exclusion criteria for the ACTION trial.

Inclusion criteria:

1. Histologically confirmed diagnosis of:
    a. Lung cancer:
        - Small cell – extensive disease/ Stage III or IV*
        - Non-small cell – stage III or IV*
    b. Colorectal cancer: Stage IV or metachronous metastases*,
    *according to the 7th edition of TNM classification and staging system
2. Written informed consent to participate,
3. WHO performance status of 0-3.

Exclusion criteria:

1. Age <18 years,
2. Unable to provide consent,
3. Unable to complete questionnaire in country's language,
4. Less than 3 months anticipated life expectancy,
5. Taking part in a research study that is evaluating palliative care services or communication strategies.

Measures

Sociodemographic and clinical variables

Patients provided information about their age, educational level, gender, living situation and religion. Their healthcare providers provided information on the type and stage of the disease and the time since diagnosis of both the primary tumor and the current stage of the disease. Additionally, they gave information on which treatment patients received and their WHO performance status, ranging from 0 to 3.[28]

Coping

We measured patients' coping strategies with the subscales Denial and Acceptance of the COPE Inventory and the subscales Planning and Active coping of the Brief COPE.[7 29] Patients were asked to rate the items according to the best description of how they had been coping with their disease during the past two months. Items were rated on a four point Likert scale, ranging from 1 ("I don't do this at all"), 2 ("I do this a little bit"), 3 ("I do this a medium amount") to 4 ("I do this a lot").

Following questionnaire instructions, we confirmed the subscales of the underlying coping strategies,[7] by conducting a principal components analysis with the twelve selected items of the COPE Inventory and Brief COPE. The analysis identified three distinct factors, each with eigenvalues above 1. The analysis confirmed the subscales Denial (explained variance 29%) and Acceptance (explained variance 14%), which were also described by the developers of the COPE Inventory.[7] The analysis also showed that the subscale Active coping and the subscale Planning of the Brief COPE loaded on the same factor (explained variance 23%), which is in accordance with the structure of the questionnaire as described by the developers.[29] We therefore combined Active coping and Planning, and, following previous research,[30] labelled the resulting subscale as Problem-focused coping (see Box 2 for an overview of the identified subscales and included questions). We subsequently summed the responses per subscale to create subscale scores. This resulted in a range of 4 to 16 for each subscale. Higher scores indicate more use of that particular coping strategy.

Box 2. Overview of the subscales and items of the COPE and Brief COPE after the principal component analysis.

Denial:
(1) I act as though this hasn't even happened.
(2) I say to myself "this isn't real".
(3) I pretend that this hasn't really happened to me.
(4) I refuse to believe that this happened to me.

Acceptance:
(1) I accept the reality of the fact that this has happened to me.
(2) I learn to live with my situation.
(3) I get used to the idea that this has happened to me.
(4) I accept that this has happened to me and that it can't be changed.

Problem-focused coping
(1) I concentrate my efforts on doing something about my situation.
(2) I take action to try to make my situation better.
(3) I try to come up with a strategy about what to do in my situation.
(4) I think hard about what steps to take in my situation.

Statistical methods

Missing items are common in palliative care trials.[31] Given the low percentage of missing items (<5%) in our study, we carried out a complete case analysis by including only the data of patients with full responses on all items of the three respective coping subscales.

We used the Statistical Package for the Social Sciences version 24 (SPSS, Chicago, IL) for the analyses. We summarized patients' sociodemographic and clinical characteristics with means and standard deviations for the continuous variables and counts and percentages for the categorical variables. The distribution of scores on the coping subscales is presented with mean sum scores and standard deviations. We calculated Pearson correlation coefficients to assess the linear correlation between the coping strategies.

A multivariate multilevel regression model was used to analyze associations between coping strategies and sociodemographic and clinical variables. This type of model allows accounting for clustering at the hospital level and thus for non-independency of observations.[32] First, univariate multilevel models were used to test associations between sociodemographic and clinical variables and distinct coping strategies. A significance level of $p<0.20$ was used to select variables for the final model. For the final multivariate model, the significance level was set at $p<0.05$. Betas, 95% confidence intervals and *p*-values are reported.

RESULTS

Descriptive statistics

The analyses included 675 patients who were enrolled in the control arm of the ACTION trial. Numbers of patients per country ranged from n=25 (Slovenia) to n=168 (the Netherlands). Sociodemographic and clinical characteristics are shown in Table 1. Patients' average age was 66 (SD 9.6) years and the majority of patients were male (60%). Most of the patients were living with a partner (76%) and had children (87%). About half of the patients described themselves as being religious (52%). The majority of patients were diagnosed with lung cancer stage III or IV (51%). On average, patients were diagnosed with their primary tumor 1.7 years earlier (2.4 SD). At the time of inclusion, most patients received systemic antitumor treatment (92%).

Prevalence of coping strategies

655 patients were included in the analysis of Denial; this number was 659 for Acceptance and 643 for Problem-focused coping. On average, patients scored low on the use of Denial (mean sum score 6.6 (SD 3.1) and high on Acceptance and Problem-focused coping (mean sum score 12.6 (SD 2.7) and 12.2 (SD 2.9), respectively; Table 2). Higher scores on Acceptance were correlated with higher scores on Problem-focused coping ($r=0.36$; $p<0.001$) and higher scores on Problem-focused coping were correlated with higher scores on Denial ($r=0.11$; $p<0.001$). The use of Denial and Acceptance was not correlated ($r=0.04$; $p=0.27$).

Table 1. Sociodemographic and Clinical Characteristics per Country

	Belgium (n = 135)	Denmark (n = 68)	Italy (n = 139)	Netherlands (n = 168)	Slovenia (n = 25)	United Kingdom (n = 140)	Total (N = 675)
Age in years, mean (SD)	65.3 (9.5)	65.5 (9.0)	65.5 (9.6)	65.4 (8.1)	71.1 (9.5)	68.4 (11.0)	66.2 (9.6)
Years of education, mean (SD)	13.9 (4.4)	13.5 (5.9)	11.4 (5.2)	13.2 (3.7)	9.9 (3.3)	13.5 (4.7)	12.9 (4.7)
Gender (male), n (%)	91 (67.4)	35 (51.5)	90 (64.7)	111 (66.1)	10 (40.0)	70 (50.4)	407 (60.4)
Living with a spouse, n (%)	106 (79.1)	55 (80.9)	99 (73.9)	129 (78.2)	15 (62.5)	93 (69.9)	497 (75.5)
Having children, n (%)	114 (85.1)	62 (91.2)	118 (86.8)	146 (86.9)	21 (84.0)	60 (44.1)	583 (87.3)
Religion, n (%)							
Prefers not to specify	31 (23.8)	9 (13.6)	16 (11.7)	17 (10.1)	2 (8.0)	18 (13.2)	93 (14.0)
Not religious	30 (23.1)	38 (57.6)	24 (17.5)	76 (45.2)	2 (8.0)	58 (42.6)	228 (34.4)
Religious	69 (53.1)	19 (28.8)	97 (70.8)	75 (44.6)	21 (84.0)	60 (44.1)	341 (51.5)
Diagnosis, n (%)							
Lung cancer, stage III or IV	79 (58.5)	34 (50.0)	71 (51.1)	76 (45.2)	0 (0.0)	82 (58.6)	342 (50.7)
Colorectal cancer, stage IV	56 (41.5)	34 (50.0)	68 (48.9)	92 (54.8)	25 (100)	58 (41.4)	333 (49.3)
Years since diagnosis, mean (SD)	1.5 (1.7)	2.7 (3.2)	2.0 (3.5)	1.9 (1.9)	2.3 (2.4)	0.9 (1.4)	1.7 (2.4)
Years since diagnosis of current stage, mean (SD)	1.1 (1.4)	1.6 (2.2)	0.8 (1.1)	1.2 (1.4)	1.3 (1.9)	0.4 (0.7)	1.0 (1.4)
Current systemic antitumor treatment,[1] n (%)	126 (96.2)	68 (100.0)	135 (97.1)	144 (86.2)	8 (53.3)	115 (87.8)	596 (91.6)
WHO performance status,[2] n (%)							
3	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.2)	1 (4.0)	5 (3.6)	8 (1.2)
2	7 (5.5)	1 (1.5)	2 (1.4)	12 (7.1)	13 (52.0)	20 (14.3)	55 (8.3)
1	56 (44.1)	40 (58.8)	65 (47.1)	122 (72.6)	10 (40.0)	49 (35.0)	342 (51.4)
0	64 (50.4)	27 (39.7)	71 (51.4)	32 (19.0)	1 (4.0)	66 (47.1)	261 (39.2)

NOTE:

[1] Includes chemotherapy, immunotherapy and targeted therapy.

[2] 0-Fully active, able to carry on all pre-disease performance without restriction, 1-Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g. light house work, office work, 2-Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours, 3-Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.

Missings total: Age (n=6), Education (n=89), Gender (n=1), Living with a spouse (n=15), Having children (n=6), Religion (n=13), Years since diagnosis (n=1), Years since diagnosis of current stage (n=6), Systemic treatment (n=24), WHO performance status (n=9)

Multilevel model: Associations between coping strategies and sociodemographic and clinical variables

Associations between Denial and sociodemographic and clinical variables

For Denial, the univariate multilevel models showed significant associations (p<0.20) with age, years of education, having children, years since the diagnosis of the primary tumor and country of residence (S-Table 1). These variables were included in the final multivariate model. That multivariate multilevel model (Table 3) showed that older patients scored higher on Denial than younger patients (β=0.05; 95% CI, 0.2 to 0.7, p<0.001) and that patients in Italy (β=1.57; 95% CI, 0.76 to 2.39; p<0.001) and Denmark (β=1.81; 95% CI, 0.88 to 2.75; p<0.001) scored higher on Denial than patients in other countries.

Table 2. Patients Mean Sum Scores (SD) on each coping subscale by sociodemographic and clinical characteristic and country of residence

	Denial[1] (n=655)	Acceptance[1] (n=659)	Problem-focused[1] (n=643)
Patient Mean Sum Score (SD)	6.6 (3.1)	12.6 (2.7)	12.2 (2.9)
Age in years			
18-64	6.1 (2.8)	12.6 (2.9)	12.6 (2.7)
65-79	6.9 (3.2)	12.6 (2.5)	12.0 (2.8)
≥80	7.3 (3.9)	13.3 (3.0)	11.5 (3.6)
Years of education			
0-4	6.4 (2.8)	12.5 (2.2)	10.4 (3.3)
5-12	7.0 (3.3)	12.3 (2.8)	12.2 (2.8)
≥13	6.1 (2.8)	12.9 (2.5)	12.3 (2.9)
Gender			
Male	6.6 (3.1)	12.5 (2.7)	12.0 (3.0)
Female	6.6 (3.2)	12.8 (2.8)	12.6 (2.7)
Living with a spouse			
Yes	6.6 (3.0)	12.6 (2,7)	12.2 (2.8)
No	6.7 (3.5)	12.6 (2.6)	12.1 (3.1)
Having children			
Yes	6.7 (3.2)	12.6 (2.7)	12.2 (2.9)
No	5.8 (2.5)	12.8 (2.7)	12.4 (2.9)
Religion			
Prefers not to specify	6.5 (3.0)	12.0 (2.9)	11.7 (3.0)
Not religious	6.3 (3.1)	12.7 (2.7)	12.2 (2.9)
Religious	6.9 (3.1)	12.7 (2.6)	12.5 (2.8)
Diagnosis			
Lung cancer, stage III or IV	6.7 (3.1)	12.4 (2.6)	12.1 (2.8)
Colorectal cancer, stage IV	6.6 (3.1)	12.8 (2.8)	12.3 (3.0)
Years since diagnosis			
≤1 year	6.5 (3.0)	12.7 (2.7)	12.3 (2.8)
> 1 year	6.5 (3.1)	12.8 (2.8)	12.4 (3.1)
Years since diagnosis of current stage			
≤0.5 year	6.5 (3.0)	12.6 (2.6)	12.4 (2.6)
>0.5 year	6.7 (3.3)	12.7 (2.7)	12.0 (3.1)
Current systemic treatment[2]	6.6 (3.1)	12.6 (2.6)	12.2 (2.8)
WHO performance status[3]			
3	5.8 (2.4)	13.4 (2.1)	11.3 (1.9)
2	7.2 (3.6)	12.5 (2.8)	11.8 (2.9)
1	6.6 (3.1)	12.3 (2.7)	12.2 (2.8)
0	6.6 (3.0)	12.9 (2.7)	12.4 (3.1)
Country of residence			
Belgium (n=135)	6.5 (2.9)	11.7 (2.8)	10.4 (3.0)
Denmark (n=68)	7.6 (3.5)	13.3 (2.4)	12.6 (2.9)
Italy (n=138)	7.5 (3.1)	12.5 (2.5)	12.8 (2.3)

Table 2. Patients Mean Sum Scores (SD) on each coping subscale by sociodemographic and clinical characteristic and country of residence (continued)

	Denial[1] (n=655)	Acceptance[1] (n=659)	Problem-focused[1] (n=643)
Netherlands (n=166)	6.0 (2.9)	12.5 (2.6)	13.0 (2.4)
Slovenia (n=25)	7.3 (3.5)	12.6 (2.5)	12.4 (2.6)
United Kingdom (n=139)	6.1 (3.0)	13.4 (2.8)	12.2 (3.2)

NOTE:

[1] The range for the coping strategies is 4 to 16. A higher score on the subscale indicates a greater use of the particular coping strategy.

[2] Includes chemotherapy, immunotherapy, and targeted therapy.

[3] 0-Fully active, able to carry on all pre-disease performance without restriction, 1-Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g. light house work, office work, 2-Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours, 3-Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.

Missing range: Age (5-6), Education (n=79-89), Gender (n=1), Living with a spouse (n=14-15), Children (n=6-), Religion (n=12-13), Time since diagnosis (n=1), Time since diagnosis of current stage (n=6), Systemic treatment (n=20-23), WHO performance status (n=8-9)

Table 3. Multivariate multilevel analysis of the coping strategy Denial (n=655)

	β	95% CI	*p*
Explanatory Variables			
Age in years	.05	.02, .07	<.001*
Years of education	-.04	-.10, .01	.129
Having children			.074
Yes	.67	-.07, 1.41	
No	Ref		
Years since diagnosis	.04	-.06, .14	.418
Country of residence			<.001*
Netherlands	.08	-.66, .82	.831
Belgium	.69	-.11, 1.49	.090
Slovenia	1.07	-.36, 2.50	.141
Italy	1.57	.76, 2.39	<.001
Denmark	1.81	.88, 2.75	<.001
United Kingdom	Ref		

[*] *p<0.05*, and thus significant

Associations between Acceptance and sociodemographic and clinical variables

The univariate multilevel models for Acceptance showed significant associations (p<0.20) with years of education, being religious or not, primary diagnosis, years since the diagnosis of the primary tumor and diagnosis of the current stage, WHO performance status and country of residence (S-Table 1). These variables were included in the final multivariate model. The multivariate multilevel model (Table 4) showed that patients with higher education scored higher on Acceptance than patients with lower education (β=0.05; 95% CI 0.005 to 0.100; p=0.030).

Table 4. Multivariate multilevel analysis of the coping strategy Acceptance (n=659)

	β	95% CI	*p*
Explanatory Variables			
Years of education	.05	.005, .100	.030*
Religion			.277
Prefers not to specify	-.55	-1.23, .13	
No	-.08	-.58, .42	
Yes	Ref		
Diagnosis			.463
Lung cancer, stage III or IV	-.18	-.67, .30	
Colorectal cancer, stage IV	Ref		
Years since diagnosis	.02	-.09, .12	.758
Years since diagnosis of current stage	.16	-.03, .34	.100
WHO performance status[1]			.075
3	.88	-1.26, 3.02	
2	-.54	-1.52, .44	
1	-.59	-1.09, -.09	
0	Ref		
Country of residence			.060
Netherlands	-.84	-1.90, .21	
Belgium	-1.88	-2.99, -.77	
Slovenia	-.80	-2.33, .74	
Italy	-.66	-1.77, .45	
Denmark	-.19	-1.56, 1.19	
United Kingdom	Ref		

* *$p<0.05$*, and thus significant

[1] 0-Fully active, able to carry on all pre-disease performance without restriction, 1-Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g. light house work, office work, 2-Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours, 3-Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.

Associations between Problem-focused coping and sociodemographic and clinical variables

For Problem-focused coping, the univariate multilevel models showed significant associations ($p<0.20$) with age, years of education, gender, being religious or not, years since the diagnosis of the primary tumor, WHO performance status and country of residence (S-Table 1). These variables were included in the final multivariate model. This model (Table 5) showed that patients with a WHO status of 1 ($\beta=-0.75$; 95% CI -1.27 to -0.23; $p=0.005$) or 2 ($\beta=-1.33$; -2.33 to -0.34 95% CI, $p=0.009$, i.e. patients who were somewhat restricted in their activities and selfcare) scored lower on Problem-focused coping than patients with a WHO status of 0 (i.e. patients who were fully active).

Table 5. Multivariate multilevel analysis of the Problem-focused coping strategy(n=643)

	β	95% CI	*P*
Explanatory Variables			
Age in years	-.02	-.04, .01	.222
Years of education	.04	-.01, .09	.135
Gender			.187
Male	-.32	-.81, .16	
Female	Ref		
Religion			.272
Prefers not to specify	-.39	-1.10, .33	
No	-.40	-.93, .13	
Yes	Ref		
Years since diagnosis	-.01	-.11, .08	.772
WHO performance status[1]			.009*
3	-1.54	-3.82, .73	.183
2	-1.33	-2.33, -.34	.009*
1	-.75	-1.27, -.23	.005*
0	Ref		
Country of residence			.086
Netherlands	1.28	-.56, 3.12	
Belgium	-1.68	-3.68, .32	
Slovenia	.80	-1.66, 3.25	
Italy	.52	-1.48, 2.52	
Denmark	.53	-1.94, 3.00	
United Kingdom	Ref		

* $p<0.05$, and thus significant

[1] 0-Fully active, able to carry on all pre-disease performance without restriction, 1-Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g. light house work, office work, 2-Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours, 3-Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.

CONCLUSIONS

We found that patients with advanced lung or colorectal cancer predominantly use Acceptance and Problem-focused coping. Coping strategies used by patients with advanced cancer appear to be influenced by age, level of education, WHO status and country of origin.

Prevalence of coping strategies

Our finding that patients scored low on Denial and higher on Acceptance and Problem-focused coping aligns with observations in patients with early stage cancer,[33] patients who were recently diagnosed with incurable cancer[34] and cancer survivors.[35]

Our results also show that coping strategies were correlated: higher scores on Acceptance were correlated with higher scores on Problem-focused coping. Endler and colleagues observed that patients with acute health problems predominantly used one coping strategy, in an effort to soothe their symptoms.[8] Contrarily, patients with chronic health problems relied on more than one coping strategy, possibly because they have to adjust their life styles to a new situation.[8] A similar challenge might apply to the situation of patients with advanced cancer. The seemingly contradictory coping strategies Denial and Problem-focused coping were also positively correlated, be it only weakly. Problem-focused coping includes taking action to make a situation better.[6] Possibly, this mechanism is also used as a means to distract oneself from the actual situation.

Associations between coping strategies and sociodemographic and clinical variables

We identified different patterns in the use of coping strategies across various subpopulations. Older patients scored higher on Denial than their younger counterparts. The same finding has been observed in patients with lung cancer.[36] It has been hypothesized that older patients use 'threat minimization' more often, which includes keeping feelings to oneself and avoiding emotional distress by trying to forget.[37] We also found that patients with higher education scored higher on Acceptance. Patients with higher education might have higher cognitive abilities and therefore be more able to manage the multiple demands of a terminal illness. Higher education has also been found to be related to increased prognostic awareness[38] and more communication and involvement in end-of-life decision-making.[39] Possibly, having better abilities in managing the multiple demands of a terminal illness and better involvement in the decision-making contribute to the use of Acceptance.

We also found that patients with a worse WHO performance status scored lower on Problem-focused coping than patients who were fully active and did not experience restrictions. The behavioral efforts that are linked to Problem-focused coping might become more challenging when patients' physical abilities decline.

Patients in Italy and Denmark scored higher on Denial than patients in other countries. A review about culture and end of life care demonstrated that patients in Italy and Norway (a Scandinavian country with supposedly shared values and cultural resemblance to Denmark) showed a general reluctance to talk about death, as well as a trend towards partial or no disclosure of patients' diagnosis and prognosis.[40] This was related to respect for privacy and/ or to a strong death taboo.[40] Not disclosing a diagnosis and a general taboo to talk about death could facilitate the use of Denial, which entails thinking that the disease is not real. Denial itself has been found to be related to both negative and positive outcomes. One study showed that patients with asthma who scored high on Denial tended to disregard symptoms of breathing difficulty, resulting in a higher rate of hospitalizations.[41] Yet, in another study with patients with lung cancer high scores on denial were related to a better overall perception of health and less pain.[9]

Implications for clinical practice

The results of our study can inform healthcare providers about individual differences in the use of coping strategies. As Walshe and colleagues stressed,[14] a major conceptual issue in current interventions is that they largely ignore the coping strategies of patients with advanced cancer, which might worsen their psychological experience.[14] Our results might be used to start discussions of how to support patients with different coping strategies. Next to tailoring interventions accordingly, our findings may help to design interventions on coping support and to decide which elements of coping to include. In a trial investigating coping support as an element of a palliative care intervention for patients with advanced cancer, the coping support included for instance the improvement of behavioral strategies.[11] Ultimately, patients' quality of life improved when coping was addressed more often.[11] Interestingly, clinicians highlighted behavioral coping strategies less and counseling more throughout the intervention.[11]

Based on our results we advise to take the tendency of older patients to use Denial into account, as well as patients' health status. Targeted coping support considering patients' individual coping strategies has the potential to be more efficient in improving patient outcomes. Using information on patients' coping strategies could be extended towards information provision or psychoeducation on, for example, pain control. Since it has been suggested that healthcare providers often lack the appropriate skills to assess patients' coping strategies, psychologists could support them in diagnosing and integrating the information into daily care where needed.[17 42]

Strengths

This paper presents unique data of patients who suffer from an advanced stage of one of two common types of cancer types in six European countries. We were able to collect detailed sociodemographic and clinical information, which allowed a thorough analysis of self-reported coping strategies.

Limitations

To minimize questionnaire burden, we restricted the assessment of coping strategies to three subscales. Future research should include additional coping strategies, such as the use of spirituality or seeking social support. This might give more information about cultural sensitivity and relevance of coping strategies in different countries. Besides, since we observed patients using a combination of coping strategies, future research should investigate to what extent combinations of coping strategies are beneficial for patients.

Conclusion

We investigated the prevalence of coping strategies and associated sociodemographic and clinical characteristics in patients with advanced cancer in six European countries. We found that patients with advanced cancer predominantly use Acceptance and Problem-focused coping and also use different strategies simultaneously. Denial was used less often. Being aware of the variance in the use of coping strategies can help healthcare professionals to coordinate and finetune their care more efficiently. Further, the design and implementation of interventions should be tailored to patients' coping strategies.

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SUPPLEMENTARY MATERIAL

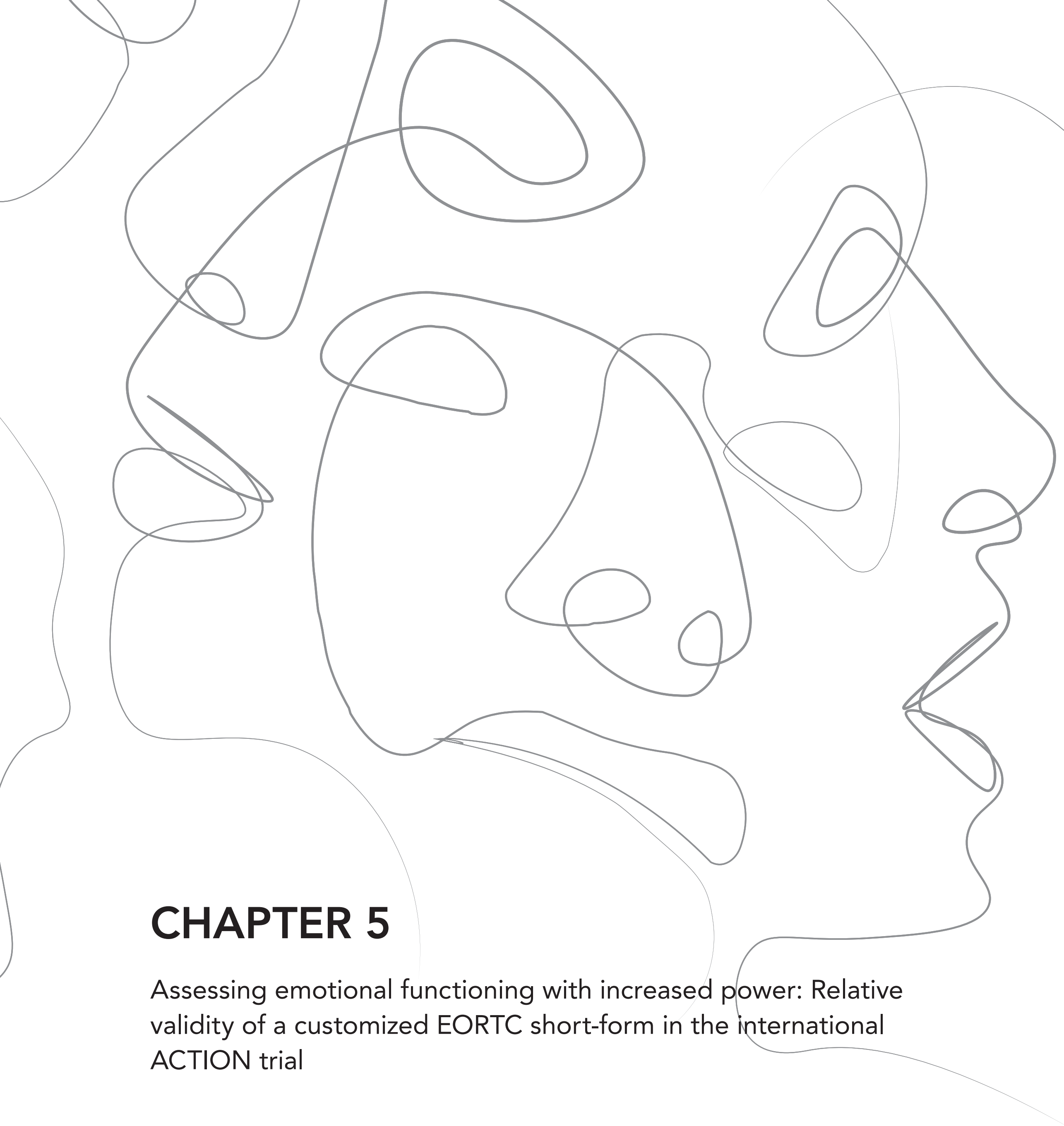
S-Table 1. Univariate multilevel analysis of the association between sociodemographic characteristics, clinical characteristics and country of residence, and coping strategies (online only)

	Denial (n=655)			Acceptance (n=659)			Problem-focused (n=643)		
	β	95% CI	*p*	β	95% CI	*p*	β	95% CI	*p*
Sociodemographic Characteristic									
Age in years	.05	.03, .08	<.001*	-.00	-.02, .02	.807	-.03	-.05, -.01	.007*
Years of education	-.06	-.12, -.01	.021*	.06	.01, .11	.010*	.05	.00, .10	.057*
Gender			.845			.434			.024*
Male	.05	-.44, .54		-.17	-.58, .25		-.50	-.93, -.06	
Female	Ref			Ref			Ref		
Living with a spouse			.503			.740			.548
Yes	-.19	-.74, .36		.08	-.39, .56		.15	-.35, .65	
No	Ref			Ref			Ref		
Having children			.011*			.462			.480
Yes	.92	.21, 1.63		-.23	-.83, .38		-.23	-.87, .41	
No	Ref			Ref			Ref		
Religion			.344			.153*			.101*
Prefers not to specify	-.27	-.99, .46		-.61	-1.24, .01		-.49	-1.15, .16	
Not religious	-.40	-.94, .15		-.20	-.67, .27		-.48	-.96, .01	
Religious	Ref			Ref			Ref		
Clinical Characteristic									
Diagnosis			.535			.092*			.822
Lung cancer, stage III or IV	.15	-.33, .64		-.36	-.77, .06		-.05	-.49, .39	
Colorectal cancer, stage IV	Ref			Ref			Ref		
Years since diagnosis	.08	-.02, .18	-.106*	.08	-.00, .17	.060*	.08	.00, .17	.061*
Years since diagnosis of current stage	.08	-.09, .25	.374	.20	.05, .34	.009*	-.03	-.18, .13	.750
Systemic treatment[1]			.751			.374			.484
Yes	.14	-.74, 1.03		.36	-.43, 1.14		-.29	-.52, 1,10	
No	Ref			Ref			Ref		
WHO performance status[2]			.245			.043*			.012*
3	-.23	-2.42, 1.96		-.16	-2.03, 1.71		-1.66	-3.72, .40	
2	.99	.02, 1.96		-.65	-1.50, 1.90		-.92	-1.80, -.05	
1	.15	-.38, .67		-.63	-1.08,-1.83		-.70	-1.17, -.23	
0	Ref			Ref			Ref		
Country of residence			<.001*			.098*			.044*
Netherlands	-.12	-.81, .58		-.95	-2.13, .24		.88	-.55, 2.30	
Belgium	.43	-.31, 1.16		-1.83	-3.10, -.56		-1.73	-3.28, -.19	
Slovenia	1.24	-.07, 2.55		-.82	-2.43, .79		.23	-1.69, 2.14	
Italy	1.40	.67, 2.13		-.95	-2.22, .32		.62	-.92, 2.17	
Denmark	1.49	.59, 2.38		-.15	-1.71, 1.40		.45	-1.45, 2.34	
United Kingdom	Ref			Ref			Ref		

* *p<0.20,* and thus included in the final model.

[1] Includes chemotherapy, immunotherapy, and targeted therapy.

[2] 0-Fully active, able to carry on all pre-disease performance without restriction, 1-Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g. light house work, office work, 2-Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours, 3-Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.



CHAPTER 5

Assessing emotional functioning with increased power: Relative validity of a customized EORTC short-form in the international ACTION trial

Jabbarian LJ, Groenvold M, Petersen MA, Arnfeldt Christensen C, Deliens L, van der Heide A, Kars MC, Miccinesi G, Payne S, Wilcock A, Korfage IJ, on behalf of the ACTION consortium

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ABSTRACT

Objectives

There is a need to improve the assessment of emotional functioning (EF). In the international an Innovative Palliative Care Intervention to Improve Quality of Life in Cancer Patients - a Multi-Centre Cluster Randomized Clinical Trial (ACTION) trial involving patients with advanced cancer, EF was assessed by a customized 10-item short form (EF10). The EF10 is based on the European Organisation for Research and Treatment of Cancer (EORTC) EF item bank and has the potential for greater precision than the common EORTC Quality of Life Questionnaire Core 30 four-item scale (EF4). We assessed the relative validity (RV) of EF10 compared with EF4.

Methods

Patients from Belgium, Denmark, Italy, the Netherlands, Slovenia and the United Kingdom completed EF10 and EF4, and provided data on generic quality of life, coping, self-efficacy, and personal characteristics. Based on clinical and sociodemographic variables and questionnaire responses, 53 "known groups" that were expected to differ were formed, for example, females versus males. The EF10 and EF4 were first independently compared within this known group, for example, the EF10 score of females vs the EF10 score of males. When these differences were significant, the RV was calculated for the comparison of the EF10 with the EF4.

Results

A total of 1028 patients (57% lung, 43% colorectal cancer) participated. Forty-five of the 53 known-groups comparisons were significantly different and were used for calculating the RV. In 41 of 45 (91%) comparisons, the RV was more than 1, meaning that EF10 had a higher RV than EF4. The mean RV of EF10 compared with that of EF4 was 1.41, indicating superior statistical power of EF10 to detect differences in EF.

Conclusions

Compared with EF4, EF10 shows superior power, allowing a 20 to 34% smaller sample size without reducing power, when used as a primary outcome measure.

INTRODUCTION

Assessing the quality of life of patients with cancer is common practice in clinical trials and is strongly suggested as a screening instrument for detecting distress and improving care.[1, 2] Commonly used questionnaires often lack precision[3, 4] and may have problems with floor and/or ceiling effects, limiting their ability to detect differences between groups and change over time.

Computerized adaptive testing (CAT) is a relatively new technique that enables more efficient data collection for example, of patient-reported outcomes. The content and the number of questions presented are selected according to the participant's previous responses; that is, they are restricted to those relevant to that specific participant.[5, 6] For example, if a participant's responses indicate severe emotional problems, the next item will be one that is relevant for people with such severe problems.[6] The items used in CAT are derived from so-called item banks.[6] These items have been calibrated (estimated) to an item-response theory model,[7, 8] which means that scores based on any subset of the items are comparable.[6]

Because CAT has a higher validity (i.e., the statistical power) than traditional measures, it has the potential to reduce trial sample size requirements without reducing power.[6] Even when it is not possible to complete questions on a computer, the item banks underlying CAT can be useful. Taking into consideration the participant's characteristics, such as age or type and stage of cancer, relevant items can be selected from the item bank and used in pen and paper questionnaires, so-called customized short-forms.

Currently, several organizations work on the enhancement of clinical outcomes research by developing efficient measures of patient-reported outcomes using item banks. In the United States, the Patient-Reported Outcomes Measurement Information System (PROMIS) has developed item banks. In Europe, the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group has developed 14 item banks for each of the domains (excluding overall physical condition/quality of life) covered by its core quality-of-life measure, the Quality of Life Questionnaire Core 30 (QLQ-C30). This includes one of its key domains: emotional functioning (EF).[6, 9] Traditionally, EF is assessed with the QLQ-C30 four-item EF scale (EF4), measuring depression, anxiety and general distress,[10, 11] or with a shortened two-item version (EF2) as included in the Quality of Life Questionnaire Core 15 Palliative Care (QLQ-C15-PAL) questionnaire, an abbreviated version of the QLQ-C30 for use in palliative care.[12] To date, the EF item bank has only been tested in the data set used for its development and no external validation has been performed. This study is the first to test a customized 10-item short form (EF10) based on the EORTC EF item bank in an external, independent and international data set.

Our hypothesis is that the customized EF10 will provide more precise results, that is, better discrimination between groups, and thus higher relative validity (RV) and lower expected sample size requirements than the original QLQ-C30 EF scale (EF4). The primary aim was to compare the RV, which is also known as the relative efficiency, of the EF10 with that of the EF4. The secondary aims were to compare the RV of the EF10 with that of the EF2 and to compare the RV of the EF4 with that of the EF2.

METHODS

Sample

The Advance Care Planning: an Innovative Palliative Care Intervention to Improve Quality of Life in Cancer Patients - a Multi-Centre Cluster Randomized Clinical Trial (ACTION) cluster randomized clinical trial investigates an adapted version of the Respecting Choices advance care planning program. Patients were recruited in pulmonology and oncology departments in hospitals in Belgium, Denmark, Italy, the Netherlands, Slovenia and the United Kingdom between June 2015 and May 2017. Patients were invited by their treating health care professional. The ACTION study protocol has been described elsewhere.[13]

Eligibility requirements included a histologically verified cancer diagnosis of either lung cancer stage III or IV, or colorectal cancer stage IV, being aged at least 18 years and being physically and mentally competent to give consent and complete the questionnaire. Patients had to have a World Health Organization/ Eastern Cooperative Oncology Group performance status of 0 to 3.[14] Written informed consent was obtained. Ethics committees of the participating countries approved the study.

Patients provided information about their age, sex, living situation, and educational level. Their health care professionals provided clinical information, such as the date of diagnosis, current disease stage, and current treatment.

Assessment of the RV

See Table 1.

We used the method of known-groups validation to evaluate the RV (i.e., statistical power to detect group differences) of the EF10 compared with those of the EF4 and the EF2.[18] EF is a multidimensional and complex construct that is influenced by various characteristics on the patient level (e.g., sex), clinical level (e.g., type of cancer), coping, satisfaction and experience with care, and patient involvement. For each patient characteristic and for each questionnaire item (except for the EF items), participants were divided into “known groups”: two groups based on a priori formulated expectations on differences with regard to EF. For example, we hypothesized that patients who felt nauseated would have a worse EF than would patients who did not feel nauseated. In case of continuous variables, such as age, the median value was used as a cutoff for the dichotomization. For example, we hypothesized that older patients would have a better EF than would younger patients.[19] If the median was similar to the highest or the lowest score, and thus no groups could

Table 1. Scales for the assessment of emotional functioning

The EORTC QLQ-C30 EF scale (EF4) consists of four items asking about feeling tense, worrying, feeling depressed, and being irritable.[11] The EF4 was scored using sum scoring following the EORTC scoring manual.[15]

The two-item EF version in the QLQ-C15-PAL (EF2) consists of the items about feeling depressed and feeling tense.[12] The EF2 was scored using an appendix to the EORTC scoring manual.[16]

A customized 10-item EF short form (EF10) was composed for the trial, including the original 4 QLQ-C30 items (EF4) and 6 additional items from the EORTC EF item bank.[6, 9] The EORTC EF item bank includes 24 items and is based on the response of 1023 patients from different countries. The development of the item bank has been described elsewhere in more detail.[6] The items for this study were selected by methodological and clinical experts, based on characteristics of the target population, such as age and type of cancer.[17] The selection of items based on these population characteristics is aimed at making the measure more applicable for the specific population in this study (i.e., patients with advanced cancer). Based on results of observed[6] and simulated data (currently in press) put together, asking fewer than 5 to 6 items might give notable loss in power, whereas asking more than about 14 items would give only negligible gain in power. Hence, 10 items were chosen as a good compromise between response burden and optimal measurement precision. The EF10 was scored using the item-reponse theory model model calibrated for the EORTC EF item bank.[6] The complete questionnaire is included in the Supplementary Materials found at https://doi.org/10.1016/j.jval.2018.07.002. All EF items concern the experiences "during the past week" and use a four-point response scale ranging from "not at all" to "very much".

EORTC, European Organisation for Research and Treatment of Cancer; Quality of Life Questionnaire Core 30 (QLQ-C30); Quality of Life Questionnaire Core 15 Palliative Care (QLQ-C15-PAL).

be created on the basis of median value, we calculated the mean value and used it as the cutoff to create two groups. In total, we formed 53 pairs of known groups for the comparison. The EF10, EF4, and EF2 were then each compared within these known groups (e.g., the EF10 of patients who felt nauseated vs the EF10 of patients who did not feel nauseated).

We used the two-sample *t* test (assuming equal variances) to assess significant differences between the known groups for the comparison. The RV was calculated when the *t* test for at least one of the measures being compared (EF10, EF4, or EF2) showed a significant difference ($P < 0.05$).[18] For each comparison, the *t* statistic was calculated and subsequently squared. The ratio (= RV) was calculated for each comparison by using the squared *t*-statistic of the EF10 as the numerator and the squared *t* statistic of the EF4 or the EF2 as the denominator.[6] We used the EF10 as the numerator because we wanted to evaluate the potential gain (or loss) in measurement precision and power using the customized EF scale (EF10) compared with the two existing scales (EF4 and EF2). Hence, RV > 1 would confirm the expectation that EF10 is the more precise measure. The mean RV across all characteristics or variables was calculated with a bootstrap-based 95% confidence interval.[20] A mean RV above 1 indicates that the EF10 has higher RV than the EF4 or the EF2. With increasing RV, one can expect more power gained by using the EF10. On the basis of the mean RV, we estimated the potential savings in sample size requirements using the EF10 compared with using the EF4 or the EF2.[21] See Table 2.

Known-group comparisons

The known-group comparisons were based on the following measures and characteristics.

Table 2. Example for the translation of the relative validity into a percentage of sample size reduction

Because the RV is calculated as $RV = \frac{t^2\,(EF10)}{t^2\,(EF4)}$, if RV=1.21 for the E10 vs the EF4, it means that the t test for the EF10 was ($\sqrt{1.21} = 1.1$) 1.1 times that of the EF4, or equivalent with $SD(EF10) = \frac{SD\,(EF4)}{1.1}$. We used this SD-ratio to calculate an estimate of the required sample for the EF10 compared with the EF4. As an example, if the EF4 with N = 128 had power = 80% at $\alpha = 5\%$ to detect a specific difference, then it can be calculated from the SD ratio using standard sample size calculations that the EF10 would need N = 106 to obtain the same power, or 106/128 = 83% of the sample of the EF4.
We used power = 80%, $\alpha = 5\%$, and effect size (ES) = 0.5 in the calculations. The expected savings for any combination of power and ES will be similar to those presented here, except in very extreme cases with very low power or large ES.

Sociodemographic and clinical characteristics

Patients provided information about their age, sex, marital status, whether they had children or not, educational level and religiosity. Their health care professionals provided clinical background information on the type and current stage of the disease and the time since diagnosis of both the primary tumor and the current stage of the disease. In addition, they indicated whether the patient received chemotherapy.

Quality of life and symptoms

The EORTC Quality of Life Questionnaire Core 15 Palliative Care (QLQ-C15-PAL), an abbreviated version of the EORTC QLQ-C30 for palliative care, was used to measure patients' quality of life and symptoms.[12] Fourteen items use a four-point response scale, ranging from "not at all" to "very much". The final and 15th item concerns a rating of the overall quality of life during the past week, with response options on a seven-point scale ranging from 1 "very poor" to 7 "excellent".

Coping

Patients completed three scales, that is problem-focused coping, acceptance, and avoidance (denial) COPE and brief COPE.[22, 23] The 12 questions have a four-point response scale.

Satisfaction with care

Items from the European Organization for Research and Treatment of Cancer Inpatient Satisfaction with care (EORTC IN-PATSAT) Questionnaire were used to assess patients' satisfaction with care, their appraisal of hospital doctors and nurses, and aspects of care organization and services.[24] The questions have a five-point response scale.

Experience of cancer care

The "Assessment of Patients' Experience of Cancer Care" assesses patients' perceptions of the quality of their cancer care.[25] To assess medical decision-making of the treatment and care, we selected five items measuring the quality of the medical decision-making. Responses are given on a five-point scale.

Patient involvement

We developed four questions on patient involvement in treatment and care and the awareness of relatives and physicians of the patients' wishes and preferences, which can be answered on a five-point scale.

RESULTS

Patient characteristics

Characteristics of the 1028 participants in the study are presented in Table 3. The majority of the sample was male (60%), married (70%), and living in a private household (95%). Most patients had lung cancer stage IV (45%) or colorectal cancer stage IV (29%). Most had a World Health Organization performance status of 1 (52%).

Table 3. Sociodemographic and clinical characteristics of the study sample (*N* = 1028)

Characteristic*	Value
Age (y), mean ± SD Range	65.91 ± 9.85 18-91
Sex, n (%)	
Male	592 (60.2)
Country of residence, n (%)	
Belgium	180 (18.1)
Denmark	134 (13.6)
Italy	147 (14.9)
The Netherlands	229 (23.2)
Slovenia	74 (7.5)
The United Kingdom	218 (22.1)
Civil status, n (%)	
Married, civil partnership	683 (70.1)
Divorced, separated	110 (11.3)
Widowed	96 (9.8)
Unmarried	86 (8.8)
Living with partner, n (%)	717 (74.1)
Living conditions	
Private household	915 (94.4)
Institutionary care	6 (0.6)
Other	48 (5.0)
Having children, n (%)	848 (86.8)
Education	
Years of education, mean ± SD Range	13.17 ± 4.59 0-45
Interquartile range	10.0, 13.0, 16.0
Religion, n (%)	

Table 3. Sociodemographic and clinical characteristics of the study sample (*N* = 1028) (continued)

Characteristic[*]	Value
Religious	491 (50.5)
Not-religious	353 (36.3)
Prefers not to specify	128 (13.2)
Ethnicity, n (%)	
No ethnic minority	943 (99.0)
Cancer type and current stage, n (%)	
Lung cancer (stage III or IV)	534 (57.6)
Colorectal cancer (stage IV or metachronous metastases)	393 (42.4)
Time since diagnosis in years, mean ± SD Range	1.4 ± 1.82 0-11
Time since diagnosis of current stage in years, mean ± SD Range	0.85 ± 1.16 0-9.69
Current treatment, n (%)[✝]	
Chemotherapy	301 (29.3)
Targeted therapy	866 (84.2)
Immunotherapy	897 (87.3)
Radiotherapy	921 (89.6)
WHO performance status, n (%)	
0: fully active	318 (34.4)
1: restricted in physically strenuous activity	486 (52.6)
2: ambulatory and capable of all self-care	107 (11.6)
3: capable of only limited self-care	13 (1.4)

NOTE:

[*] Missing: Age (n=11), Gender (n=6), Country of residence (n=7), Civil status (n=14), Living with partner (n=21), Living conditions (n=20), Having children (n=12), Education (n=130), Religion (n=17), Ethnicity (n=36), Cancer type and stage (n=62), WHO performance status (n=65)

✝ Several options may apply.

Relative validity

The results of the known-group comparisons of the three scales (EF10, EF4, EF2) are summarized in Table 4. The table presents the *t* statistics and the RV per known-group comparison as well as the mean RV for the comparisons of the EF10 with the EF4, the EF10 with the EF2, and the EF4 with the EF2, respectively.

Of the 53 pairs of known groups considering the EF10 and the EF4, 45 showed a statistically significant difference for at least one of the two measures. For these 45 pairs we calculated the RV for the EF10 compared with the EF4 and found that RV ranged from 0.47 to 3.71. In 41 out of the 45 (91%) comparisons, the RV was above 1, indicating that the EF10 had a higher RV than did the EF4. The mean RV for the comparison of the EF10 with the EF4 was 1.41, with a bootstrap-based 95% confidence interval of 1.28 to 1.57. Transforming this confidence interval to sample size requirements resulted in a 20% to 34% reduction in sample size without loss of power.

Table 4. Relative validity of the three scales to assess emotional functioning

Patient characteristics	Scale			Relative validity		
	EF10 *t* statistic	EF4 *t* statistic	EF2 *t* statistic	EF10 /EF4	EF10 /EF2	EF4 /EF2
Age[*]	1.43	2.09	1.54	0.47	–	1.84
Sex	3.90	3.72	4.31	1.10	0.82	0.75
Spouse[†]	–	–	–	–	–	–
Children: yes/ no[†]	–	–	–	–	–	–
Education	2.06	3.01	3.02	0.47	0.46	0.99
Religious	–4.47	–4.43	–3.81	1.02	1.38	1.35
Lung cancer vs colorectal cancer	–3.04	–2.94	–2.86	1.07	1.13	1.06
Stage[†]	–	–	–	–	–	–
Chemotherapy yes/ no[†]	–	–	–	–	–	–
Time since diagnosis	2.99	2.27	2.16	1.73	1.92	1.11
Time in stage	3.43	2.88	2.51	1.41	1.86	1.31
WHO status	4.69	3.95	4.07	1.41	1.33	0.94
Quality of life (EORTC QLQ-C15-PAL)						
Physical functioning: trouble taking a short walk	–10.69	–9.07	–8.19	1.39	1.70	1.23
Physical functioning: need to stay in bed or a chair	–8.53	-6.63	–6.43	1.65	1.76	1.06
Physical functioning: help with eating, dressing, washing	–7.34	-7.00	–6.69	1.10	1.20	1.09
Dyspnea	–8.65	-7.41	–6.66	1.36	1.68	1.24
Pain	–8.21	-8.12	–7.28	1.02	1.27	1.24
Insomnia	–8.29	-7.95	–7.76	1.09	1.14	1.05
Fatigue	–13.70	-11.04	–10.54	1.54	1.69	1.10
Lack of appetite	–11.78	-9.82	–9.29	1.44	1.61	1.12
Nausea	–10.25	-9.10	–8.77	1.27	1.37	1.08
Constipation	–5.63	-5.21	–5.54	1.17	1.03	0.88
Tiredness	–14.88	-13.20	–13.46	1.27	1.22	0.96
Interference due to pain	–11.31	-10.65	–10.42	1.13	1.18	1.04
Overall quality of life	15.41	12.80	12.51	1.45	1.52	1.05
Coping (COPE)						
Active: efforts on doing something about it	3.20	2.91	3.01	1.21	1.13	0.94
Acceptance: accepting the reality	5.44	4.65	4.47	1.37	1.48	1.08
Planning: coming up with a strategy	2.66	2.99	3.72	0.79	0.51	0.65
Active: taking action	3.34	2.92	2.90	1.31	1.33	1.01
Denial: acting as though it hasn't happened[†]	–	–	–	–	–	–
Denial: saying "this isn't real"	–3.08	–3.19	–3.42	0.94	0.81	0.87
Denial: pretending this hasn't happened [‡]	–1.84	–1.88	–1.98	–	0.86	0.90
Acceptance: learning to live with it	8.15	6.40	6.13	1.62	1.77	1.09
Planning: thinking about what steps to take[†]	–	–	–	–	–	–
Denial: refusing to believe that it has happened	–3.36	–2.78	–2.73	1.46	1.51	1.04
Acceptance: getting used to the idea	4.94	4.28	3.51	1.33	1.98	1.48
Acceptance: accepting that it has happened	4.43	3.92	3.43	1.28	1.67	1.30

Table 4. Relative validity of the three scales to assess emotional functioning (continued)

Patient characteristics	Scale			Relative validity		
	EF10 *t* statistic	EF4 *t* statistic	EF2 *t* statistic	EF10 /EF4	EF10 /EF2	EF4 /EF2
Satisfaction with care (IN-PATSAT)						
Information about illness (by doctors)	5.50	4.42	3.62	1.55	2.31	1.49
Information about medical tests (by doctors)	5.90	4.53	3.94	1.70	2.24	1.32
Information about treatment (by doctors)	5.82	4.90	3.97	1.41	2.15	1.52
Information about medical tests (by nurses)	5.79	4.88	4.68	1.41	1.53	1.09
Information about care (by nurses)	5.46	4.14	3.68	1.74	2.20	1.26
Information about treatment (by nurses)	5.94	4.83	4.27	1.51	1.93	1.28
General rating of received care	6.71	4.95	4.39	1.84	2.34	1.27
Experience of cancer care (APECC)						
Detailed discussions	6.88	5.80	5.09	1.41	1.83	1.30
Concerns/ questions	6.73	5.07	4.78	1.76	1.98	1.13
Preferred option	7.31	6.32	5.58	1.34	1.72	1.28
Work out differences	6.24	5.29	4.52	1.39	1.90	1.37
Responsible for final decision	5.34	4.36	3.58	1.50	2.22	1.48
Patient Involvement						
Friends are aware of wishes[§]	3.40	1.77	1.20	3.71	8.03	–
Doctors are aware of wishes[*]	–	–	–	–	–	–
Involvement as preferred	5.16	3.79	3.61	1.85	2.04	1.10
Great influence on care	3.65	2.26	1.97	2.60	3.43	1.32
Mean ratio				1.41	1.74	1.16
95% CI				1.28–1.57	1.48–2.10	1.11–1.26

APECC, Assessment of Patients' Experience of Cancer Care; COPE; EORTC IN-PATSAT, the European Organization for Research and Treatment of Cancer Inpatient Satisfaction with care (EORTC IN-PATSAT) Questionnaire; Quality of Life Questionnaire Core 15 Palliative Care (QLQ-C15-PAL); WHO, World Health Organization.

NOTE:

* not significant for the comparison of E10 with E2 ($P > 0.05$)
† not significant for any comparison ($P > 0.05$)
‡ not significant for the comparison of E10 with E4 ($P > 0.05$)
§ not significant for the comparison of E4 with E2 ($P > 0.05$)

When calculating the RV of the EF10 in comparison with that of the EF2, we found significant differences in EF in 45 of 53 known-group comparisons; 44 of these 45 comparisons were also significant when comparing the EF10 with the EF4. The RV was calculated for these 45 pairs and the EF10 had a higher RV than the EF2 in 40 out of 45 (89%) significant comparisons. The mean RV for the EF10 compared with that for the EF2 was 1.74 (95% CI 1.48–2.10). This would allow for a 31% to 52% reduction in sample size when using the EF10 instead of the EF2, without loss of power.

Comparison of the EF4 with the EF2 revealed higher RV of the EF4 in 36 out of 45 (80%) significant comparisons. These 45 comparisons differed from the previous comparisons (Table 4). The mean RV for the comparison of the EF4 with the EF2 was 1.16 (95% CI 1.11–1.26). Based on this confidence interval, using the EF4 instead of the EF2 would allow for a 9% to 20% reduction in sample size without loss of power.

DISCUSSION

One of the most powerful implications of using CAT is the more precise and efficient estimate of a patient's quality of life by tailoring the items to the patient's individual characteristics. The aim of this study was to compare the RV of the customized EF10 with the original validated EF4 using the method of known-groups comparison.

The results of the study confirm our hypothesis that the EF10 has a better RV compared with those of the EF4 and the EF2. This means that the EF10 has superior power to detect differences between groups, which allows for a smaller sample size to detect differences without reducing power. Ninety-one percent of the known-group comparisons indicated higher RV of the EF10 compared with the EF4, with an average RV of 1.41. This allows for a smaller sample size of about 20% to 34% when using the EF10 instead of the EF4. This indicates that clinical trials having EF as primary outcome and using the EF10 instead of the EF4 scale of the QLQ-C30 can be carried out with considerably smaller sample sizes without loss of power.

The EF10 had a higher RV in 89% of the comparisons with the EF2. We also found that the EF4 had a higher RV than did the EF2. Although this finding was expected and hypothesized when the EF2 was developed 11 years ago,[12, 26] it had not been confirmed empirically.

Mapping the quality of life of patients is important for the improvement of care and to inform treatment decisions. Quality of life is often an important outcome measure in randomized clinical trials and observational studies. The savings in sample size that can be obtained by using the customized short-form EF10 are particularly important when the study concerns a vulnerable group of patients, such as patients with advanced cancer, because the reduced required sample sizes can address the often-encountered problems with reaching target numbers in studies. Many palliative care trials have failed because of problems with recruitment.[27, 28] An additional benefit is that when fewer study participants are required while maintaining the same power, innovative findings may become ready for implementation sooner.

Using a customized short form has many benefits, yet it comes with the costs of the complex development (e.g., the creation of an item bank or the selection of items based on the samples' characteristics). Besides, although the items might lead to less missing values, because the questions are more applicable to the respondents' situation, the questionnaires tend to be somewhat longer, which is adding some burden to respondents. Therefore, as is generally the case in patient-reported outcome assessments, it is important to weigh the practical gain (i.e., increased power) of a longer, more precise measure against minimizing the burden to respondents. Note that we aimed here to improve measurement precision by adding relevant items, but customized short forms can also be used to form shorter measures if, for example, the minimum response burden has priority.

The EORTC CAT has been designed for international use in patients with cancer, and we tested it for the first time in a large sample of patients with advanced cancer in various European countries. This makes generalizability of the results possible. Another strength of this study was the high number of known-group comparisons (53 pairs, of which 45 were significant), which makes the findings robust and reduces the risk that conclusions are influenced by chance findings. In addition, we calculated the RV only when the *t* test for at least one of the measures being compared (EF10, EF4, or EF2) showed a significant difference.

Although this study used cross-sectional data, extending and replicating our approach based on longitudinal ACTION data will be possible in due course. We used the EORTC item bank on EF, which has the structure of the original QLQ-C30 scale with respect to the number of response options and phrasing of items. One might consider this a limitation in comparison to, for example, the PROMIS item banks that were developed from scratch, while aiming for the optimal way to address concepts. However, because of its design (being a new measurement system), the PROMIS item banks do not allow comparison to a pre-existing, validated instrument measuring exactly the same construct, using the same wording. Instead they need to compare the RV to alternative instruments measuring a similar construct. In our study, we were able to assess the RV of the EF10 to a validated instrument measuring exactly the same construct.

Conclusions

We found that the customized EF10 based on the EORTC CAT item bank performs better than the EF4 in detecting differences in EF between groups of patients with advanced cancer. Compared with the EF4, the EF10 showed superior power, allowing a 20% to 34% smaller sample size without reducing power, when used as a primary outcome measure.

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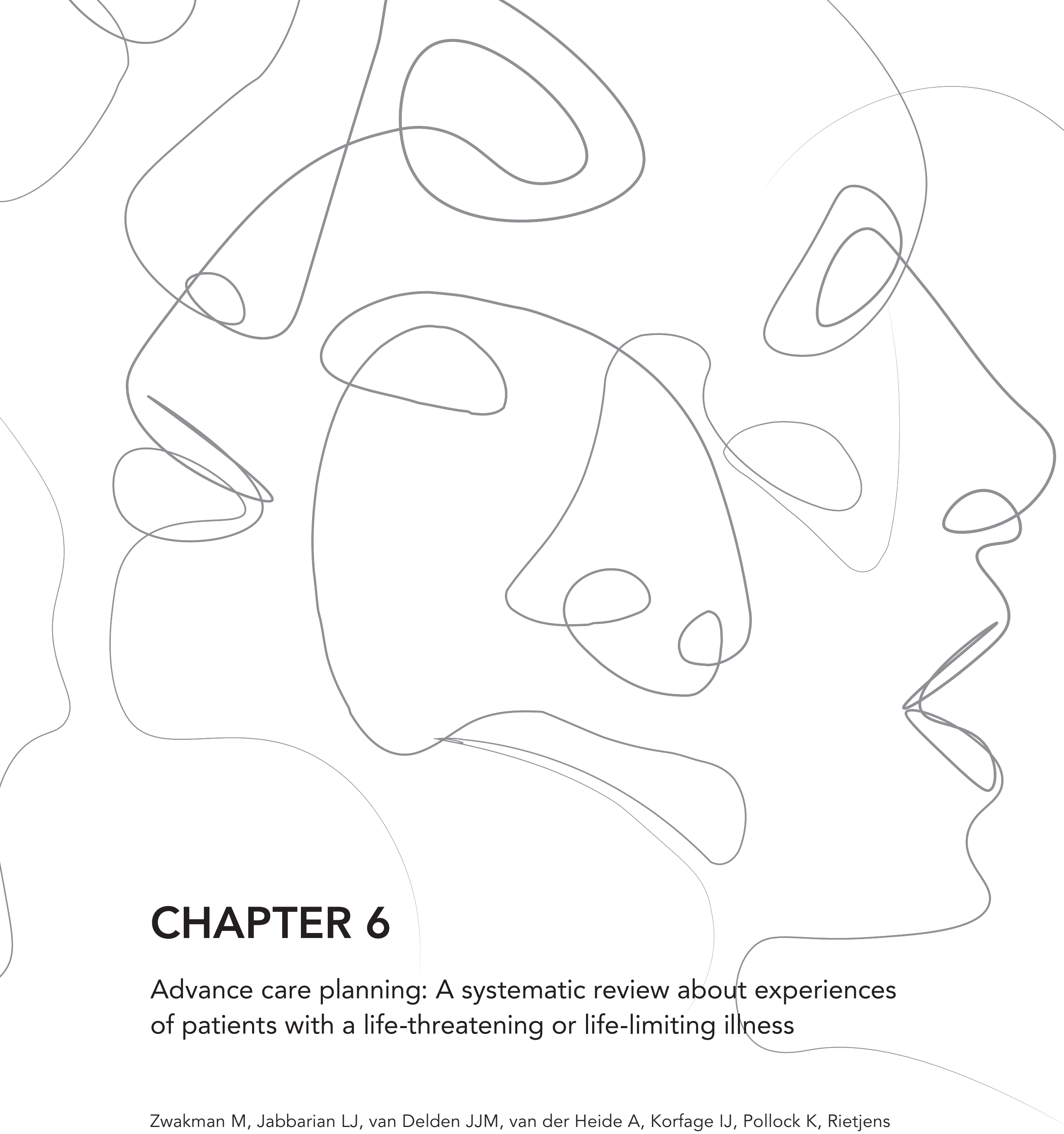

CHAPTER 6

Advance care planning: A systematic review about experiences of patients with a life-threatening or life-limiting illness

Zwakman M, Jabbarian LJ, van Delden JJM, van der Heide A, Korfage IJ, Pollock K, Rietjens JAC, Seymour J, Kars MC

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ABSTRACT

Background

Advance care planning is seen as an important strategy to improve end-of-life communication and the quality of life of patients and their relatives. However, the frequency of advance care planning conversations in practice remains low. In-depth understanding of patients' experiences with advance care planning might provide clues to optimise its value to patients and improve implementation.

Aim

To synthesise and describe the research findings on the experiences with advance care planning of patients with a life-threatening or life-limiting illness.

Design

A systematic literature review, using an iterative search strategy. A thematic synthesis was conducted and was supported by NVivo 11.

Data sources

The search was performed in MEDLINE, Embase, PsycINFO and CINAHL on 7 November 2016.

Results

Of the 3555 articles found, 20 were included. We identified three themes in patients' experiences with advance care planning. 'Ambivalence' refers to patients simultaneously experiencing benefits from advance care planning as well as unpleasant feelings. 'Readiness' for advance care planning is a necessary prerequisite for taking up its benefits but can also be promoted by the process of advance care planning itself. 'Openness' refers to patients' need to feel comfortable in being open about their preferences for future care towards relevant others.

Conclusion

Although participation in advance care planning can be accompanied by unpleasant feelings, many patients reported benefits of advance care planning as well. This suggests a need for advance care planning to be personalised in a form which is both feasible and relevant at moments suitable for the individual patient.

BACKGROUND

The growing interest in advance care planning (ACP) has resulted in a variety of ACP interventions and programmes.[1] Most definitions of ACP incorporate sharing values and preferences for medical care between the patient and healthcare professionals (HCPs), often supplemented with input from and involvement of family or informal carers. Differences are seen in whether ACP focuses only on decision-making about future medical care or also incorporates decision-making for current medical care. Furthermore, there are different interpretations about for whom ACP is valuable, ranging from the general population towards a more narrow focus on patients at the end of their lives.[2–5] A well-established definition of ACP is presented in Box 1.[3]

Box 1.
ACP refers to the whole process of discussion of end-oflife care, clarification of related values and goals, and embodiment of preferences through written documents and medical orders. This process can start at any time and be revisited periodically, but it becomes more focused as health status changes. Ideally, these conversations occur with a person's health care agent and primary clinician, along with other members of the clinical team; are recorded and updated as needed; and allow for flexible decision making in the context of the patient's current medical situation.[3]

ACP is widely viewed as an important strategy to improve end-of-life communication between patients and their HCPs and to reach concordance between preferred and delivered care.[6–8] Moreover, there is a high expectation that ACP will improve the quality of life of patients as well as their relatives as it might decrease concerns about the future.[1] Other potential benefits, which have been reported, are that ACP allows patients to maintain a sense of control, that patients experience peace of mind and that ACP enables patients to talk about end-of-life topics with family and friends.[9–13]

Despite evidence on the positive effects of ACP, the frequency of ACP conversations between patients and HCPs remains low in clinical practice.[14–18] This can partly be explained by patient-related barriers.[9,11,13,19,20] Patients, for instance, indicate a reluctance to participate in ACP conversations because they fear being confronted with their approaching death; they worry about unnecessarily burdening their families and they feel unable to plan for the future.[9,11,13,19,20] In addition, starting ACP too early may provoke fear and distress.[21] However, current knowledge of barriers to ACP is initially derived from patients' responses to hypothetical scenarios or from studies in which it remains unclear whether patients really had participated in such a conversation.[9,11,13,15,19,20] More recent research has shifted towards studies on the experiences of patients who actually took part in an ACP conversation. These studies can give a more realistic perspective and a better understanding of the patients' position when having these conversations.

To our knowledge, there is only one review that summarises the perceptions of stakeholders involved in ACP and which includes some patients' experiences. However, this review is limited to oncology.[21] Given the fact that ACP may be of particular value for patients with a progressive disease due to the unpredictable but evident risk of deterioration and dying,[2,22,23] this study focuses on the experiences of the broader population of patients with a life-threatening or life-limiting disease with ACP.

We aim to perform a systematic literature review to synthesise and describe the research findings concerning the experiences of patients with a life-threatening or life-limiting illness who participated in ACP. Our analysis provides an indepth understanding of ACP from the patients' perspective and might provide clues to optimise its value to patients.

METHOD

Design

A systematic literature search was conducted, the analysis relying on the method of thematic synthesis in a systematic review.[24]

Search strategy

In collaboration with the Dutch Cochrane centre, we used a recently developed approach that is particularly suited to systematically review the literature in fields that are challenged by heterogeneity in daily practice and poorly defined concepts and keywords, such as the field of palliative care.[25] The literature search strategy consisted of an iterative method. This method has, like all systematic reviews, three components: formulating the review question; performing the literature search and selecting eligible articles. The literature search, however, consists of combining different information retrieval techniques such as contacting experts, a focused initial search, pearl growing[26,27] and citation tracking.[25,27] These techniques are repeated throughout the process and are interconnected through a recurrent process of validation with the use of so-called 'golden bullets'. 'Golden bullets' are articles that undoubtedly should be part of the review and are identified by the research team in the first phase of the search (phase question formulating). These 'golden bullets' are used to guide the development of the search string and to validate the search.

First, we undertook an initial search in PubMed and asked an internationally composed set of experts, who are actively involved in research and practice of ACP (n = 33) to provide articles that in their opinion, should be part of this review. These articles were used to refine the eligibility criteria. Based on these refined criteria, the 'golden bullets' (n = 7)[28–34] were selected from the articles identified from the initial search and by the experts. Second, the analysis of words used in the title, abstract and index terms of the 'golden bullets' were used to improve the search string. A new search was then conducted. The validation of this search was carried out by identifying whether all the 'golden bullets' were retrieved in this search. Not all 'golden bullets' could be identified in the retrieved citations after this first search. Therefore, the search string was adjusted several times and the process of searching and validation was repeated until the validation test was successful.

Once the validation test was successful, the final search was carried out on 7 November 2016 using four databases namely MEDLINE (Ovid), Embase Classic & Embase, PsycINFO (Ovid) and CINAHL (EBSCOhost) (see Table 1 for search terms). Finally, the reference list of all included articles was cross referenced in order to identify additional relevant articles.

Table 1. Database search and strategy

Database	Keywords
MEDLINE (Ovid)	((qualitative or focus group* or case stud* or field stud* or interview* or questionnaire* or survey* or ethnograph* or grounded theory or action research or 'participant observation' or narrative* or (life and (history or stor*)) or verbal interaction* or discourse analysis or narrative analysis or social construct* or purposive sampl* or phenomenol* or criterion sampl* or 'story telling' or (case adj (study or studies)) or 'factor analysis' or 'self-report').ti,ab,kf. OR (conversation adj2 analys*).ti,ab,kf. OR qualitative research/ or exp questionnaire/ or self report/ or health care survey/ or 'nursing methodology research'/ or 'Interviews as Topic'/) AND (exp advance care planning/ OR ((advance adj preferences) or 'advance care planning' or advance directive* or living will* or end-of-life planning or (future care adj3 planning)).ti,ab,kf.)
Embase Classic & Embase	(qualitative or focus group$ or case stud$ or field stud$ or interview$ or questionnaire$ or survey$ or ethnograph$ or grounded theory or action research or 'participant observation' or narrative$ or (life and (history or stor$)) or verbal interaction$ or discourse analysis or narrative analysis or social construct$ or purposive sampl$ or phenomenol$ or criterion sampl$ or 'story telling' or (case adj (study or studies)) or 'factor analysis' or 'self-report' or (conversation adj2 analys*)).ti,ab,kw,hw. exp qualitative research/data collection method/ or exp interview/ or exp questionnaire/ health care survey/self-report/nursing methodology research/exp ethnography/discourse analysis/((advance adj preferences) or 'advance care planning' or advance directive* or living will* or end-of-life planning or (future care adj3 planning)).ti,ab,kw,hw.
PsycINFO (Ovid)	(qualitative or focus group$ or case stud$ or field stud$ or interview$ or questionnaire$ or survey$ or ethnograph$ or grounded theory or action research or 'participant observation' or narrative$ or (life and (history or stor$)) or verbal interaction$ or discourse analysis or narrative analysis or social construct$ or purposive sampl$ or phenomenol$ or criterion sampl$ or 'story telling' or (case adj (study or studies)) or 'factor analysis' or 'self-report' or (conversation adj2 analys*)).ti,ab,id,hw. 'Consumer Opinion & Attitude Testing'.cw. exp Questionnaires/exp Self Report/exp Surveys/exp Ethnography/exp Grounded theory/exp Phenomenology/ qualitative research/ or exp interviews/ or observation methods/((advance adj preferences) or 'advance care planning' or advance directive* or living will* or end-of-life planning or (future care adj3 planning)).ti,ab,hw,id.
Cinahl search (EBSCOhost)	SU ((qualitative or focus group* or case stud* or field stud* or interview* or questionnaire* or survey* or ethnograph* or grounded theory or action research or 'participant observation' or narrative* or (life and (history or stor*)) or verbal interaction* or discourse analysis or narrative analysis or social construct* or purposive sampl* or phenomenol* or criterion sampl* or 'story telling' or (case N1 (study or studies)) or 'factor analysis' or 'self-report') OR (conversation N2 analys*)) AB ((qualitative or focus group* or case stud* or field stud* or interview* or questionnaire* or survey* or ethnograph* or grounded theory or action research or 'participant observation' or narrative* or (life and (history or stor*)) or verbal interaction* or discourse analysis or narrative analysis or social construct* or purposive sampl* or phenomenol* or criterion sampl* or 'story telling' or (case N1 (study or studies)) or 'factor analysis' or 'self-report') OR (conversation N2 analys*)) TI ((qualitative or focus group* or case stud* or field stud* or interview* or questionnaire* or survey* or ethnograph* or grounded theory or action research or 'participant observation' or narrative* or (life and (history or stor*)) or verbal interaction* or discourse analysis or narrative analysis or social construct* or purposive sampl* or phenomenol* or criterion sampl* or 'story telling' or (case N1 (study or studies)) or 'factor analysis' or 'self-report') OR (conversation N2 analys*)) (MH 'Qualitative Studies +')(MH 'Clinical Assessment Tools +') OR (MH 'Questionnaires +') OR (MH 'Interview Guides +')(MH 'Surveys')(MH 'Interviews +')(MH 'Self Report')(MH 'Advance Care Planning') TI((advance adj preferences) or 'advance care planning' or advance directive* or living will* or end-of-life planning or (future care N3 planning)) AB((advance adj preferences) or 'advance care planning' or advance directive* or living will* or end-of-life planning or (future care N3 planning)) SU((advance adj preferences) or 'advance care planning' or advance directive* or living will* or end-of-life planning or (future care N3 planning)) excluding MEDLINE records

Inclusion and exclusion criteria

Papers were included based on the following inclusion criteria: the study must be an original empirical study; published in English; it must concern patients diagnosed with a life-threatening (illnesses for which curative treatment may be feasible but can fail)[35] or a life-limiting illness (illnesses for which there is no reasonable hope of cure)[36] and report experiences of patients who actually participated in ACP. We considered an activity to be ACP when it concerned a conversation which at least aimed at clarifying patients' preferences, values and/or goals for future medical care and treatment. This conversation could have been conducted either by an HCP, irrespective of whether they were involved in the regular care for that particular patient or by persons who are not directly related to the patients' care setting.

Studies reporting the experiences of multiple actors were excluded when the patients' experiences could not be clearly distinguished. Studies in which only a part of the respondents had participated in ACP were also excluded when their experiences could not be distinguished from those patients who did not participate in ACP. Because of the difficulty of assessing the level of competence of the respondents, it was decided to exclude studies focusing on children aged under 18 and patients with dementia or a psychiatric illness.

Search outcomes

We identified 3555 unique papers. Two researchers (M.Z., L.J.J.) independently selected studies eligible for review based on the title and abstract using the inclusion criteria. Thereafter, the full text of the remaining studies (n = 80) was reviewed (M.Z., L.J.J.). The researchers discussed any disagreements until they achieved consensus. Remaining disagreements were resolved in consultation with a third researcher (M.C.K.). Finally, 20 articles were found to meet the inclusion criteria (Figure 1). The web-based software platform Covidence supported the selection process.[37]

Quality assessment

The methodological quality of the qualitative studies was assessed using the Critical Appraisal Skills Programme (CASP) checklist,[38] a commonly used tool in qualitative evidence syntheses.[39] The CASP checklist consists of 10 questions covering the aim, methodology, design, recruitment strategy, data collection, relationship between researcher and participants, ethical issues, data analysis, findings and value of the study.[38] A 'yes' was assigned when the criterion had been properly described (score 1), a 'no' when it was not described (score 0) and a 'can't tell' when the report was unclear or incomplete (score 0.5). Total scores were counted ranging from 0 to 10. We considered a score of at least 7 as indicating satisfying quality.

The methodological quality of mixed-method studies was assessed using the multi-method assessment tool developed by Hawker et al.[40] This tool consists of nine categories: abstract and title; introduction and aims; method and data; sampling; data analysis; ethics and bias; results; transferability or generalisability; and implications. Each category was scored on a 4-point scale,

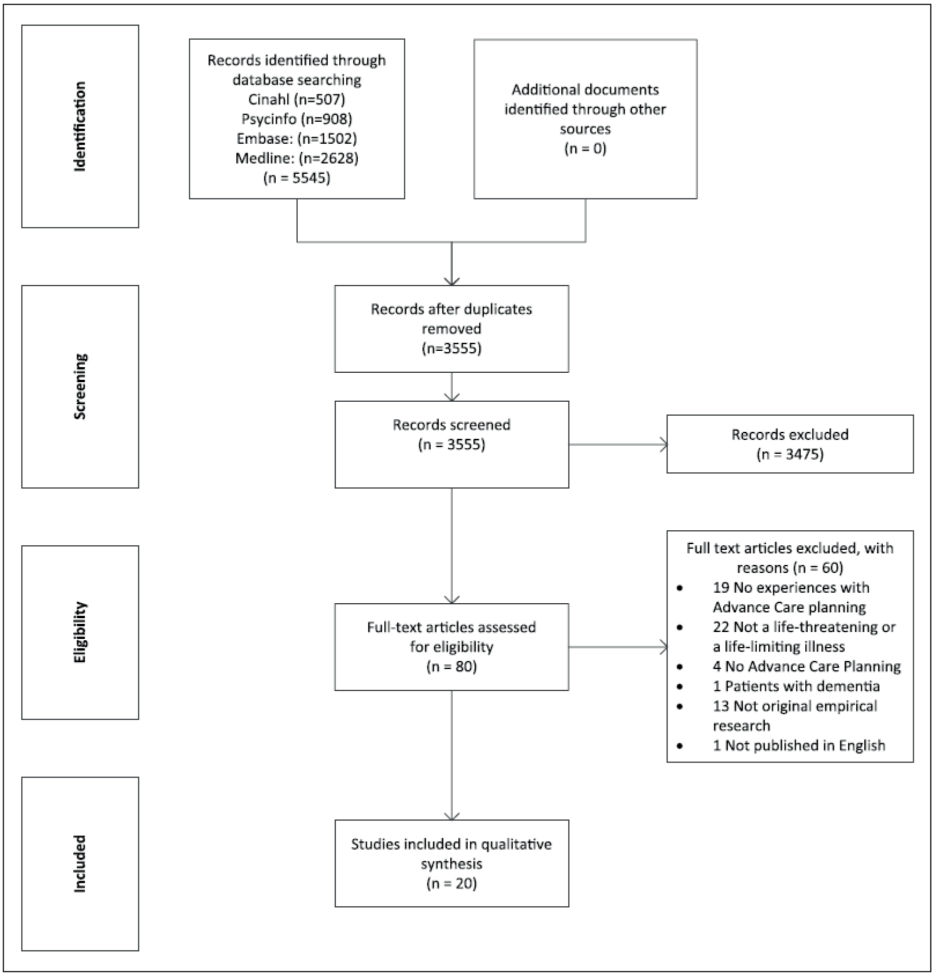

Figure 1. Flow diagram illustrating the inclusion of articles for this review.

ranging from 1–4, resulting in a total score from 9 (very poor) to 36 (good). We consider a score of at least 27 (=fair) as indicating satisfactory quality.

Two authors (M.Z., L.J.J.) independently assessed all included articles. Discrepancies were encountered in 33 of the 190 items assessed with the CASP and in 3 of the 9 items assessed with the Hawker scale. These were resolved by discussion.

The mean score of the methodological quality of the qualitative studies[28–34,41–52], according to the CASP, was 8 out of 10 (range: 6.5–9.5). Main issues concerned limitations describing ethical issues[30,33,34,41–45,47,49,51,52] and the lack of information concerning the relationship between researchers and respondents[28–30,32–34,41,42,44,46–50,52] (Table 2). The quality of the mixed-method study[53] was 29 (out of 36) according to the scale of Hawker (Table 3).[40] Points were in particular lost in the categories 'method and data' and 'data analysis'.

The appraisal scores are meant to provide insights into the methodological quality of the included studies. They were not used to exclude articles from the systematic review because a qualitative article with a low score could still provide valuable insights and thus be highly relevant to the study aim.[54,55]

Table 2. Quality assessment CASP

	Aim	Methodology	Design	Recruitment	Data Collection	Relationship	Ethical	Data analysis	Finding	Values	Score
Abdul-Razzak et al.[28]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Valuable	9
Almack et al.[29]	Yes	Yes	Yes	Yes	Can't tell	No	Yes	Can't tell	Yes	Valuable	8
Andreassen et al.[41]	Yes	Yes	Yes	Can't tell	Can't tell	No	Can't tell	Can't tell	Yes	Valuable	7
Bakitas et al.[42]	Yes	Yes	Yes	Can't tell	Can't tell	No	Can't tell	Yes	Yes	Valuable	7.5
Barnes et al.[43]	Yes	Yes	Yes	Can't tell	Yes	Yes	Can't tell	Can't tell	Yes	Valuable	8.5
Brown et al.[44]	Yes	Yes	Can't tell	Yes	Can't tell	No	Can't tell	Can't tell	Yes	Valuable	7
Burchardi et al.[45]	Yes	Yes	Yes	Can't tell	Yes	No	Can't tell	Can't tell	Yes	Valuable	8.5
Burge et al.[30]	Yes	Yes	Yes	Can't tell	Can't tell	No	Can't tell	Yes	Yes	Valuable	7.5
Chen and Habermann[46]	Yes	Yes	Can't tell	Yes	Yes	No	No	Yes	Yes	Valuable	7.5
Epstein et al.[47]	Yes	Yes	Yes	Yes	Yes	No	Can't tell	Yes	Yes	Valuable	8.5
Horne et al.[32]	Yes	Yes	Yes	Yes	Can't tell	No	Yes	Can't tell	Yes	Valuable	8
MacPherson et al.[31]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Valuable	9.5
Martin et al.[34]	Yes	Yes	Yes	Yes	Yes	No	Can't tell	Yes	Yes	Valuable	8.5
Metzger et al.[48]	Yes	Yes	Yes	Can't tell	Yes	No	Yes	Can't tell	Yes	Valuable	8
Robinson[49]	Yes	Yes	Can't tell	Can't tell	Can't tell	No	Can't tell	Can't tell	Yes	Valuable	6.5
Sanders et al.[50]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Valuable	9
Simon et al.[51]	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Valuable	9
Simpson[52]	Yes	Yes	Yes	Can't tell	Can't tell	No	Can't tell	No	Yes	Valuable	6.5
Singer et al.[33]	Yes	Yes	Yes	Yes	Can't tell	No	Can't tell	Yes	Yes	Valuable	8

Table 3. Quality assessment Hawker

	Michael, et al.[53]
Abstract and title	3
Introduction and aims	3
Method and data	3
Sampling	4
Data analysis	3
Ethics and bias	3
Results	3
Transferability or generalisability	4
Implications and usefulness	3
Total	29

4: Good; 3: fair; 2: poor; 1: very poor.

Data extraction and analysis

To achieve the aim of this systematic review, information was extracted on general study characteristics and the patients' experiences and responses (Table 4). To provide context and to facilitate the interpretation of the results, the number of patients refusing participation in the study and the number of dropouts were identified, as well as the underlying reasons. This process was undertaken and discussed by two authors (M.Z., L.J.J.). Disagreements remained on three papers[28,31,46] and were resolved in discussion with a third author (M.C.K.).

The thematic synthesis consisted of three stages.[24] By using the software program for qualitative analysis, NVivo 11, a transparent link between the text of the primary studies and the findings was created. First, the relevant fragments, with respect to the focus of this systematic review, were identified and coded. Second, the initial codes were clustered into categories and the content of these clusters was described. Finally, the analytical themes were generated.[24] This analysis was performed by the first author (M.Z.) in collaboration with the last author (M.C.K.).

RESULTS

Study characteristics

Of the 20 articles selected,[28-34,41-53] 19 had a qualitative study design [28-34,41-52] and one a mixed-methods design.[53] All included studies were conducted in Western countries, mostly in Canada (n=6) (Table 4).[28,33,34,49,51,52] The studies included patients with cancer[28,29,32,42,43,47,49,53] as well as patients with other life-threatening or life-limiting illnesses (e.g. chronic obstructive pulmonary disease (COPD)[31,44,52] human immunodeficiency virus (HIV)[34,50] amyotrophic lateral sclerosis (ALS))[45] (Table 4).[28-31,33,34,41,43,44,46,48-52] Most studies reported the experiences of patients in an advanced stage of their illness.[28,29,32,41-44,46-49,51-53] A total of 14 studies reported patients' experiences with an ACP intervention in a research context,[30,32-34,41-43,47-53] the remaining six articles focused on ACP experiences in daily practice (Table 4).[28,29,31,44-46] The studies labelled the conversations as ACP conversations [29-34,41-53] (n=19) or as end-of-life conversations (n=1).[28]

Eight studies reported the number of refusals and/or the reasons why patients refused to participate in the study.[30,31,33,34,42,45,51,53] The total number of eligible patients in these eight studies was 579 of which 206 patients refused to participate. Patients refused for 'practical' reasons (n=44)[30,42] or felt too ill to participate (n=42).[33,34,53] Other reasons concerned logistics (e.g. could not be reached by phone:n=42)[33,42,45,51,53] and some patients (n=25) died during the period of recruitment.[33, 34, 45] Eleven patients (5%) were reported to have refused because they felt not ready to participate or were too upset by the word "palliative".[31,53] The number of dropouts remained unclear. Three studies reported reasons for drop-out[29,33,41] showing that some patients were too disturbed by the topic to proceed with ACP.[33] One patient reported feeling better and was, therefore, reluctant to follow-up the end-of-life conversation.[29]

Table 4. Extraction data form

Reference	**Country**	**Aim**	**Method**	**Sample**	**Intervention/ setting**	**Data collection**	**Findings**
Abdul-Razzak et al.[28]	CA	To understand patient perspectives on physician behaviours during EOL communication.	Qualitative study	Seriously ill hospitalized patients (cancer and non-cancer) with an estimated 6-12 month mortality risk of 50% (*n*=16)	Experiences with EOL communication in regular care, including ACP, in the moment decision-making and related information sharing processes.	Semi-structured face-to-face interviews	Two types of HCP behavior were felt to be beneficial during EOL communication. (1) 'Knowing me' relates to the importance of the family involvement during the EOL conversation by the HCP and the social relationship between the patient and the HCP. (2) 'Conditional candour', relates to the process of information sharing between the HCP and the patient including an assessment of the patients' readiness to participate in an EOL conversation.
Almack et al.[29]	UK	To explore the factors influencing if, when and how ACP takes place between HCP's, patients and family members from the perspectives of all parties involved and how such preferences are discussed and are recorded.	Qualitative study	Patients from palliative care register (cancer and non-cancer) and who were expected to die in the next year according to the HCP (*n*=18)	Experiences with ACP in regular care (focus on Preferred Place of Care tool).	Semi-structured face-to-face interviews	Nine out of 13 cancer patients had a degree of open awareness of which three patients had some preferences recorded in a written document. A few patients had initial conversations about future plans, but did not revisit these over time. When a HCP initiated an EOL conversation, patients wondered if they were close to dying. Patients who felt relatively better, were reluctant to participate in an ACP conversation.
Andreassen et al.[41]	DK	To explore nuances in long-term impact of ACP as experienced by patients and relatives.	Qualitative study	Patients with a life-limited disease (*n*=3) and relatives (*n*=7)	An ACP discussion in research context	Semi-structured face-to-face and phone interviews	ACP impacted patients and relatives in three ways. (1) Positive impact, such as better communication; awareness of dying and empowerment. (2) No impact, described as ACP being insignificant and not relevant yet. (3) Negative impact, less communication about the EOL.
Bakitas et al., [42]	USA	To elicit patient and caregiver participants' feedback on the clarity and overall usefulness of the commercially available PtDA when introduced soon after a new diagnosis of advanced cancer.	Qualitative study	Patients with an advanced solid tumor or hematological malignancy (prognosis between 6 and 24 months) (*n*=57 patients, *n*=20 caregivers)	Looking ahead: Choices for Medical Care When You're seriously Ill patient decision aid (PtDA).	Semi-structured phone interviews	Patients who participated in the programme 'Looking ahead' felt empowered, informed and 'in charge'. Patients needed to be ready to participate in this programme. Some patients had felt not ready before the start, but in hindsight mentioned that it was the right time. After the programme some patients started to talk with their healthcare proxy or their HCP.

Table 4. Extraction data form (continued)

Reference	Country	Aim	Method	Sample	Intervention/ setting	Data collection	Findings
Barness et al.[43]	UK	To inform the nature and timing of an ACP discussion intervention delivered by an independent trained mediator.	Qualitative study	Patients with clinically detectable, progressive disease (*n*=40)	An ACP intervention: ACP discussions with a trained planning mediator using a standardized topic guide. All patients received up to three sessions.	Verbatim transcripted audio-tapes of the face-to-face ACP intervention.	A third of the patients said the ACP discussion had been helpful and thought-provoking. Many patients found the information valuable and some found it challenging to think about dying. A few patients talked with their family about their future, some patients did not want to burden or upset their relatives and others were not yet ready to discuss this topic with family or the HCP. Over a third of the patients said their doctors were reluctant to introduce such topics.
Brown et al.[44]	AU	To explore issues relating to EOL decisions and ACP	Qualitative study	Patients with advance COPD (GOLD stage IV) (*n*=15)	Experiences in regular care with ADs and ACP in regular care.	Semi-structured face-to-face interviews	Two of the 15 patients had conversations with their HCP about CPR. One couple completed an AD and was well informed about future decision-making. Some patients talked with their family about their wishes and appointed a decision-maker. Others did not because of the feeling that the family would feel uncomfortable to make a decision.
Burchardi et al.[45]	DE	To investigate how neurologists provide information about LWs to ALS patients and to explore if their method of discussing it met the patients' needs and expectations.	Qualitative grounded theory study	ALS patients (*n*=15)	Experiences with LW in regular care.	Semi-structured face-to-face interviews	Six out of 15 ALS patients completed a LW, mostly after symptoms had worsened. Patients described ADs as important and necessary, but they also considered ADs as closely connected to forthcoming death. The patients preferred information given in a way that would minimise the anxiety. Some patients felt that a LW is contrary with the work of a HCPs. Family involvement was by some described as a process of discussion and coping, which led to completing a LW. Others only gave a copy of the LW.
Burge et al.[30]	AU	To evaluate the introduction of a structured ACP information session from the perspective of participants in PR&M programmes.	Qualitative study	Patients having chronic respiratory impairment, in PR&M (*n*=67).	A structured group ACP information session presented by two trained facilitators.	Semi-structured face-to-face Interviews	Seventeen patients described the PR&M programme as an appropriate place to receive information about ACP. Participants valued the received information and highlighted the importance of the educator. Twenty-four patients started to think about their personal decision-making and initiated a discussion with family members.

Table 4. Extraction data form (continued)

Reference	Country	Aim	Method	Sample	Intervention/ setting	Data collection	Findings
Chen and Habermann, 2013[46]	USA	To explore how couples living with advanced MS approach planning for future health changes together.	Qualitative study	Patients with advanced MS and their care-giver spouses (*n*=20)	Experiences with ACP among couples	Semi-structured face-to-face interviews	Three out of 10 couples with advanced MS had an AD or LW and communicated their wishes to their loved ones. These MS couples felt confident in knowing each other's wishes. Most couples had some thoughts about aspects of ACP, but had not a written AD. Expressed difficulties were to make a choice, communication and the hope for a cure.
Epstein et al.[47]	USA	To better understand the more general problem, and potential solutions to, barriers to communicate about EOL care.	Qualitative study	Patients with advanced hepatopancreatico-biliary cancers (*n*=54) (*n*=26 articulated questions or/ and comments)	One-time educational video or narrative about CPR.	Face-to-face open interview following the intervention.	Video education was seen by patients as an appropriate means of starting an ACP conversation. ACP should start early because, it is better to discuss these topics when you are reasonably healthy. Patients found ACP sometimes difficult to discuss, but they considered it as important. The information was helpful and HCPs should be involved in ACP in order to realize life goals and to plan practically.
Horne et al.[32]	UK	To develop and pilot an ACP intervention for lung cancer nurses to use in discussing EOL preferences and choices for care with patients diagnosed with inoperable lung cancer.	Qualitative grounded theory study	Patients with inoperable lung cancer (*n*= 9) and their family members (*n*=6)	An ACP discussion with a trained lung cancer nurse using an ACP interview guide, an ACP record and an ACP checklist.	Semi-structured face-to-face Interviews	Most participants reported that they felt better after the ACP discussion. Nursing attributes enabled patients to talk about EOL issues. Some patients found it a 'personal thing' to discuss ACP with the nurse. Patients appreciated the information they received and accepted the recording of their preferences. These were shared with the HCP and sometimes with family.
MacPherson et al.[31]	UK	To answer whether people with COPD think that ACP could be a useful part of their care, and to explore their reasoning behind this view, as well as their thoughts about future and any discussions about future care that had taken place.	Qualitative grounded theory study	Patients with severe COPD (*n*=10) of these two respondents reported experiences with ACP	Experiences with ACP in regular care.	Semi-structured face-to-face interviews	2 out of 10 patients reported some discussion about future care. These discussions initially upset them. This was caused by being unfamiliar with ACP and the exploration of the patient's prognosis led the patient to think more about mortality. Patients felt uncomfortable documenting their wishes.

Table 4. Extraction data form (continued)

Reference	Country	Aim	Method	Sample	Intervention/ setting	Data collection	Findings
Martin et al.[34]	CA	To develop a conceptual model of ACP by examining the perspectives of individuals engaged in it.	Qualitative grounded theory study	Patients with HIV or AIDS (n=140)	An educational video with a generic Centre for bioethics LW or the disease-specific HIV LW or both ADs.	Semi-structured face-to-face Interviews	ACP was seen as confronting, but helpful. It helped patients to prepare to face death and helped them to confront and to accept the prospect of their death. Patients mentioned that they learned more about themselves and achieved feelings of "peace". Both ACP and an AD provided a language and framework that can help to organise patients' thoughts about their preferences for care, thus enabling a degree of control. ACP strengthened relationships with patients' loved ones.
Metzger et al.[48]	USA	To increase the understanding of patients' and surrogates' experiences of engaging in ACP discussions, specifically how and why these discussions may benefit patients with LVADs and their families.	Qualitative study	Patients with a LVAD (n=14) and their surrogates (n=14)	An ACP intervention: SPIRIT-HF	Semi-structured phone interviews	Three themes were identified. (1) Nearly all patients reported that sharing their Heart Failure stories was a positive and essential part of SPIRIT-HF. (2) SPIRIT-HF brought patients an increased peace of mind. It allowed patients to clarify their wishes which created a feeling of being more prepared for the future. (3) ACP discussions should be an individual approach, the best timing may vary.
Michael et al.[53]	AU	To assess the feasibility and acceptability of an ACP intervention.	Mixed methods study (Qualitative grounded theory study)	Patients with cancer stage III/IV (n=30)	A 5-step guided ACP intervention	Questionnaire and semi-structured face-to-face interviews	This ACP intervention may motivate participants to consider thoughts about their future health care. Many patients said that the intervention helped them to feel respected, heard, valued, empowered, and relieved. The intervention was both informative and distressing. Most patients welcomed the opportunity to involve their family during this conversation. A barrier to complete a written document was, e.g., not feeling ready.
Robinson, 2011[49]	CA	To explore the applicability and usefulness of a promising ACP intervention and examined the ACP process.	Qualitative study	Patients newly diagnosed with advanced lung cancer (n=18) and their loved one.	RC tool	Semi-structured face-to-face Interviews	The RC tool was addressed as difficult, but helpful. ACP is a family affair. Patients wanted to avoid burdening their family and they felt safe knowing that their wishes were clearly understood by a trusted loved one. ACP brought an enhanced sense of closeness. None of the patients had involved a HCP.

Table 4. Extraction data form (continued)

Reference	Country	Aim	Method	Sample	Intervention/ setting	Data collection	Findings
Sanders et al.[50]	UK	To examine the impact of incorporating the subject of planning for death and dying within self-management intervention.	Qualitative study	Patients with a long term health condition (n=31) and patients with HIV (n= 12)	Education group session about ACP within a much wider generic 'expert patient' course designed to teach people how to manage a long term health condition.	Semi-structured Interviews	A group educational session is a valuable form of social support. However, the session about LWs was disruptive and the introduction of the educational material was confrontational. One patient said it was traumatic, but relevant. Some patients thought that talking about LWs would be more acceptable for older people with chronic conditions or people with a terminal illness.
Simon et al.[51]	CA	To explore and understand what it is like to go through an ACP process as a patient.	Qualitative grounded theory study	Patients with end-stage renal disease who had completed a health region quality initiative, pilot project of facilitated ACP (n=6)	RC tool	Semi-structured face-to-face interviews	Patients addressed ACP as logical. One patient described an initial shock when being invited. One felt it was: "a positive thing: peace of mind" which contained three categories.(1) Witnessing an illness in oneself or in others and acknowledging mortality; (2) I don't want to live like that or to be a burden to oneself or others; and (3) the process. The awareness of the EOL allowed patients to participate in ACP, the workbook was viewed as central to discussions and the facilitator was seen as a paperwork reviewer. Some patients initiated a discussion with a HCP.
Simpson[52]	CA	To give insight in what is required for a meaningful, acceptable advance care planning in the context of advance COPD.	Qualitative research methodology	Patients with a primary diagnosis of COPD in an advance stage (n=8) and their informal caregivers (n=7)	Loosely structured conversations with the help of the brochure 'Patient and Family Education Document,: Let's Talk About ADs including an AD template.	An open interview	Despite the initial resistance of patients to participate in the ACP conversation positive outcomes of ACP occurred. ACP with a facilitator was an opportunity to learn about several factors. These included: the options for EOL care; considering or documenting EOL care preferences so the decision-maker would offer tangible guidance; countering the silence around the EOL through social interaction; and sharing concerns about their illness with the HCP.

Table 4. Extraction data form (continued)

Reference	Country	Aim	Method	Sample	Intervention/ setting	Data collection	Findings
Singer et al.[33]	CA	To examine the traditional academic assumptions by exploring ACP from the perspective of patients actively participating in the planning process.	Qualitative grounded theory study	Patients who are undergoing hemodialysis (*n*=48)	An educational video about ADs and patients receive an AD form.	Semi-structured face-to-face Interviews	Through the use of open communication, ACP is a helpful means of preparing for incapacity and death. Resulting in peace of mind. The awareness of life's frailty allowed patients to participate in ACP. ACP is based on autonomy, maintaining control and relieve of the burden on the loved ones. The result of ACP is not simply to complete an AD; the discussion about the patient's wishes is also meaningful in itself.

Abbreviations

ACP: Advance Care Planning; AD: Advance Directive; AIDS: acquired immunodeficiency syndrome; ALS: Amyotrophic Lateral Sclerosis; AU: Australia; CA: Canada; COPD: Chronic Obstructive Pulmonary Disease; CPR: Cardiopulmonary resuscitation; DE: Germany; DK; Denmark; EOL: end-of-life; GOLD: Global Initiative for Obstructive Lung Disease; HCP: Health Care Professional; HIV: Human immunodeficiency virus; PtDA: Patient Decision Aid; LVAD: a Left Ventricular Assist Devices; LW: Living Wills; MS: multiple sclerosis; PR&M: Pulmonary Rehabilitation and Maintenance; PtDA: Looking Ahead Patient Decision Aids; RC: Respecting Choices; SPIRIT-HF: 'Sharing the Patient's Illness Representations to Increase Trust in Heart Failure'; UK: United Kingdom

Synthesis of results

Three different, but closely related, main themes were identified which reflected the experiences of patients with ACP conversations namely: 'ambivalence', 'readiness' and 'openness'. Themes, subordinated themes and subthemes, are presented in Table 5. 'Ambivalence' was identified in 18 studies[28-34,41-43,45,47-53] and 'readiness' in 18 studies.[28-34,42-48,50-53] The theme 'openness' was found in all studies.

Table 5. Themes

Main theme	Subordinate theme	Subtheme
Ambivalence		
	Positive aspects	
		Receiving information
		Being in control
		Thinking about end of life
		Learning
		Confrontation
	Unpleasant feelings	
		It's not easy to talk about
		Confrontation
	Possible solution	
		Group session
Readiness		
	Being ready	
		Readiness is needed for ACP to be useful
	Not being ready	
		Invitation
		Resistance in advance
		In hindsight pleased
	Documentation	
	Timing of ACP	
		Assess readiness
Openness		
	Positive aspects	
		Relatives: Enables to become a surrogate decision-maker
		Relatives: Actively engage family in the ACP process
	Difficulties	
		Relatives: Feeling uncomfortable to be open
		HCP: Feeling uncomfortable to be open
	Overcoming difficulties	
		Attitude facilitator

ACP: advance care planning; HCP: healthcare professional.

Ambivalence

Several studies reported the patients' ambivalence when involved in ACP. From the invitation to participate in an ACP conversation to the completion of a written ACP document, patients simultaneously experienced positive as well as unpleasant feelings. Such ambivalence was identified as a key issue in five studies.[34,43,47,49,53] Irrespective of whether the illness was in advanced stage, patients reported ACP to be informative and helpful in the trajectory of their illness, while participation in ACP was also felt to be distressing and difficult.[47,49,53] 'It's not easy to talk about these things at all, but...information is power.'[43] Thirteen studies showed that patients who participated in ACP were positive about participation or felt it was necessary for them to participate in ACP also described negative experiences. However, the nature of these was not specified further.[28-33,41,42,45,48,50-52]

Positive aspects

Looking at why patients experienced ACP as positive, studies mentioned the information patients received during the ACP conversation and the way it was provided.[28,29,32,42,43,47,52,53] Information that made patients feel empowered was clear, tailored towards the individual patient's situation, and framed in such a way that patients felt it was delivered with compassion and with space for them to express accompanying feelings and emotions.[28,45] Another positive aspect of ACP was that it provided patients a feeling of control. This was derived from their increased ability to make informed healthcare decisions [28,32,47] and to undertake personal planning.[28,32,42] Patients also mentioned that the ACP process offered them an opportunity to think about the end of their life. This helped them to learn more about themselves and their situation, such as what kind of care they would prefer in the future. In addition, participating in ACP made them feel respected and heard.[32–34,41–43,48,49,51–53] One patient summarised it by saying that ACP allowed him to feel that 'everything was in place'.[34]

Unpleasant feelings

Turning to the unpleasant feelings evoked during the process of ACP, these were often caused by the difficulty to talk about ACP, especially because of the confrontation with the end of life. Patients particularly experienced this confrontation at the moment of invitation and during the ACP conversation. Eleven studies,[29,31,33,34,43,45,47,49–51,53] of which eight concerned an ACP intervention in a research context,[33,34,43,47,49,50,51,53] reported that being invited and involved in ACP made patients realise that they were close to the end of their lives and this had forced them to face their imminent death.[29,31,33,34,43,45,47,49,50,51,53] Four of these studies found that this resulted in patients feeling disrupted.[31,33,50,53] In particular, an increased awareness of the seriousness of their illness and that the end-of-life could really occur to them, was distressing.[31,33,50,53] A notable finding was that some patients in five studies,[34,43,47,52,53] labelled the confrontation with their end-of-life as positive because it had helped them to cope with their progressive illness.

Possible solution

In order to overcome, or to soften, the confrontation with their approaching death, some patients offered the solution of a more general preparation. These patients had received general information on ACP through participation in a group ACP session with trained facilitators.[30,50] They believed that the introduction of ACP in a more general group approach or by presenting it more as routine information was less directly linked with the message that they themselves had a life-threatening disease.[30,50] In addition, patients who participated in a group setting mentioned that questions from other patients had been helpful to them.[30] Particularly, those that they had not thought of themselves but of which the answers proved to be useful.[30]

Readiness

During our analysis we noticed how influential the patients' ability and willingness to face the life-threatening character of the disease and to think about future care was during this process. Patients, both in earlier and advanced stages of their disease, refer to this as their readiness to participate in an ACP conversation.[28,29,42,43,45,48,50,51,53]

Being ready

One study involving seriously ill patients looked at their preferences regarding the behaviour of the physician during end-of-life communication.[28] In response to their own ACP experience, several patients in this study suggested that an ACP conversation is only useful and beneficial when patients are ready for it.[28]

Not being ready

Of the patients in the studies which addressed 'readiness', some had not yet felt ready to discuss end-of-life topics at the moment they were invited for an ACP conversation.[29,31,42,43,45,50–53] This was true both for an ACP intervention in a research context or an ACP conversation in daily practice, irrespective of the stage of illness. These patients reported either an initial shock when first being invited[31,50,51] or their initial resistance to participate in an ACP conversation.[29,43,45,51–53] This was particularly true because of them being confronted with the life-threatening nature of their disease.[29,31,33,42,45,50–53] In addition, some patients were worried about the possible relationship between the process of ACP and their forthcoming death.[29,31,42,45,53] The patients in one study reported that introducing ACP at the wrong moment could both harm the patient's well-being and the relationship between the patient and the HCP.[28]

In spite of the initial resistance of some patients to participate in an ACP conversation, most patients completed the conversation and in hindsight felt pleased about it.[42,43,50–53] In two studies, a few patients felt too distressed by the topic and, as a consequence, had not continued the ACP conversation.[29,33]

Documentation

In nine studies, patients' experiences in writing down their values and choices for future medical care were reported.[32–34,44–46,51–53] Patients who participated in an ACP conversation and did not write a document about their wishes and preferences did not do so because they felt uncomfortable about completing such a document.[45,51,53] This was particularly due to their sense of not feeling ready to do so.[45,51,53] In addition, they mentioned their difficulty with planning their care ahead and their need for more information. Some patients felt reluctant to complete a document about their wishes and preferences due to their uncertainty about the stability of their end-of-life preferences in combination with their fear of no longer having an opportunity to change these.[31,45,51,53] However, the patients who completed a document indicated it as a helpful way to organise their thoughts and experienced it as a means of protecting their autonomy.[32–34,44–46,51,52] In a study about the experiences of ALS patients with a living will, a few said that they had waited until they felt ready to complete their living will. This occurred when they had accepted the hopelessness of the disease or when they experienced increasingly severe symptoms.[45]

Timing of ACP

In addition, in three studies investigating patients' experiences with an ACP intervention in a research context, patients emphasised that an ACP conversation should take place sooner rather than later.[42,47,51] In a study among cancer patients about a video intervention as part of ACP, patients mentioned that 'It is better to deal with these things when you are reasonably healthy'.[47] In two studies, patients suggested that it would be desirable to assess the patient's readiness for an ACP conversation by just asking patients how much information they would like to receive.[28,48]

Openness

In all included studies, it appeared that besides sharing information with their HCP or the facilitator who conducted the ACP conversation, patients were also stimulated to share personal information and thoughts with relatives, friends or informal carers.[28–34,41–53] 'Openness' in the context of ACP refers to the degree to which patients are willing to or feel comfortable about sharing their health status and personal information, including their values and preferences for future care, with relevant others.

Positive aspects

Some patients, including a number who were not yet in an advanced stage of the illness, positively valued being open towards the HCP about their options and wishes. An open dialogue enabled them to ask questions related to ACP and to plan for both current and future medical care.[28,29,32,44,45,47,51] Openness towards relatives was also labelled as positive by many patients.[28,30,33,34,42–44,46,48,49,52,53] Patients appreciated the relatives' awareness of their wishes and preferences, which enabled them to adopt the role of surrogate decisionmaker in future, should the patient become too ill to do so his or herself.[28,30,33,34,42–44,46,48,49,52,53] Most patients thought their openness would reduce the burden on their loved ones.[28,33,34,46,47,49,51,52] In two studies, patients described a discussion with family members that led to the completion of the patients' living wills.[45,53] Because of these positive aspects of involving a relative in the ACP process, some patients emphasised that the facilitator should encourage patients to involve relatives in the ACP process and to discuss their preferences and wishes openly.[28,43]

Difficulties

On the other hand, openness did not always occur. Eight studies reported patients' difficulties being open about their wishes and preferences towards others.[32,33,41,43–45,49,53] Some patients had felt uncomfortable about discussing ACP with their HCP because they considered their wishes and preferences to be personal.[32,33,49] Others felt that an ACP conversation concerned refusing treatment and, as such, was in conflict with the work of a doctor.[43,45]

The difficulties reported about involving relatives derived from patients' discomfort in being open about their thoughts.[32,33,44,53] Some patients consciously decided not to share these. For instance, patients felt that the family would not listen or did not want to cause them upset.[32,33,43,44] The ACP conversation did occasionally expose family tensions such as feelings of being disrespected or about the conflicting views and wishes of those involved.[41,53]

Overcoming difficulties

According to the patients, the facilitator who conducted the ACP conversation had the opportunity to support patients to overcome some of these difficulties.[28,30,32,48,52] Patients highlighted that when the facilitator showed a degree of informality towards the patient during the conversation, was supportive and sensitive – which in this context meant addressing difficult issues without 'going too far' – they felt comfortable and respected.[28,30,32,48] This enabled them to be open about their wishes and thoughts.[28,30,32,48]

DISCUSSION

Main findings

This systematic review of research findings relating to the actual experiences with ACP of patients with a life-threatening or life-limiting illness shows that 'ambivalence', 'readiness' and 'openness' play an important role in the willingness and ability to participate in ACP. Previous studies involving hypothetical scenarios for ACP indicate that it can have both positive and negative aspects for patients.[9,11,13,19,20] This systematic review now takes this further showing that individual patients can experience these positive and unpleasant feelings simultaneously throughout the whole ACP process. However, aspects of the ACP conversation that initially are felt to be unpleasant can later be evaluated as helpful. Albeit that patients need to feel some readiness to start with ACP, this systematic review shows that the ACP process itself can have a positive influence upon the patient's readiness. Finally, consistent with the literature concerning perceptions of ACP,[9,11,13,19,20] sharing thoughts with other people of significance to the patient was found to be helpful. However, this systematic review reveals that openness is also challenging and patients need to feel comfortable in order to be open when discussing their goals and plans for future care with those around them.

What this study adds

All three identified themes hold challenges for patients during the ACP process. Patients can appraise these challenges as unpleasant and this might evoke distress.[56–58] For example, the confrontation with being seriously ill and/or facing death, which comes along with the invitation and participation in an ACP conversation, can be a major source of stress. In addition, stress factors such as sharing personal information and wishes with significant others or, fearing the consequences of written documents which they feel they may not be able to change at a later date, may also occur later in the ACP process. All these stress factors pose challenges to coping throughout the ACP process.

The fact that the process of ACP in itself may help patients to discuss end-of-life issues more readily, might be related to aspects of the ACP process which patients experience as being meaningful to their specific situation. It is known from the literature on coping with stress that situational meaning influences appraisal, thereby diminishing the distress.[58] Participation in the ACP process suggests that several perceived stress factors can be overcome by the patient. Although ACP probably does not take away the stress of death and dying, participation in ACP, as our results show, may bring patients new insights, a feeling of control, a comforting or trusting relationship with a relative or other experiences that are meaningful to them.

Patients use a variety of coping strategies to respond to their life-threatening or life-limiting illness and, since coping is a highly dynamic and individual process, the degree to which patients' cope with stress can fluctuate during their illness.[59–61]

ACP takes place within this context. Whereas from the patients' perspective ACP may be helpful, HCPs should take each individual patients' barriers and coping styles into account to help them pass through the difficult aspects of ACP in order to experience ACP as meaningful and helpful to their individual situation.

The findings of this systematic review suggest that the uptake and experience of ACP may be improved through the adoption of a personalised approach, reflectively tailored to the individual patient's needs, concerns and coping strategies.

While it is widely considered to be desirable that all patients approaching the end of life should be offered the opportunity to engage in the process of ACP, a strong theme of this systematic review is the need for 'readiness' and the variability both in personal responses to ACP and the point in each personal trajectory that patients may be receptive to such an offer. Judging patients' readiness', as a regular part of care, is clearly a key skill for HCPs to cultivate in successfully engaging patients in ACP. An aspect of judging patients' 'readiness' is being sensitive to patients' oscillation between being receptive to ACP and then wishing to block this out. Some patients may never wish to confront their imminent mortality. However, it is evident that ACP may be of great value, even for patients who were initially reluctant to engage, or who found the experience distressing. Therefore, HCPs could provide information about the value of participation in ACP, given the patient's individual situation.

If patients remain unaware of ACP, they are denied the opportunity to benefit. Consequently, it is important that information about the various ACP options should be readily available in a variety of formats in each local setting. Given the challenges of ACP and the patient's need to feel comfortable in sharing and discussing their preferences, HCPs should be sensitive and willing to openly discuss the difficulties involved.

Several additional strategies can be helpful. First, ACP interventions can include a variety of activities, for example, choosing a surrogate decision-maker, having the opportunity to reflect on goals, values and beliefs or to document one's wishes. Separate aspects can be more or less relevant for patients at different times. Therefore, HCPs could monitor patients' willingness to participate in ACP throughout their illness, before starting a conversation about ACP or discussing any aspect of it. Second, the option of participating in a group ACP intervention could be a helpful means of introducing the topic in a more 'hypothetical' and non-threatening way, especially for patients who are reluctant to participate in an individual ACP conversation. An initial group discussion could lower the barriers to subsequently introducing and discussing personal ACP with the HCP.[30,50]

The reality remains that discussing ACP with patients requires initiative and effort from HCPs. Even skilled staff in specialist palliative care roles experience reluctance to broach the topic and difficulty in judging how and when to do so.[29,62,63] Therefore, it is important that HCPs are provided with adequate knowledge and training about all aspects of ACP (e.g. appointment of proxy decision-makers as well as techniques for sensitive discussion of difficult topics). It may be helpful for HCPs to have access to different practical tools or ACP interventions which they can use in the care of patients during their end-of-life trajectory. For example, an interview guide with questions that have been established to be helpful could offer guidance to HCPs when asking potentially difficult questions. For that reason, it is important for future research to study the benefits of (different aspects of) ACP interventions in order to improve the care and decision-making processes of patients with a life-threatening or life-limiting illness.

Limitations of the study

Some limitations of this systematic review should be taken into account. First, the articles included were research studies offering an ACP intervention in a research context or studies evaluating daily practice with ACP. It is likely that the patients included here were self-selected for participation in these studies because they felt ready to discuss ACP. This would represent a selection bias, influencing patients' experiences with ACP positively. However, from the studies that reported patients' refusals to participate, we learnt that part of the patients felt initial resistance to ACP and a small number of patients refused participation because they felt not ready. Second, our search was limited to articles published in English.

Conclusion

This systematic review of the evidence of patients' experiences of ACP showed that patients' 'ambivalence', 'readiness' and 'openness' play an important role in their willingness and ability of patients to participate in an ACP conversation. We recommend the development of a more personalised ACP, an approach which is reflectively tailored to the individual patient's needs, concerns and coping strategies. Future research should provide insights in to the potential for ACP interventions in order to benefit the patient's experience of end-of-life care.

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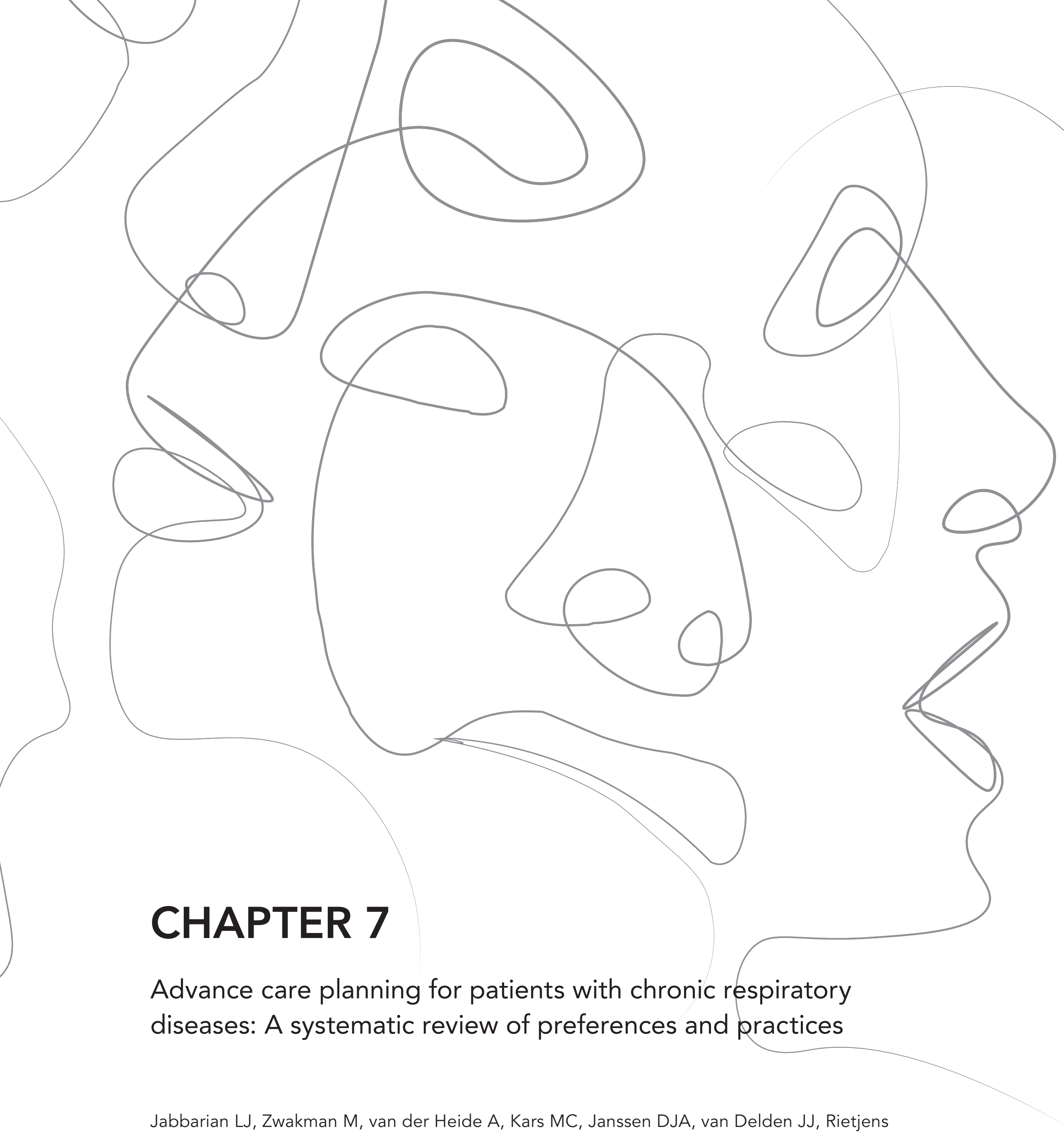

CHAPTER 7

Advance care planning for patients with chronic respiratory diseases: A systematic review of preferences and practices

Jabbarian LJ, Zwakman M, van der Heide A, Kars MC, Janssen DJA, van Delden JJ, Rietjens JAC*, Korfage IJ*

** Equal contributors*

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ABSTRACT

Background

Advance care planning (ACP) supports patients in identifying and documenting their preferences and timely discussing them with their relatives and healthcare professionals (HCPs). Since the British Thoracic Society encourages ACP in chronic respiratory disease, the objective was to systematically review ACP practice in chronic respiratory disease, attitudes of patients and HCPs and barriers and facilitators related to engagement in ACP.

Methods

We systematically searched 12 electronic databases for empirical studies on ACP in adults with chronic respiratory diseases. Identified studies underwent full review and data extraction.

Results

Of 2509 studies, 21 were eligible: 10 were quantitative studies. Although a majority of patients was interested in engaging in ACP, ACP was rarely carried out. Many HCPs acknowledged the importance of ACP, but were hesitant to initiate it. Barriers to engagement in ACP were the complex disease course of patients with chronic respiratory diseases, HCPs' concern of taking away patients' hopes and lack of continuity of care. The identification of trigger points and training of HCPs on how to communicate sensitive topics were identified as facilitators to engagement in ACP.

Conclusions

In conclusion, ACP is surprisingly uncommon in chronic respiratory disease, possibly due to the complex disease course of chronic respiratory diseases and ambivalence of both patients and HCPs to engage in ACP. Providing patients with information about their disease can help meeting their needs. Additionally, support of HCPs through identification of trigger points, training, and system-related changes can facilitate engagement in ACP.

INTRODUCTION

Chronic respiratory diseases have grown in prevalence and are major causes of health burden and death.[1 2] Chronic pulmonary disease (COPD), for example, has become the fourth leading cause of death worldwide.[3] Patients with chronic respiratory diseases, such as COPD or pulmonary fibrosis, experience a complex and often unpredictable disease course,[4] which is characterized by a gradual decline, interrupted by sudden and life-threatening exacerbations.[5 6] As the disease progresses, complications may become more frequent and complex.[7] Disease progression may also lead to a variety of symptoms, such as dyspnoea and comorbidities, which can reduce the quality of life of patients substantially.[7] Patients, their relatives and healthcare professionals (HCPs) are faced with treatment decisions throughout the disease course. Acute deterioration of health can,[7] for instance, result in respiratory failure requiring mechanical ventilation and the necessity of having to make ad hoc decisions on how to proceed.[8]

Since patient preferences for treatments such as mechanical ventilation vary,[9] patient-centred discussions about goals of care are needed, while taking into account patients' preferences for content and timing of such discussions.[10] The British Thoracic Society and American College of Chest Physicians acknowledge advance care planning (ACP) as an integral part of cardiopulmonary medicine and encourage end-of-life discussions about goals of care.[11 12] ACP is a means to support patients in identifying their preferences of care, discussing these preferences timely with their relatives and HCPs and, if desired, documenting them in an advance directive (AD). In other disease groups, such as frail nursing home residents, ACP has been found to have beneficial effects on the communication between patients and HCPs and patients' quality of life.[13] ACP has also been found to have the potential to increase patients' satisfaction with care and care being delivered in accordance with patients' preferences.[13]

To date, there is no thorough overview of the use of ACP for patients with chronic respiratory diseases, of the attitudes towards ACP of those who may be involved in it and of comprehensive ACP programmes in this context. This systematic review aims to describe ACP practice in chronic respiratory disease, summarising findings on (1) how ACP is defined in chronic respiratory disease, (2) the experiences with and attitudes towards ACP of patients and HCPs, (3) the barriers and facilitators related to engagement in ACP and (4) the effects of ACP programmes.

METHODS

Registration of the review

This systematic review was registered at the PROSPERO register (registration number: CRD42016039787). The full form can be accessed online at https://www.crd.york.ac.uk/PROSPERO/

Inclusion and exclusion criteria

We conceptualised ACP following the comprehensive definition of the National Academy of Medicine (NAM):

> *Advance care planning refers to the whole process of discussion of end-of-life care, clarification of related values and goals, and embodiment of preferences through written documents and medical orders. This process can start at any time and be revisited periodically, but it becomes more focused as health status changes. Ideally, these conversations (1) occur with a person's healthcare agent and primary clinician, along with other members of the clinical team; (2) are recorded and updated as needed; and (3) allow for flexible decision making in the context of the patient's current medical situation.*[14]

Based on this definition, we identified four core elements of ACP (see box).

We included studies with interventions, programmes, or activities that were labelled as 'advanced care planning' by the authors or studies addressing one or more core elements of ACP as defined by the NAM.[14] This concerned standalone programmes or activities, as well as activities or programmes as part of a bigger (palliative care) intervention. However, if the ACP components in such a bigger intervention were not clearly described, we excluded the study.

Box Inclusion and exclusion criteria for the current review

Inclusion criteria:

1. Original empirical research on the definitions of advance care planning (ACP), the experiences with and attitudes towards ACP of patients and healthcare professionals (HCPs), the barriers and facilitators related to engagement in ACP and the effects of ACP programmes.
2. Research in the field of chronic respiratory disease.
3. Studies must address ACP, defined as:
    a. Interventions, programmes, or activities that the authors label as 'advance care planning' or
    b. Studies addressing one or more core elements of ACP as defined by the National Academy of Medicine[14]
        1. discussing values and goals for future medical care and treatment with an HCP
        2. clarifying values and goals for future medical care and treatment
        3. involving a personal representative
        4. documenting patients' wishes.
4. Studies published in English.

Exclusion criteria:

1. Studies in which ACP is only an element of a more complex care programme, such as palliative care, and specific content on ACP are not clearly described.
2. Studies involving children and adolescents.

Information sources and search

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist for reporting systematic reviews was used as the underlying structure of this review.[15] A systematic search strategy was developed with the aid of a biomedical information specialist of the Erasmus MC medical library. The following electronic databases were used: Embase, MEDLINE, Web of Science, Scopus, CINAHL EBSCO, PsycINFO, Cochrane, PubMed, LILACS, SciELO, ProQuest and Google Scholar.

The search was conducted on 26 June 2015. The search terms for the databases can be found in the online supplementary file (S-box 1–11).

Study selection

Duplicates of the retrieved studies were removed. Based on the inclusion and exclusion criteria (box), two reviewers (LJJ and MZ) independently screened titles and abstracts for eligibility. Thereafter, they reviewed the full text of the remaining studies. Disagreements were discussed, if necessary including IJK and JACR, and solved. The reviewers used the web-based software platform Covidence (www.covidence.org) for screening and reviewing the studies.

Data extraction

We developed a data extraction form for this systematic review and used it to extract data on the study characteristics and results of the studies. We extracted the elements of ACP that were described in the conducted studies. Furthermore, we extracted data on the patients' as well as the HCPs' perspective on ACP, organising the results into experiences with and attitudes towards ACP, barriers and facilitators related to engagement in ACP and the effects of ACP programmes. We defined barriers and facilitators as predisposing factors reported by either patients, HCPs or both that hamper or facilitate engagement in ACP. We solely included those barriers and facilitators that were endorsed by at least 10% of the participants of the particular study. We chose for the cut-off point of 10% of participants to include as much information as possible, while at the same time keeping the information relevant and meaningful. The extraction was completed by one author (LJJ) and checked by another author (MZ). Disagreements were discussed and solved.

Risk of bias assessment and quality appraisal

Risk of bias assessment

The quantitative studies were assessed by two reviewers (LJJ and MZ) with a standardised form of seven items in a modified version of the guidelines for methodological quality assessment of the Dutch Cochrane Centre.[16] The checklist assesses the (1) research hypothesis, (2) study population, (3) selection bias, (4) exposure, (5) outcome, (6) confounding and (7) a general opinion on the study's validity and applicability. A score of 1 was assigned when the criterion had been met sufficiently, a score of 0 when the criterion had not been met sufficiently and a question mark when the information for rating the criterion was lacking. The rating resulted in a total score from 0 to 7. A score of three or less was considered a study of low quality.

Quality appraisal

For the quality appraisal of the qualitative studies, two reviewers (LJJ and MZ) used the 'Consolidated criteria for reporting qualitative research' (COREQ) list,[17] which is recommended by Cochrane Netherlands. The COREQ is a 32-item checklist, developed to promote explicit and comprehensive reporting of qualitative studies. The checklist evaluates qualitative studies on three domains: (1)

research team and reflexivity, (2) study design and (3) analysis and findings. A plus (+) was assigned when the criterion had been properly described (score 1), a minus (–) when it was described unclearly (score 0), and a plus-minus (+/–) when the description was incomplete (score 0.5). Points were added for a total score ranging from 0 to 32.

RESULTS

Study selection

Our systematic search identified 4031 studies as potentially eligible for this review. After removing duplicates, 2509 studies remained, which were screened based on title and abstract. 2264 studies were excluded, mostly because ACP was only an element of an overarching intervention, such as a palliative care programme, and the ACP-specific components were not clearly described. Full text of 245 studies was assessed for eligibility. In the end, 21 studies were included for the analysis (see figure 1).

Study characteristics

Of the 21 studies, 10 had a quantitative study design (table 1).[18-27] Out of these 10 studies, eight were observational, cross-sectional and retrospective.[19 20 22-27] Nine studies had been conducted in the USA.[18 20-23 25 26 28 29] Studies involved patients with COPD (n=13),[18 19 23-25 27 30-36] chronic lung diseases (n=5),[20-22 29 37], cystic fibrosis (n=2),[26 28] and progressive idiopathic fibrotic interstitial lung disease (n=1).[38] Sixteen studies described the patients' perspective on ACP,[18 21-26 28-30 33-38] nine described the perspective of HCPs.[19 20 24 25 27 29 31 32 38] Sixteen studies had been conducted in an outpatient setting.[18-26 29 30 32 33 35-37] Sample sizes varied from 17 to 513 in the studies with a quantitative design and from 7 to 67 in those with a qualitative design. Five studies evaluated an ACP programme.[18 21 33 35 37] Studies were published between 1996 and 2014.

Online supplementary tables 1 and 2 present the results of the risk of bias assessment of the quantitative studies and the results of the quality appraisal of the qualitative studies, respectively. One study, that was described in a 'short communication', was of low quality (score of 2), due to concerns about the rationale of the study, study population and selection bias, as well as potential confounding.[27] The quality scores of the remaining quantitative studies ranged from 4 to 7, indicating overall good quality of the studies. One study had the maximum score of 7.[24] Four studies had a score of 6. The results of these studies should be interpreted in the light of concerns about confounding[18 21] and selection bias.[23 25] These concerns were also the most prominent quality issues of the quantitative studies in general (risk of possible confounding in 6 out of 10 studies, concerns about selection bias in 4 out of 10 studies).

The mean quality appraisal score of the qualitative studies was 16.5 of 32 (range 12–26.5). Almost all studies had poor ratings on the first domain, 'Research team and reflexivity'. Studies with the

Figure 1. Flow diagram of article inclusion for this review. ACP, advance care planning.

lowest scores also provided insufficient information on the domains 'Study design' and 'Analysis and finings'. The first domain 'research team and reflexivity' was reported the poorest throughout all studies, which clearly had a detrimental impact on the overall quality of the studies.

Synthesis of results

Core elements of ACP studied in chronic respiratory disease

Our first aim was to summarise how ACP is defined in chronic respiratory disease. We therefore gathered which elements of ACP were described in the conducted studies (table 2). The vast majority of studies investigated the discussion of end-of-life care in their studies. The documentation of patients' wishes was investigated in about half of the studies.

Table 1. Study characteristics of the included studies

First author (year)	Study design	Country	Setting	Type of disease	Sample size (response rate (%))
Quantitative study design					
Target group: patients					
Au (2012)[18]	Experimental Longitudinal Prospective	USA	Outpatient clinic	COPD	306 (81)
Heffner (1997)[21]	Experimental Longitudinal Prospective	USA	Outpatient clinic	Chronic lung diseases	93 (ns)*
Heffner (1996)[22]	Observational Cross-sectional Retrospective	USA	Outpatient clinic	Chronic lung diseases	105 (100)
Janssen (2011)[23]✝	Observational Cross-sectional Retrospective	NL/USA	Outpatient clinic	COPD	513 (ns)*
Sawicki (2008)[26]	Observational Cross-sectional Retrospective	USA	Outpatient clinic	Cystic fibrosis	234 (77)
Target group: patients and healthcare professionals					
Janssen (2011)[24]	Observational Cross-sectional Retrospective	NL	Outpatient clinic	COPD	105 patients (63), 101 HCPs (96)
Knauft (2005)[25]	Observational Cross-sectional Retrospective	USA	Outpatient clinic	COPD	115 patients (40), 56 HCPs (86)
Target group: healthcare professionals					
Gaspar (2014)[19]	Observational Cross-sectional Retrospective	Portugal	Inpatient and outpatient clinic	COPD	136 (29)
Heffner (1996)[20]	Observational Cross-sectional Retrospective	USA	Outpatient clinic	Chronic lung diseases	218 (63)
Smith (2014)[27]	Observational Cross-sectional Retrospective	Australia	Inpatient clinic	COPD	17 (41)
Qualitative study design					
Target group: patients					
Brown (2012)[30]	Semi-structured interviews	Australia	Outpatient clinic	COPD	15
Dellon (2010)[28]	Semi-structured interviews	USA	Inpatient clinic	Cystic fibrosis	36
MacPherson (2012)[36]	Semi-structured interviews	UK	Inpatient clinic, GP practices	COPD	10
Seamark (2012)[34]	Semi-structured interviews	UK	Inpatient clinic	COPD	16
Simpson (2011)[35]	Semi-structured interviews	Canada	Outpatient clinic	COPD	8
Nguyen (2013)[33]	Qualitative descriptive	Canada	Outpatient clinic	COPD	12

Table 1. Study characteristics of the included studies (continued)

First author (year)	Study design	Country	Setting	Type of disease	Sample size (response rate (%))
Burge (2013)[37]	Prospective semi-structured interviews	Australia	Inpatient and outpatient clinic	Chronic lung diseases	67
Target group: patients and healthcare professionals					
Bajwah (2012)[38]	Semi-structured interviews	UK	Inpatient clinic	PIF-ILD	8 patients 6 HCPs
Hajizadeh (2014)[29]	Semi-structured interviews	USA	Outpatient clinic	Chronic lung diseases	11 patients five physicians
Target group: healthcare professionals					
Crawford (2010)[31]	Semi-structured interviews	UK	Inpatient clinic	COPD	7
Gott (2009)[32]	Focus group	UK	GP practices	COPD	39

*ns=response rate not specified.
✝Data of a part of the included patients in this study were also used in the analysis of the study by Jansen et al. 2011[24]
COPD, chronic obstructive pulmonary disease; GP,general practitioner; PIF-ILD,progressive idiopathic fibrotic interstitial lung disease; NL, the Netherlands.

Experiences with and attitudes towards ACP in chronic respiratory disease from a patient perspective

Involvement in discussions about end-of-life care preferences was addressed in 11 articles. Six of these studies had a quantitative study design. Seven studies involved patients with COPD. Per study, 12%–32% of patients could recall involvement in end-of-life care discussions.[18 23-26] The qualitative studies found that patients could rarely recall these discussions.[29 30 34 36]

Eight studies addressed patients' interest in discussing end-of-life care preferences. Two quantitative studies, each of high quality, involved patients with COPD and chronic lung diseases in an outpatient setting and found that 68% and 99% of the patients, respectively, were interested in discussing end-of-life care preferences (online supplementary table 3).[18 22] In five qualitative studies patients with a variety of chronic respiratory diseases expressed willingness to discuss end-of-life care preferences.[29 30 34 36 38] Two of these qualitative studies revealed some hesitation of patients to talk about end-of-life care preferences, mainly due to uncertainty about the stability of their preferences and the sensitive nature of the topic.[34 36]

Seven studies addressed the documentation of preferences. Two quantitative studies of high quality, in an outpatient setting with patients with chronic lung diseases and cystic fibrosis, found that 30% and 42% of patients reported documentation of their wishes through an AD.[22 26] Documentation of patients' wishes however did not always result in those wishes being discussed with the HCP, merely 19% of the patients in this study discussed their ADs with their HCPs.[22] In four qualitative studies, involving patients with a variety of chronic respiratory diseases in inpatient as well as outpatient clinics, only a minority of the interviewed patients had heard of an AD.[29 30 34 38]

Table 2. Core elements of advance care planning studied in chronic respiratory disease (n=21)

	Specific core elements of advance care planning as addressed in studies in chronic respiratory disease (n=21)
Core elements of advance care planning	
1) Discussing end-of-life care	20[18-36 38]
2) Clarifying values and goals	7[18 19 23 24 27 29 33]
3) Involving a personal representative	7[18 26 27 29 30 35 37]
4) Documenting patients' wishes	11[19-22 26 29 30 33-36]

Experiences with and attitudes towards ACP in chronic respiratory disease from a HCP perspective

Eight studies addressed the experiences with and attitudes towards ACP from the HCP perspective (online supplementary table 4). Four of these were quantitative studies, in both inpatient as well as outpatient settings, and addressed the engagement of HCPs in ACP discussions.[19 20 24 27] The percentage of self-reported engagement in ACP was 20%–33% in the three high-quality studies[19 20 24] and 13% in a pilot study of low quality.[27]

Two of these high-quality studies and the pilot study of lower quality found that 42-77% of HCPs recognised the importance of discussing end-of-life care topics.[19 20 27]

The vast majority of HCPs in two qualitative studies with patients with COPD and chronic lung diseases in an outpatient setting endorsed the need of discussing end-of-life care.[29 32] HCPs in one of these studies stated that not discussing end-of-life care would limit patient choice.[32] The pilot study that was carried out in Australia found that 41% of HCPs thought that their patients would be willing to discuss their wishes.[27]

The same Australian study found that 77% of HCPs felt comfortable to talk about end-of-life care,[27] while a high-quality study from Portugal revealed that 89% of HCPs found it difficult to engage in discussions on end-of-life care preferences.[19] Two qualitative studies, that involved patients with COPD and progressive idiopathic fibrotic interstitial lung disease (PIF-ILD) in an inpatient clinic showed that HCPs had doubts about the right moment to initiate these discussions on end-of-life care preferences[31 38] and felt uncomfortable to share prognostic estimates such as life expectancy.[29] In one qualitative study[31] that involved COPD inpatients, HCPs emphasized that the timing of engaging in these discussions was crucially dependent on the patients' disease pathway and highlighted a clear difference between diseases.[31]

Barriers and facilitators related to patient and HCPs' engagement in ACP

Table 3 shows the most frequently described barriers and facilitators related to patient and HCPs' engagement in ACP.[19 21 23 25 27-34 37 38] The barriers and facilitators described in these 13 studies were related to the level of the patient, the HCP and the healthcare system.

Table 3. Barriers and facilitators related to engagement in ACP

	Patient related	HCP related	System related
Barriers	Insufficient patient knowledge about their own disease.[23,25,29,32,38]	Perceived hesitance of HCPs to discuss preferences and engage in ACP.[21,23]	Ethos of 'cure at all costs' in health care.[32]
	Unpredictable disease course and difficult prognostication.[19,25,27,31,32]	HCP's perceived fear of taking away patients' hope.[19,25]	Perceived HCP's time constraints.[23,25,27,29,32,34,38]
	Perceived patient hesitation for considering and discussing treatment preferences.[19,25,27]		Lack of organisational support and formal training on communicating end-of-life care options.[19,22,32,37,38]
			Lack of continuity and coordination of care including uncertainty on whose responsibility it is to initiate and follow-up on ACP discussions.[21,23,25,30,32,38]
Facilitators	Increased patient knowledge on terminal nature of their disease.[28,33]	Advanced stage of disease.[23,25,27,29]	Patient initiation of ACP (as experienced by HCPs),[31] HCP initiation of ACP (as experienced by patients).[23,25,28]
	Patients accepting their disease, increasing readiness to discuss end-of-life care.[27,31,33]	Identification of the right moment and setting to engage in an ACP discussion.[28,31,32]	Implementation of trigger points to discuss ACP.[32]
	Patient worry to become a burden for the family.[23,25]	HCPs' experience with care for patients at the end of life/ with lung diseases.[23,25,34]	Continuity of care, including good HCP–patient relationship.[23,25,31,33,34]
	Patient experience with end of life.[23,25,33]		

Two high-quality quantitative studies and three qualitative studies, involving patients with COPD and PIF-ILD, and their HCPs described insufficient awareness of patients about the nature of their disease, especially about its severity, as a barrier to ACP.[23,25,29,32,38] Four studies, among which one high-quality quantitative study, found that the unpredictable disease course of these diseases, particularly COPD, makes it difficult for HCPs to define and communicate the prognostic estimates to patients.[19,27,31,32] The same four studies and an additional high-quality quantitative study found that the complex disease course of chronic respiratory diseases also makes it difficult for HCPs to identify trigger points for the initiation of ACP, especially in chronic lung diseases.[19,25,27,31,32] Besides, HCPs perceive patients to be hesitant to consider and discuss end-of-life care,[19,25,27] while patients perceived HCPs to be reluctant to initiate ACP discussions.[21,23] This impression by patients aligns with HCPs acknowledging their fear of taking away patients' hope. This might be related to an ethos of 'cure at all costs', as identified by three studies in the UK, USA and Portugal involving patients with COPD.[19,25,32]

Seven studies reported system-related barriers to ACP, among which time constraints,[23,25,27,29,32,34,38] a lack of structural support, such as a lack of continuity of care,[21,23,25,30,32,38] and a lack of formal training in communicating end-of-life care options.[19,22,32,37,38] Two quantitative and two qualitative studies found that both patients and HCPs perceived lack of continuity and coordination of care as a barrier,[23,25,30,38] resulting in uncertainty about whose responsibility it is to initiate ACP discussions and to follow-up on these discussions.[21,32]

Two qualitative studies, involving patients with COPD and cystic fibrosis, identified patient knowledge and understanding of the nature of their disease as a facilitator for engagement in ACP.[28 33] Patients' acceptance of their disease was mentioned as another facilitator.[27 31 33] Three studies with patients with COPD and cystic fibrosis found that patient acceptance might increase with disease progression.[23 25 28] Two high-quality quantitative studies suggested that with disease progression, patients' worries about becoming a burden for loved ones increased, which in turn was found to be a facilitator for engagement in ACP.[23 25] Engagement in ACP was more acceptable to patients who previously experienced loved ones having to decide about end-of-life care or who had experienced loved ones dying.[23 25 33]

Three quantitative studies, among which two of high quality and one qualitative study, found that patients as well as HCPs perceived talking about ACP to be easier when patients had an advance disease stage.[23 25 27 29] The identification of the right moment and setting to engage in ACP discussions was perceived as beneficial by both,[28 31 32] as well as the HCPs' expertise in caring for patients with lung disease or end-of-life care.[23 25 34]

While patients with COPD and cystic fibrosis preferred ACP discussions to be initiated by HCPs,[23 25 28] one qualitative study with patients with COPD in the UK found that HCPs preferred patients to start discussions on end-of-life care.[31] The implementation of trigger points to discuss ACP, such as the start of oxygen therapy, could help to overcome this dilemma.[32] Patients and HCPs experienced a good patient–HCP relationship, characterised by trust and continuity, as supportive for engagement in ACP.[23 25 31 33 34]

Effects of ACP programmes

Five studies, two quantitative and three qualitative, evaluated the effects of an ACP programme (online supplementary table 5).[18 21 33 35 37] Two high-quality quantitative studies evaluated a patient-specific feedback form to stimulate ACP conversations in patients with COPD[18] and educational workshops on ADs and other end-of-life topics for patients with chronic lung diseases.[21] The interventions increased quality of end-of-life care communication[18] and resulted in an increased number of completed living wills.[21]

The three qualitative studies evaluated programmes ranging from delivering video material to patients with COPD,[33] to ACP conversations based on a conversation guide for patients with chronic lung diseases and COPD.[35 37] Some patients perceived the information presented as confrontational, nevertheless they agreed about the need to gain a thorough understanding of treatment options.[33 35 37] Considering the timing of the discussions, a study on the effects of a DVD movie covering information on end-of-life care options found that most patients wished their HCPs to mainly be sensitive to their individual needs.[33]

DISCUSSION

This is the first systematic review thoroughly describing ACP practice in chronic respiratory disease, summarising findings on how ACP is defined in chronic respiratory disease, the experiences with and attitudes towards ACP of patients and HCPs, the barriers and facilitators related to engagement in ACP and the effects of ACP programmes. We summarised the findings of 21 studies. Only five of these studies, which mostly had a qualitative study design, evaluated an ACP programme, suggesting that ACP programmes are less commonly studied in chronic respiratory disease than in other disease groups such as motor neuron disease and with nursing home residents.[39 40] By looking at the definitions of ACP in chronic respiratory disease and the elements being investigated in the 21 studies themselves, we found that only 10 studies provided an explicit operationalisation of ACP. The remaining studies did not mention the term ACP at all. This suggests that the concept of ACP is not widely known or used in chronic respiratory disease.

The assessment of the elements of ACP described in the conducted studies revealed that in contrast to the NAM definition most of the studies did not include the clarification of patients' values and goals in their studies. According to the American Thoracic Society, comprehensive ACP however is a holistic approach, tailored to individual needs. Solely discussing treatment options without grounding these in the discussion about patients' values and goals lowers the chance that patient-centred treatment decisions are made.[8] We also found that the descriptions of ACP only rarely included the involvement of a personal representative in ACP. While traditionally ACP focused mainly on the completion of written documents, the American Thoracic Society[8] nowadays acknowledges the importance of patient-centred conversations about treatment decisions as well as the involvement of a personal representative. Involving family caregivers can ensure that patient preferences will still be taken into account, even if patients lose their decision-making capacity.[8]

ACP is widely embraced by professional bodies such as the British Thoracic Society, American Thoracic Society and the American College of Chest Physicians.[8 11 12] Cumulative evidence, predominantly from studies in other disease groups, has established the positive effect of communication between patients and HCPs on patients' quality of life.[13] Our systematic review shows that many patients with chronic respiratory diseases and their HCPs are interested in engaging in ACP, while less patients reported to have had such conversations. The low uptake of these discussions seems to be comparable with other disease groups: 20% of general medicine patients and 29% of hospitalised cancer patients reported having had ACP discussions.[41 42] Apparently, there is a discrepancy between the expressed interest in ACP discussions and the extent to which ACP discussions take place. Our systematic review suggests three main explanations for this phenomenon.

First of all, chronic respiratory diseases are often characterised by a complex and unpredictable disease course.[4 5] Murray *et al*[6] describe the illness trajectory of lung failure as long-term limitations with intermittent serious episodes. Patients with chronic respiratory diseases are usually ill for a longer period of time, interrupted by occasional acute and often severe exacerbations. As a result, it is difficult for HCPs to provide the patient with prognostic estimates,[6] hence complicating the choice of timing and content of ACP discussions.

Stapleton and Curtis[1] advise to engage in ACP in any case earlier than it is usually done. They advise to start when patients are still relatively well and able to participate in decision making[8] to prevent that the impact of their decisions on their (end-of-life) care is limited.[43] This advice might be of particular importance for patients with COPD, since Lau et al[44] found 26.9% of patients having their first ACP discussions only 3 days before death. While indeed ACP discussions can start any time, they can become more targeted as the patient's health condition worsens.[45] To support HCPs in finding a good moment for ACP discussions, Bernacki and Block[43] made an effort to identify trigger points for starting ACP discussions. Examples of such trigger points are ongoing oxygen requirement of patients with COPD or lack of further treatment options. A negative response on the 'surprise question' *('Would you be surprised if this patient died in the next year?')* could serve as an indication for HCPs to initiate ACP,[43] although further validation of this question is necessary in this population. Another way of enabling ACP discussions is to remain alert for patient-induced triggers. Patients reported that experiences with death and dying of family and friends facilitated their thinking about end-of-life care. Responding to and elaborating these experiences can help to initiate ACP discussions.

The second explanation for the low frequency of ACP in chronic respiratory disease is that despite of HCPs recognising the importance of engaging in ACP, they often fear taking away patients' hope. Related to this, HCPs also reported a lack of training on communicating sensitive topics such as end-of-life care options without threatening the patients' emotional wellbeing and feelings of hope. However, a qualitative study on the perspectives of nurses on meeting patients' needs for hope and illness information[46] and a review on hope in palliative care found that honest information about the patient's illness can contribute to patient hope.[47] Patients were, for example, hoping to live to the fullest in the time they have left.[47] In fact, being able to talk about death and dying gave patients a sense of control and made them less afraid of the process of decision making.[47] Our review also found that patients do not feel well informed and educated about their disease, and HCPs confirmed that patients lack knowledge particularly about the severity of their disease. Patients seem to appreciate information about their disease, if sensitively introduced. This also highlights the importance of good communication skills and training for HCPs. Providing information on the disease, possible disease course and treatment options, can be the first step of ACP.

The third explanation for the low frequency of ACP discussions in chronic respiratory disease is that system-related barriers such as time constraints and lack of continuity of care limit the opportunity for both patients and HCPs to engage in ACP during medical encounters. Patients' care trajectory is often characterised by profound breaks in care settings and HCPs. These breaks in care make it a complex task for HCPs to assess patients' level of awareness and readiness to engage in ACP. Continuity of care can be strengthened by documenting discussions on diagnosis, prognosis, treatment, and care options in the medical file. A reliable system for storing written advance care documents can ensure that these documents can be retrieved and transferred easily. Besides, it can be valuable to look for settings in which patients with chronic respiratory diseases are treated throughout their disease trajectory, such as pulmonary rehabilitation.[21 22] Due to their long-term relationship with the patient, general practitioners might be in a good position to be involved in ACP as well.[48]

Limitations

This review however has some limitations. First, we aimed at a comprehensive search strategy by searching in 12 electronic databases and also including studies that addressed the core elements of ACP without explicitly mentioning the term 'advance care planning'. However, if ACP was part of a larger palliative care programme and it was not possible to answer our research questions regarding specific ACP elements of the programme, we had to exclude the respective paper. This may have affected our results to some extent. Second, since the studies were mainly descriptive, statements of causality cannot be made. Finally, our search was limited to published articles in English language, which creates the possibility of publication bias.

Conclusion

This systematic review, summarising findings of 21 studies, provides, for the first time, an in-depth picture of ACP practice in chronic respiratory disease, summarising findings on how ACP is defined in chronic respiratory disease, the experiences with and attitudes towards ACP of patients and HCPs, the barriers and facilitators related to engagement in ACP and the effects of ACP programmes. ACP seems to be acceptable and desired, by both patients and HCPs, while the occurrence of ACP appears to be low. The complex disease course of chronic respiratory diseases and hesitance of both patients and HCPs to engage in ACP as well as system-related factors create barriers to engagement in ACP. These barriers could be overcome by, first, identifying trigger points throughout the disease course to discuss ACP and second, training HCPs on how to communicate sensitive topics such as end-of-life care. Finally, making system-related adjustments, such as enabling continuity of care, allowing the initiation of ACP in appropriate healthcare settings and taking away time pressure from HCPs can help to take away barriers preventing engagement in ACP.

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SUPPLEMENTARY MATERIAL

S-Box 1. Search strategy in Medline for the current systematic review
(exp “Advance Care Planning”/ OR (((“Decision Making”/ AND Patients/)) AND (“terminal care”/ OR “palliative care”/ OR “Terminally Ill”/)) OR (((Advance) ADJ3 (plan* OR directive*)) OR ((living) ADJ3 (will*)) OR (patient* AND (decision* OR decid* OR attitude* OR plan* OR preference* OR want OR wish* OR dilemma* OR refus* OR choos* OR choice*) ADJ6 (terminal* OR “end of life” OR palliativ* OR (life ADJ3 (saving OR saver* OR sustain* OR Prolong*))))).ab,ti.) AND (Pulmonary Medicine/ OR exp “Respiratory Tract Diseases”/ OR exp lung/ OR (copd OR bronchi* OR pulmon* OR ((lung* OR respirat*) ADJ3 (disease* OR disorder*))).ab,ti.) NOT ((exp child/ OR exp infant/ OR (child* OR infan* OR adolescen* OR pediatr* OR paediatr*).ab,ti.) NOT (exp adult/ OR (adult OR older OR elderl*).ab,ti.))

S-Box 2. Search strategy in Embase for the current systematic review
(‘living will’/exp OR ((‘patient decision making’/exp) AND (‘terminal care’/exp OR ‘palliative therapy’/exp OR ‘terminally ill patient’/exp OR ‘terminal disease’/de)) OR (((Advance) NEAR/3 (plan* OR directive*)) OR ((living) NEAR/3 (will*)) OR (patient* AND (((decision* OR decid* OR attitude* OR plan* OR preference* OR want OR wish* OR dilemma* OR refus* OR choos* OR choice*) NEAR/6 (terminal* OR ‘end of life’ OR palliativ*)) OR ((decision* OR decid* OR attitude* OR plan* OR preference* OR want OR wish* OR dilemma* OR refus* OR choos* OR choice*) NEAR/6 life NEAR/3 (saving OR saver* OR sustain*))))):ab,ti) AND (pulmonology/exp OR ‘respiratory tract disease’/exp OR ‘lung surgery’/exp OR lung/exp OR (copd OR bronchi* OR pulmon* OR ((lung* OR respirat*) NEAR/3 (disease* OR disorder*))):ab,ti) NOT ((juvenile/exp OR (child* OR infan* OR adolescen* OR pediatr* OR paediatr*):ab,ti) NOT (adult/exp OR (adult OR older OR elderl*):ab,ti))

S-Box 3. Search strategy in PsychINFO for the current systematic review
(exp “Advance Directives”/ OR (((“Decision Making”/ AND Patients/)) AND (“Terminally Ill Patients”/ OR “Palliative Care”/)) OR (((Advance) ADJ3 (plan* OR directive*)) OR ((living) ADJ3 (will*)) OR (patient* AND (decision* OR decid* OR attitude* OR plan* OR preference* OR want OR wish* OR dilemma* OR refus* OR choos* OR choice*) ADJ6 (terminal* OR “end of life” OR palliativ* OR (life ADJ3 (saving OR saver* OR sustain* OR Prolong*))))).ab,ti.) AND (exp “Lung Disorders”/ OR exp lung/ OR (copd OR bronchi* OR pulmon* OR ((lung* OR respirat*) ADJ3 (disease* OR disorder*))).ab,ti.) NOT ((100.ag. OR 200.ag. OR (child* OR infan* OR adolescen* OR pediatr* OR paediatr*).ab,ti.) NOT (300.ag. OR (adult OR older OR elderl*).ab,ti.))

S-Box 4. Search strategy in Cochrane Library for the current systematic review
((((Advance) NEAR/3 (plan* OR directive*)) OR ((living) NEAR/3 (will*)) OR (patient* AND (((decision* OR decid* OR attitude* OR plan* OR preference* OR want OR wish* OR dilemma* OR refus* OR choos* OR choice*) NEAR/6 (terminal* OR ‘end of life’ OR palliativ*)) OR ((decision* OR decid* OR attitude* OR plan* OR preference* OR want OR wish*OR dilemma* OR refus* OR choos* OR choice*) NEAR/6 life NEAR/3 (saving OR saver* OR sustain*))))):ab,ti) AND ((copd OR bronchi* OR pulmon* OR ((lung* OR respirat*) NEAR/3 (disease* OR disorder*))):ab,ti) NOT (((child* OR infan* OR adolescen* OR pediatr* OR paediatr*):ab,ti) NOT ((adult OR older OR elderl*):ab,ti))

S-Box 5. Search strategy in Web-of-science for the current systematic review
TS=(((((Advance) NEAR/2 (plan* OR directive*)) OR ((living) NEAR/2 (will*)) OR (patient* AND (((decision* OR decid* OR attitude* OR plan* OR preference* OR want OR wish* OR dilemma* OR refus* OR choos* OR choice*) NEAR/5 (terminal* OR “end of life” OR palliativ*)) OR ((decision* OR decid* OR attitude* OR plan* OR preference* OR want OR wish* OR dilemma* OR refus* OR choos* OR choice*) NEAR/5 life NEAR/2 (saving OR saver* OR sustain*)))))) AND ((copd OR bronchi* OR pulmon* OR ((lung* OR respirat*) NEAR/2 (disease* OR disorder*)))) NOT (((child* OR infan* OR adolescen* OR pediatr* OR paediatr*)) NOT ((adult OR older OR elderl*))))

S-Box 6. Search strategy in Scopus for the current systematic review
TITLE-ABS-KEY(((((Advance) W/2 (plan* OR directive*)) OR ((living) W/2 (will*)) OR (patient* AND (((decision* OR decid* OR attitude* OR plan* OR preference* OR want OR wish* OR dilemma* OR refus* OR choos* OR choice*) W/5 (terminal* OR “end of life” OR palliativ*)) OR ((decision* OR decid* OR attitude* OR plan* OR preference* OR want OR wish* OR dilemma* OR refus* OR choos* OR choice*) W/5 life W/2 (saving OR saver* OR sustain*)))))) AND ((copd OR bronchi* OR pulmon* OR ((lung* OR respirat*) W/2 (disease* OR disorder*)))) AND NOT (((child* OR infan* OR adolescen* OR pediatr* OR paediatr*)) AND NOT ((adult OR older OR elderl*))))

S-Box 7. Search strategy in Cinahl for the current systematic review
(MH “Advance Care Planning+” OR (MH “Decision Making, Patient+” AND (MH “terminal Care” OR MH “Palliative Care” OR MH “Terminally Ill Patients+”)) OR (((Advance) N3 (plan* OR directive*)) OR ((living) N3 (will*)) OR (patient* AND (decision* OR decid* OR attitude* OR plan* OR preference* OR want OR wish* OR dilemma* OR refus* OR choos* OR choice*) N6 (terminal* OR “end of life” OR palliativ* OR (life N3 (saving OR saver* OR sustain* OR Prolong*)))))) AND (MH “Respiratory Tract Diseases+” OR MH lung+ OR (copd OR bronchi* OR pulmon* OR ((lung* OR respirat*) N3 (disease* OR disorder*)))) NOT ((MH child+ OR MH infant+ OR (child* OR infan* OR adolescen* OR pediatr* OR paediatr*)) NOT (MH adult+ OR (adult OR older OR elderl*)))

S-Box 8. Search strategy in PubMed publisher for the current systematic review
(“Advance Care Planning”[mh] OR (((“Decision Making”[mh] AND Patients[mh])) AND (“terminal care”[mh] OR “palliative therapy”[mh] OR “Terminally Ill”[mh])) OR (Advance care plan*[tiab] OR Advance directive*[tiab] OR living will*[tiab] OR (patient*[tiab] AND (decision*[tiab] OR decid*[tiab] OR preference*[tiab] OR dilemma*[tiab] OR refus*[tiab] OR choos*[tiab] OR choice*[tiab]) AND (terminal*[tiab] OR “end of life” OR palliativ*[tiab] OR life saving*[tiab] OR life saver*[tiab] OR life sustain*[tiab] OR life Prolong*[tiab])))))) AND (Pulmonary Medicine[mh] OR “Respiratory Tract Diseases”[mh] OR lung[mh] OR (copd OR bronchi*[tiab] OR pulmon*[tiab] OR ((lung*[tiab] OR respirat*[tiab]) AND (disease*[tiab] OR disorder*[tiab])))) NOT ((child[mh] OR infant[mh] OR (child*[tiab] OR infan*[tiab] OR adolescen*[tiab] OR pediatr*[tiab] OR paediatr*[tiab])) NOT (adult[mh] OR (adult OR older OR elderl*[tiab]))) AND publisher[sb]

S-Box 9. Search strategy in Google scholar for the current systematic review
“Advance directive|directives”|”advance * plan|planning”|”living will|wills” copd|pulmonary|lung|respiratory

S-Box 10. Search strategy in Scielo for the current systematic review
(“Advance directive” OR “Advance directives” OR “advance care plan” OR “advance care planning” OR “living will” OR “living wills”) AND (copd OR pulmonary OR lung OR respiratory)

S-Box 11. Search strategy in ProQuest for the current systematic review
(ti(“Advance directive” OR “Advance directives” OR “advance care plan” OR “advance care planning” OR “living will” OR “living wills”) OR ab(“Advance directive” OR “Advance directives” OR “advance care plan” OR “advance care planning” OR “living will” OR “living wills”)) AND (ti(copd OR pulmonary OR lung OR respiratory) OR ab(copd OR pulmonary OR lung OR respiratory))

S-Table 1. Results of the risk of bias assessment of the quantitative studies

1st author (year)	Au (2012)[18]	Heffner (1997)[21]	Heffner (1996)[22]	Janssen (2011)[23]	Sawicki (2008)[26]	Janssen (2011)[24]	Knauft (2005)[25]	Gaspar (2014)[19]	Heffner (1996)[20]	Smith (2014)[27]
Research hypothesis	1	1	1	1	1	1	1	0	1	0
Study population	1	1	1	1	1	1	1	1	1	0
Selection bias	1	1	1	?	1	1	0	0	1	0
Exposure assessment	1	1	1	1	1	1	1	1	1	1
Outcome	1	1	1	1	0	1	1	1	0	1
Confounding	0	?	?	1	0	1	1	1	?	0
General opinion	1	1	0	1	1	1	1	1	0	0
Total quality score	6	6	5	6	5	7	6	5	4	2

1 = Criterion has been met sufficiently
0 = Criterion had not been met sufficiently
? = Information for rating the criterion was lacking

S-Table 2. Quality evaluation of included studies according to the COREQ checklist

1st author (year)	Brown (2012)[30]	Dellon (2010)[28]	MacPherson (2012)[36]	Seamark (2012)[34]	Simpson (2011)[35]	Nguyen (2013)[33]	Burge (2013)[37]	Bajwah (2012)[38]	Hajizadeh (2014)[29]	Crawford (2010)[31]	Gott (2009)[32]
Domain 1: Research team and reflexivity											
Interviewer/ facilitator	+	+	+	-	-	-	-	-	-	-	-
Credentials	+	+	-	-	-	-	-	+ / -	-	-	-
Occupation	+	-	+	+	-	-	-	-	+ / -	-	-
Gender	+	+	+	-	-	-	-	-	-	-	-
Experience & training	+	-	+	+	-	-	-	-	+	-	-
Relationship established	-	-	+	-	-	-	-	-	-	-	-
Participants knowledge of the interviewer	-	-	+	-	-	-	-	-	-	-	-
Interviewer characteristics	-	-	+	-	-	-	-	-	-	-	-
Domain 2: Study design											
Methodological orientation and theory	+	-	+	+ / -	+	+	+	+ / -	+	+	+ / -
Sampling	+	+ / -	+	+ / -	+ / -	+ / -	+	+	-	+	+
Method of approach	+ / -	+	+	+	+	+	+	+	-	-	-
Sample size	+	+	+	+	+	+	+	+	+	+	+
Non-participation	-	+	+	+ / -	-	-	+	+	+	-	-
Setting of data collection	+	+	+	+	+	+	+	-	+	+	+
Presence of non-participants	-	+ / -	+	+	+	+	+ / -	+	-	+ / -	+
Description of sample	+	+	+	+	+	+	+	+	+	-	+
Interview guide	+ / -	+ / -	+ / -	+	+	+	+ / -	+	+ / -	+ / -	+ / -
Repeated interviews	+	-	-	-	+	+	-	-	-	-	-
Recording	+	+	+	+	+	+	+	+	+ / -	+	+
Field notes	+	-	+	+	+	+	-	-	-	-	+
Duration	-	+	+	-	-	-	-	-	+	+	-
Data saturation	-	-	+	-	-	-	+	-	-	-	-
Transcripts returned	-	-	-	-	-	-	-	-	-	-	-
Domain 3: Analysis and findings											
Number of data coders	+	-	+	+	-	-	+	+	-	-	+
Description of the coding tree	-	-	+ / -	-	-	-	+ / -	+ / -	+ / -	+ / -	+ / -
Derivation of themes	+	-	+	+ / -	+ / -	+ / -	+	+	+	+ / -	+
Software	-	-	+	-	-	-	-	+	+	+ / -	+
Participant checking	-	-	-	-	-	-	-	-	-	-	-
Quotations present	+ / -	+ / -	+ / -	+	+	+	+	+	+	+	+
Data and findings consistent	+	+	+	+	+	+	+	+	+	+	+
Clarity of major themes	+	+	+	+	+	+	+	+	+	+	+
Clarity of minor themes	+ / -	-	+	+	+	+	+	+ / -	+	+ / -	+ / -
Total +	17	12	25	15	14	14	15	14	13	9	13
Total + / -	4	4	3	4	2	2	3	4	4	6	4
Total -	11	16	4	13	16	16	14	14	15	17	15
Total score	19.0	14.0	26.5	17.0	15.0	16.0	16.5	16.0	15.0	12.0	15.0

+	= Criterion had been properly described
+ / -	= Description of the criterion was incomplete
-	= Description of the criterion was unclearly

S-Table 3. Incidence of and attitudes towards ACP: patient perspective

First author (year)	Attitudes towards ACP	Experiences with ACP
Quantitative study design		
Au (2012)[18]	Discussing EOL care - 68% would like to discuss EOL care preferences with their HCPs.	Discussing EOL care - 15% had EOL discussions.
Heffner (1996)[22]	Discussing EOL care - 69% wished to learn more explicit details about life-sustaining treatment options. - Most patients wished to actively participate in decisions about life support. Documenting patients' wishes - 89% were interested in learning more about ADs. - 78% found discussions about ADs informative. - 22% found discussions about ADs anxiety provoking but worthwhile. - 99% found discussions with HCPs about ADs acceptable. - 86% wanted to learn more about ADs, 12% had initiated these discussions. - 51% felt that physicians should initiate discussions about ADs. 68% found that discussions about ADs and life-support should occur in the outpatient setting.	Discussing EOL care - 15% had discussions about life-support. - 14% believed physicians understood their wishes. Documenting patients' wishes - 95% heard of ADs. - 42 % completed ADs. - 19% had discussed ADs with HCPs.
Janssen (2011)[23]		Discussing EOL care - 12-18% discussed life-sustaining treatments with HCPs. - Quality of EOL care communication was rated very low (median score 1.1 (IQR 0.0-2.9) for patients with mild to moderate COPD and median score 1.4 (IQR 0.0-3.4) for patients with severe to very severe COPD). - HCPs did not ask about: o feelings about getting sicker (53-73%) o important things in life (85-80%) o what dying might be like (89-92%) o spiritual, religious beliefs (87-91%). - 69-84% reported no involvement in treatment discussion.

S-Table 3. Incidence of and attitudes towards ACP: patient perspective (continued)

First author (year)	Attitudes towards ACP	Experiences with ACP
Sawicki (2008)[26]	Discussing EOL care - 50% thought that the clinician should initiate the discussion on EOL care. - Patients felt necessity of considering their treatment options, vast majority considered treatment preferences.	Discussing EOL care - 74% spoke to someone about treatment preferences. - 13% talked with their CF clinician about treatment preferences. - 28% were asked by their CF clinicians if they would want to make decisions about their medical care if they became too ill to make their own decisions. - 79% felt comfortable talking to a CF clinician about EOL care preferences. Clarifying values & goals - 58% had specific wishes about medical treatment.. Documenting patients' wishes - 30% completed an AD. Involving a personal representative - 65% thought about whom they would like to make their healthcare proxy.
Janssen (2011)[24]		Discussing EOL care - Quality of EOL care communication was rated very low (median score 0.0). Clarifying values and goals - Patients reported that HCPs did not address religious beliefs (93%) or important things in the patients' life (83%). - 85% of patients reported no involvement in treatment discussions.
Knauft (2005)[25]		Discussing EOL care - 32% were involved in treatment discussions. Clarifying value sand goals - 75% thought physicians probably/ definitely knew their treatment preferences.
Qualitative study design		
Brown (2012)[30]	Discussing EOL care - Patients would like to discuss EOL care preferences, if sensitively introduced by well-informed HCP.	Discussing EOL care - 2 out of 15 patients had conversations with HCPs about resuscitation. Documenting patients' wishes - 11 out of 15 patients had not seen ADs before.

S-Table 3. Incidence of and attitudes towards ACP: patient perspective (continued)

First author (year)	Attitudes towards ACP	Experiences with ACP
MacPherson (2012)[36]	<u>Documenting patients' wishes</u> - Patients had doubts about documenting 'preferred priorities of care' due to uncertainty about stability of preferences. - Patients had doubts on usefulness of ADs.	<u>Discussing EOL care</u> - Most reported perceived lack of communication around time of diagnosis. - 2 out of 10 patients reported some discussion about future. - 1 out of 10 patients had discussed ACP with HCPs. - 14 out of 10 patients described consultations with HCPs being very focused on the present/ current problem; future/ treatment preferences were never discussed. - Participants had not discussed general care preferences with HCPs, but all stated they would be comfortable with doing so when asked.
Seamark (2012)[34]	<u>Discussing EOL care</u> - All patients were willing to discuss ACP and related issues such as resuscitation. - Discussing ACP was seen as a difficult but worthwhile. - Having to make concrete decisions about EOL care was perceived as being hard.	<u>Discussing EOL care</u> - No one recalled discussion in hospital about life prolonging treatment. - Patients recalled admission as being hurried with minimum of discussion with the ambulance crew or attending GP. - Actual inpatient stay was seen as chaotic by most patients with lack of recall about where care took place and by whom. <u>Documenting patients' wishes</u> - 1 out of 16 patients had a DNR order at home, however form did not accompany patient to hospital.
Bajwah (2012)[38]	<u>Discussing EOL care</u> - Patients would like to discuss EOL care preferences. - Patients felt a need for further information on e.g. prognosis. - All realised importance of discussions about EOL care preferences, but did not know how to initiate them. - Patients felt that HCPs should be able to best judge when discussions about EOL care preferences should take place.	<u>Documenting patients' wishes</u> - No patients had formulated EOL plans or considered EOL preferences.

S-Table 3. Incidence of and attitudes towards ACP: patient perspective (continued)

First author (year)	Attitudes towards ACP	Experiences with ACP
Hajizadeh (2014)[29]	Discussing EOL care - Those who had not discussed EOL decisions with their physicians were willing to do it. - Most agreed that their physicians should be involved in the EOL decision-making process. - 8 out of 11 patients found that physicians should talk about their patient's chance of dying from their disease. - 10 out of 11 patients found that physicians should talk about patients' EOL treatment options . - Patients felt that conversations should take place in advance of acute disease. - Importance of EOL decision making mostly related to experience with a family member. Documenting patients' wishes - Most expressed desire to complete an AD. - 7 out of 11 patients found that physicians should help patients to make ADs.	Discussing EOL care - 8 out of 11 patients knew that they have the right to say no to a breathing machine. - 9 out of 11 patients knew that they have the right to say no to be taken to the hospital. - 1 out of 11 patients had ever talked with HCPs physician about chance of dying from the disease. - 4 out of 11 patients had ever talked about EOL decisions with HCP. Involving a personal representative - All patients had heard of a health-care proxy. Documenting patients' wishes - 3 out of 11 patients had heard of an AD.

ACP = advance care planning
AD = advance directive
EOL = end-of-life
HCP = healthcare professional
COPD = chronic obstructive pulmonary disease
CF = cystic fibrosis
GP = general practitioner
DNR = do-not-resuscitate

S-Table 4. Incidence of and attitudes towards ACP: healthcare professional perspective

First author (year)	Attitudes towards ACP	Experiences with ACP
Quantitative study design		
Janssen (2011)[24]		Discussing EOL care - 6% of both patients and physicians reported having discussed preferences regarding life-sustaining treatment. - 20% talked about life-sustaining interventions with their patients.
Gaspar (2014)[19]	Discussing EOL care - 77% found it very important to discuss EOL care preferences with advanced COPD patients. - 89% found it (very) difficult to discuss EOL care preferences with their patients. - 99% would like EOL care preferences to be further discussed in scientific meetings.	Discussing EOL care - 62% rarely/ never initiated EOL communication. - 68% rarely/ never suggested patients to make decisions about invasive mechanical ventilation/ intubation. - 81% rarely/ never suggested patients to indicate preferences about cardio-pulmonary resuscitation. - 76% rarely/ never suggested patients to make decisions about place of death. Clarifying values and goals - 82% rarely/ never addressed spiritual/ religious beliefs. Documenting patients' wishes - 80% never suggested ADs.
Heffner (1996)[20]	Discussing EOL care - 42% programmes affirmed obligation of HCPs to inform patients regarding all aspects of health care. Documenting patients' wishes - 86% would initiate educational sessions on ADs into their programmes if supplied with appropriate teaching materials.	Documenting patients' wishes: - 33% asked patients about ADs. - 33% presented educational sessions on ADs. - 42% gave written materials on ADs. - Most rehabilitation programmes had no knowledge of their patients' ADs.

S-Table 4. Incidence of and attitudes towards ACP: healthcare professional perspective (continued)

First author (year)	Attitudes towards ACP	Experiences with ACP
Smith (2014)[27]	Discussing EOL care - 69% thought that most patients with advanced COPD wanted to know about their diagnosis, prognosis, and available care options - 41% thought that most patients with advanced COPD, if asked, wanted to discuss their wishes for EOL care. - 76% thought all adult patients with COPD should be offered the opportunity to discuss ACP. - 94% thought that ACP can improve patients' and families' satisfaction about EOL care. - 77% felt comfortable discussing issues related to death and dying with patients with advanced COPD and their families. - 71% thought it is appropriate to discuss ACP with seriously ill patients who may recover. - 35% felt that ACP could destroy a patients' sense of hope. - 12% were concerned that having ACP discussions with COPD patients would lead to them not returning for further follow up. - 18% felt that ACP conflicted with other chronic disease management goals. - 18% felt that discussing ACP conflicts with responsibility to advocate for ICU levels care/ intubation for COPD patients. - 81% felt comfortable discussing ACP with patients with advanced COPD. - 77% thought it is essential to discuss ACP after recovery in patients with respiratory failure requiring non-invasive ventilation. - 94% felt comfortable discussing DNR orders with patients. - 59% found that ACP should be discussed as a routine outpatient visit. - 71% thought that ACP is a specialist physician's responsibility. - 82% felt supported by colleagues in discussing ACP with patients and families. - 71% felt sufficiently knowledgeable about how to conduct ACP conversations with patients and their families. - 81% reported interest in further ACP education.	Discussing EOL care - 13% discussed ACP with most patients, 56% with few/ (almost) none. - >50% discussed most/ all of the time diagnosis, incurability of disease, purpose of medical treatment, symptom management options. - 47% preferred discussing ACP in outpatient setting, 80% discussed it in hospital. - 6% felt that ACP makes patients losing confidence in physicians' care. Clarifying values & goals and Involving a p - <30% discussed most/ all of the time appointment of health-care proxy, palliative care options, patients' goals, values and beliefs. - 65% had previous ACP education, 81% learnt ACP skills by adopting ACP skills from others.
Qualitative study design		
Bajwah (2012)[38]	Discussing EOL care - HCPs did not know when to best initiate discussions about EOL care preferences. - Recognized complexities of delivering information while preserving balance between hope and realism.	Discussing EOL care - Frustrations about poor communication among HCPs and recognition for needed improvement to ensure adequate coordination of end of life care.

S-Table 4. Incidence of and attitudes towards ACP: healthcare professional perspective (continued)

First author (year)	Attitudes towards ACP	Experiences with ACP
Hajizadeh (2014)[29]	Discussing EOL care - All interviewees endorsed the need of having discussions about EOL care preferences, most expressed discomfort and/ or resistance discussing prognostic estimates such as life expectancy with their patients. - 4 out of 5 doctors found that physicians should be involved in decision making about EOL care preferences. - 3 out of 5 doctors found that physicians should be required to initiate discussions about EOL care preferences with their patients. - 3 out of 5 doctors believed that discussions about EOL care preferences should take place during outpatient clinic visits. Clarifying values and goals - EOL discussions should address the following topics: patients' possible outcomes and their impact on their quality of life, patients' treatment preferences in term of treatment, patients' preferences in the case of no reasonable chance of recovery, whether patients would like to identify a health-care proxy or surrogate, whether they have previous ADs and the option of not receiving treatment.	Discussing EOL care - All doctors had discussions about EOL care preferences with patients, mostly in the context of intensive care. - All doctors discussed decision-making or preparation for EOL with patients with severe chronic diseases.
Crawford (2010)[31]	Discussing EOL care - Timing of EOL discussions was crucially dependent on patients' disease pathway. - Language distinctions: 'cancer' has terminal associations; COPD is a medical label with little meaning to patients. - Avoidance of 'death' and 'dying' words from staff and tendency to soften impact of information given to COPD patients; when patients directly asked about death, physicians were unprepared and described anxiety and discomfort. - Lung cancer patients were usually prepared for discussing EOL care preferences by 'planting a seed in their mind'. - COPD patients were not provided with the opportunity for discussing/to discuss EOL care preferences, rather HCPs look for 'cues' to start the discussion. - Patient-initiated discussions were perceived as easier. - Moral and ethical dilemmas were reported: what, who, how, when to tell, while maintaining balance between truth and hope.	

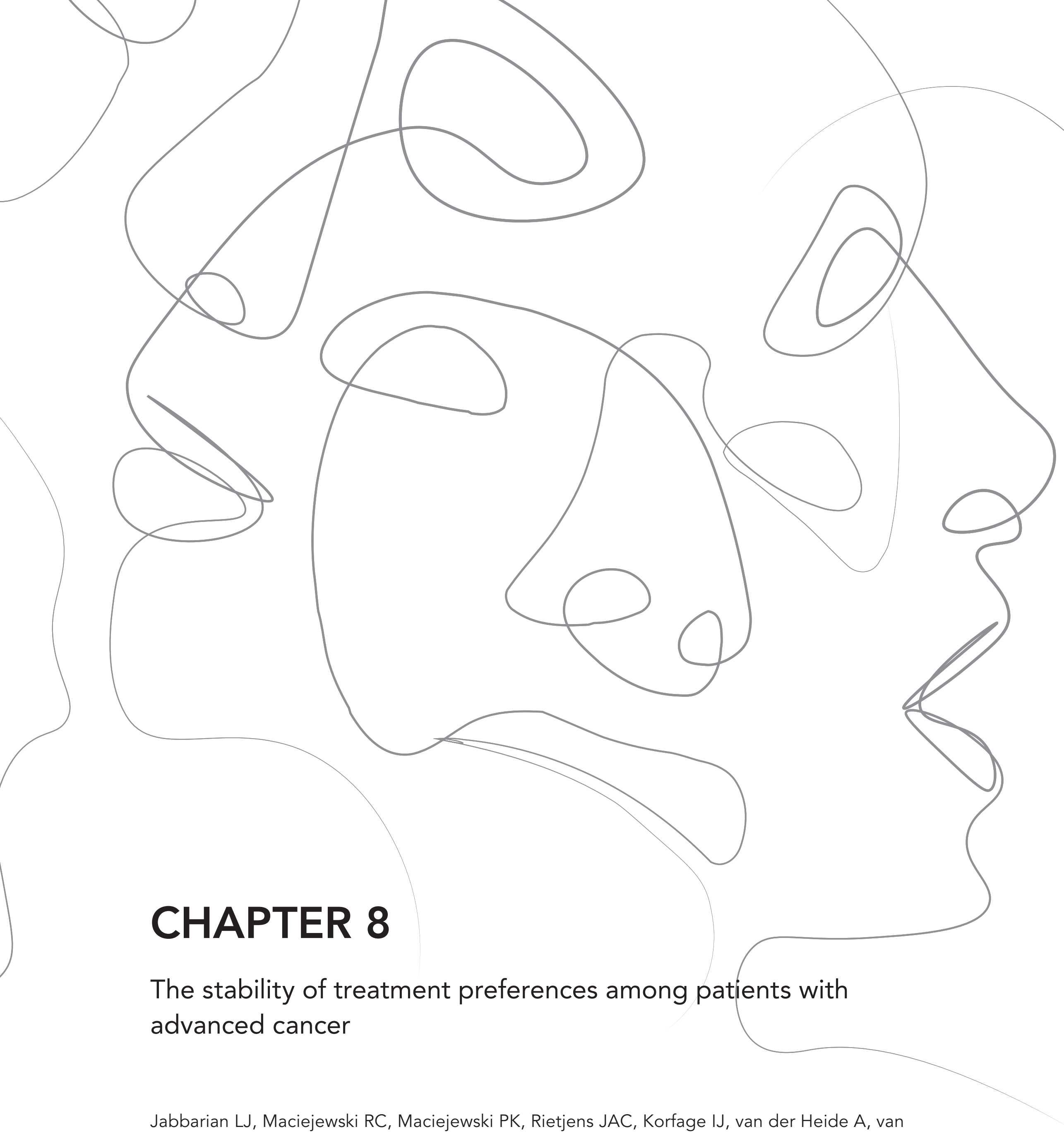
S-Table 4. Incidence of and attitudes towards ACP: healthcare professional perspective (continued)

First author (year)	Attitudes towards ACP	Experiences with ACP
Gott (2009)[32]	Discussing EOL care - Not discussing EOL could limit patient choice. - No consensus on appropriateness of rarely discussing EOL. - Majority thought that whilst they might be the right person to initiate the discussion on EOL care preferences (due to long standing relationship with the patient), there were factors identified preventing them from fulfilling this role. - Practice nurses did not feel that it was their responsibility to start the discussions on EOL care preferences, some reporting that they did not see the very 'terminal' COPD patients because these patients received home visits from the GP, and that they had never received any training in breaking bad news and therefore were ill equipped to manage such discussions. - Respiratory nurses did identify that they often 'knew' patients well and acted as a more constant point of contact in secondary care than medical staff. - Acute admission was not seen as a good time for EOL issues to be discussed.	Discussing EOL care - Discussions about EOL care preferences were rare. - Small minority of GP participants initiate discussions about EOL care preferences earlier in the disease process; typically it was 'too late' for patient to be well enough to make care choices. Most felt that people with COPD receive inadequate information about their condition. HCPs often use euphemisms when disclosing a diagnosis of COPD.

ACP = advance care planning
EOL = end-of-life
COPD = chronic obstructive pulmonary disease
AD = advance directive
ICU = intensive care unit
HCP = healthcare professional

S-Table 5. Effects of ACP programmes: Outcomes from the interventional studies (n = 6)

First author (year)	ACP programme	Study groups (n = participants)	Behavioural outcome
Quantitative study design			
Au (2012)[18]	Based on a patients' questionnaire responses, the HCP and the patient received a one-page patient specific feedback form to stimulate an ACP conversation	Intervention group (n=151) vs control group (n=155)	- Intervention group: threefold rate of EOL discussions with physicians (absolute difference 18.6%, p<.001), higher quality of EOL communication (difference 5.7 points (scale 0-100), p=.03; Cohen effect size 0.21) - No significant effect on number of discussions about patients' feelings about getting sicker, prognosis, what dying might be like, family involvement, asking about things important to patient.
Heffner (1997)[21]	Educational workshop on ADs and other EOL topics	Patients receiving workshop vs care as usual	- Educational group: significant increase (p<0.05) in number of completed living wills (OR=3.6, 95%CI 1.1,12.9), AD discussions (OR = 2.9, 95% CI 1.1,8.3), discussions with physicians about life-support (OR=2.7, 95% 1.0,7.7) and assurance that physicians understand their preferences (OR=3.7, 95%CI 1.3,13.4).
Qualitative study design			
Simpson (2011)[35]	Two loosely structured sessions based on a conversation guide. Each family also got the local health district's brochure on ACP	n=8 (+ 7 informal caregivers)	- 1 patient expressed appreciation for the sessions in terms of social interaction and opportunity for learning. - 1 patient found that the AD template offered a way to ensure that her family member, spouse and very uncertain substitute decision-maker, would have a tangible guidance about the wishes. - Between study visits 1 patient used the template to develop an AD and planned to follow-up by talking about it with her children. - 1 patient pointed out the appreciation for the facilitator's approach.
Nguyen (2013)[33]	A DVD movie to help build patients' knowledge about EOL options and to facilitate patient-physician discussion	n=12	- Most felt DVD did a good job of fulfilling information needs. - Words as 'scary' and 'shocking' were used to describe the visual portrayal of the intubation and tracheostomy processes. Nevertheless most agreed that it was necessary to gain a thorough understanding of the reality of these treatments. - Those who struggled with their diagnosis and prognosis tended to dislike the DVD and not wanting to watch it at all. Generally, the further the participant had progressed in their stages of readiness, the more they expressed that the DVD met their needs.
Burge (2013)[37]	ACP sessions	"attendees" (n=44) vs "non-attendees" (n=23) of the ACP sessions	- 17 described PR&M programmes as appropriate to receive information about ACP and preferable to an acute hospital setting. - 38 patients found information valuable and gave 'peace of mind' in relation to future care. - 34 patients felt that information about ACP is best presented in a group. - No consensus on which health professional should present the ACP information. 12 patients of the community-based group and 8 of the hospital-based group followed up with the ACP facilitators, 21 participants went on to complete documentation.



CHAPTER 8

The stability of treatment preferences among patients with advanced cancer

Jabbarian LJ, Maciejewski RC, Maciejewski PK, Rietjens JAC, Korfage IJ, van der Heide A, van Delden JJM, Prigerson HG

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ABSTRACT

Context

Stability of patients' treatment preferences has important implications for decisions about concurrent and future treatment.

Objectives

To examine the stability of treatment preferences and correlates among patients with advanced cancer.

Methods

In this cohort, 104 patients with metastatic cancer, progression after at least one chemotherapy regimen, and an oncologist-estimated life expectancy of six or fewer months participated in structured interviews after clinical visits in which patients' recent scan results were discussed. Interviews were repeated in three monthly follow-ups. At baseline, patients' age, education, sex, race, marital status, insurance status, and type of cancer were documented. At each assessment, patients reported their treatment preferences (i.e., prioritizing life-prolonging vs. comfort), quality of life, and current health status.

Results

At baseline (n = 104), 55 (53%) patients preferred life-prolonging care and 49 (47%) preferred comfort care. Patients were followed up for one (n = 104), two (n = 74), or three months (n = 44). Between baseline and Month 1, 84 patients (81%) had stable preferences. During follow-up, preferences of 71 patients (68%) remained stable (equally divided between a consistent preference for life-prolonging and comfort care). Treatment preferences of 33 (32%) patients changed at least once during follow-up. Direction of change was inconsistent. Patients' preferences at baseline strongly predicted preferences at Month 1 (odds ratio = 17.8; confidence interval = 6.7 – 47.3; $P < .001$). Description of the current health status at baseline was the only variable significantly associated with stability of preferences at Month 1.

Conclusion

Two-thirds of patients with advanced cancer had stable preferences. Changes of preferences were often inconsistent and unpredictable. Our findings suggest potential benefits of ongoing communication about preferences.

INTRODUCTION

Patients with cancer typically experience diverse symptoms and profound functional decline as their illness reaches an advanced stage.[1] Because there are often options to improve quality of life or survival,[2] patients confront decisions on the medical management of their illness.[1,3] Patients' preferences for potential interventions may vary. Timely discussions can support patients in identifying their options and prepare them for the actual decision-making.[2] Such discussions can increase the likelihood that the care is consistent with patients' (informed) preferences–a principle embedded in the patient's right to self-determination of treatment (e.g., the patient Self-Determination Act in the U.S.).[4] In practice, however, these discussions tend to occur not at all or late in the course of illness,[2] which involves the risk that patients have lost their capacity to engage in these discussions meaningfully.[3,5,6]

The American Society of Clinical Oncology acknowledges the complex nature of the discussions about patients' needs, goals and preferences.[2,7] Clinicians are in the difficult position of having to balance the fear and disappointment patients typically feel when they become aware of the progression of their illness, against an ethical duty to impart realistic information. Imparting this information is tied to fostering autonomy about the patient's prognosis and expected outcomes of treatment so that patients can make informed decisions about their treatment preferences.[8,9] Identifying the right moment in the disease trajectory to engage in these discussions is challenging.[7] One part of this challenge is tied to the stability of preferences. Clinicians must use their best judgment to decide how often preferences should be discussed to inform decision-making. They also have to determine if these preferences can be assumed to remain essentially stable and, therefore, serve as a reliable predictor for preferences in the future.

To date, evidence about the stability of general treatment preferences has been primarily based on studies outside of oncology and through the use of hypothetical scenarios.[10] In a recent review, Auriemma et al. found that treatment preferences are fairly stable among patients with illnesses other than cancer, and among students and physicians.[10] Stability of preferences was associated with the presence of an advance directive, higher level of educational attainment, and very mild and very severe health conditions. The published evidence on the association between changes in health status and stability is equivocal. Some patient groups were shown to have stable treatment preferences, despite a decline in daily activities or physical functioning. Other patient groups adjusted their preferences after a change in health status, either in favor of life-prolonging treatment or comfort care. Mixed results on stability were also found among racial/ethnic minority groups of patients.[10] A pilot study with healthy individuals on the stability of specific treatment wishes (among which cardiopulmonary resuscitation or kidney dialysis) showed a mixed pattern, with a stronger stability for cardiopulmonary resuscitation (CPR) preferences and lower stability for preferences for kidney dialysis.[11]

We identified one study explicitly investigating the stability of treatment preferences of patients with cancer.[12] The patients in this study had a life expectancy of less than two years and reported their attitudes concerning treatment on inclusion in the study, and after six and 12 months of follow-up. Overall, patients were found to have stable treatment preferences, except for patients with a recent diagnosis of cancer.[12] The extent to which they preferred treatment aimed at prolonging life decreased after six months.[12]

We aimed to extend previous findings about the stability of treatment preferences to patients with advanced cancer who are estimated to have a life expectancy of six or fewer months, a period in which patients typically experience profound functional decline.[1,3] Furthermore, we aimed to observe the stability of treatment preferences in patients actually at the end of life confronting decisions, as opposed to evaluating hypothetical scenarios.

METHODS

Sample

The Coping with Cancer-2 (CwC-2) study is a National Cancer Institute-funded, prospective, multi-institutional cohort study of patients with advanced cancer, their caregivers, and their oncology providers. It was designed to evaluate end of life communication processes and end of life care. Patients were recruited to this study to determine how clinical communication related to their coping with a serious illness. Patients were recruited from nine cancer centers across the U.S.: Dana-Farber/Harvard Cancer Center (DF/HC; Dana-Farber Cancer Institute, Brigham and Women's Hospital, and Massachusetts General Hospital, Boston, MA), Parkland Hospital (Dallas, TX), Simmons Comprehensive Cancer Center (Dallas, TX), Yale Cancer Center (New Haven, CT), Meyer Cancer Center at Weill Cornell Medical College (New York, NY), Memorial Sloan Kettering Cancer Center (New York, NY), Virginia Commonwealth University Massey Cancer Center (Richmond, VA), University of New Mexico Cancer Center (Albuquerque, NM), and Pomona Valley Hospital Medical Center (Pomona, CA). Review boards of all participating cancer centers approved the study procedures and all participating patients provided written informed consent. Patients received $25 gift cards for every post–clinical visit assessment that they completed.

Patients had to meet the following inclusion criteria: stage IV gastrointestinal, lung, or gynecologic cancer and select incurable and poor-prognosis stage III cancers (e.g., pancreas and lung); oncologist-estimated life expectancy of six or fewer months; and illness progression after at least one chemotherapy regimen or, in case of colorectal cancer, progression after at least two chemotherapy regimens. All patients were screened using the Pfeiffer Short Portable Mental Status Examine scores to determine severe cognitive impairment. Patients with severe cognitive impairments were excluded, as well as patients who appeared too weak or too ill. Children and young adults up to age 20 were ineligible.

Patients completed structured clinical baseline interviews with mostly close-ended responses after a clinical visit with their oncology provider in which their most recent scan results and treatment plans were discussed. During the baseline interviews, patients reported their treatment preferences (i.e. trade-offs of life-prolonging care vs. comfort care). The interviews occurred either in clinic (31%) or over the telephone (69%), whichever the patient preferred, between November 2010 and April 2015. Patients completed additional monthly follow-up interviews in the clinic. The follow-up interviews included questions about treatment preferences, quality of life, and their description of their current health status. For the present analysis, we selected patients from the CwC-2 cohort who completed baseline and one up to three consecutive monthly follow-up interviews (N = 104, see Figure 1 for a CONSORT flow diagram of the study).

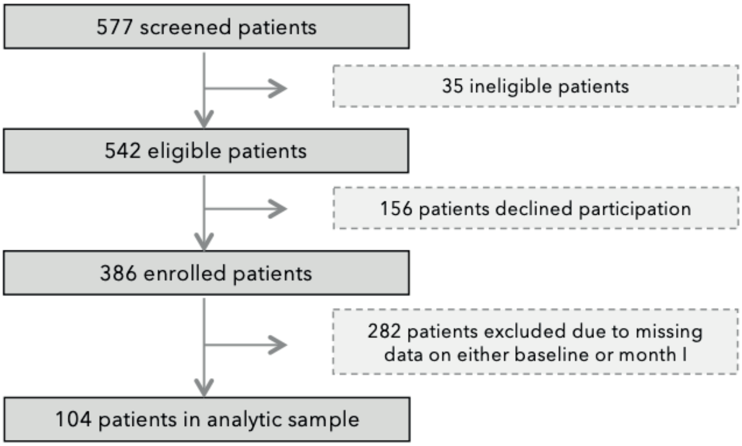

Figure 1. Flow diagram of patients.

Measures

Treatment preferences

Patients' treatment preferences were assessed with the question *"If you could choose, would you prefer A) a course of treatment that focused on extending life as much as possible, even if it meant more pain and discomfort, or B) (on) a plan of care that focused on relieving pain and discomfort as much as possible, even if that meant not living as long?"* Response options were (1) *extend life as much as possible* (classified as having a preference for life-prolonging care) or (2) *relieve pain or discomfort as much as possible* (classified as having a preference for comfort care). This question has been used in several studies of patients with terminal illnesses, including the SUPPORT trial.[13] It has been found to be associated with the number of therapeutic interventions received.[13]

We defined treatment preferences as stable when patients did not change their expressed preference throughout the follow-up period and/or until drop-out. We defined treatment preferences as unstable when patients changed their expressed treatment preference at least once during follow-up.

Predictors of the stability of treatment preferences

Patient characteristics

Patients provided information regarding their age and education (in years), sex, marital status (married or not married), and insurance status (insured or not insured). Patients also provided information on the race they consider themselves to be (white, Afro-American, or other). For the analysis, we recoded the answers into white or other.

Clinical characteristics included the type of cancer and whether patients were currently getting chemotherapy or radiation for their cancer. We summarized the answers on type of cancer into three categories: 1) lung cancer, 2) gastrointestinal cancer (also including bladder and gallbladder cancer), and 3) other cancer.

Quality of life

Patients' quality of life was assessed with the self-report McGill Quality of Life Questionnaire.[14] The questionnaire was designed for assessing quality of life of patients with life-threatening illnesses and has been validated in that setting.[14] The total quality-of-life score was calculated by taking the mean of the 15 self-report items of the questionnaire. Following guidelines, those who did not respond to four or more items were not included in the study as their scale was considered incomplete.[15] Higher scores indicate better self-reported levels of quality of life.

Description of the current health status

The patients' description of their current health status was assessed by asking *"How would you describe your current health status?"* Response options were 1) *relatively healthy,* 2) *relatively healthy and terminally ill,* 3) *relatively ill but not terminally ill,* 4) *seriously ill and terminally ill,* and 5) *do not know.* The responses 1) and 3) were re-coded into 1) *Does not understand that illness is terminal.* Responses 2) and 4) were re-coded into 2) *Understands that illness is terminal.* For this study we considered the response 5) *do not know* a missing response.

Statistical analyses

All statistical analyses were performed using SPSS, version 24 (Statistical Package for Social Sciences, Chicago, IL). *P*-values of <0.05 were considered statistically significant.

Descriptive statistics were used for analyzing patient demographics and baseline characteristics. Means and standard deviation (SD) were used for continuous variables, and frequencies and percentages for binary and categorical variables. Cross-tabulation and frequency counts were used to describe the sample and treatment preferences.

We used univariate logistic regression to calculate odds ratios (ORs) for the association between baseline treatment preferences and treatment preferences at Month 1. Given the restricted sample size at Months 2 and 3, the analysis focused on this particular study interval.

Subsequently, we created a variable on the stability of treatment preferences (stable preferences vs. unstable preferences) between baseline and Month 1 and used this variable in logistic regressions to estimate the association between the following predictors–treatment preferences, patient characteristics, quality of life, and description of the current health status, all at baseline–and stability of treatment preferences at Month 1. Owing to restrictions in sample size, multivariable analyses were not used.

RESULTS

Sample characteristics

The sample consisted of 104 patients who completed the baseline assessment and the assessment after one month of follow-up. Of these patients, 74 completed the questionnaire at Month 2, and 44 completed the questionnaire at Month 3 (see Supplementary Figure 1 for an overview of study participation). In New England, 73 patients were included, eight patients were included in Mid-Atlantic/South, and 23 patients in Southwest/West.

Most patients were female (70%), white (86%), and covered by health insurance (79%). Their average age was 61.3 years (SD 8.7 years). Most patients (89%) currently received chemotherapy or radiation for their cancer. Half of the patients described their current health status as "relatively healthy" or "seriously ill, but not terminally ill", and half of the patients described their current health status as "relatively healthy and terminally ill" or "seriously ill and terminally ill". At baseline, 55 patients (53%) preferred a course of treatment that focused as much as possible on prolonging life, whereas 49 patients (47%) preferred care that focused as much as possible on relieving pain and discomfort.

The patient characteristics are listed in Table 1, separately for patients with stable and unstable treatment preferences.

Stability of treatment preferences

In total, 71 patients (68%) had no observed changes in treatment preferences during the entire follow-up period (Month 1, Month 2, and Month 3). This stability of treatment preferences was equally divided between patients preferring life-prolonging care (35%) and patients preferring comfort care (34%, Table 2).

The remaining 33 patients (32%) changed their treatment preference over time. These patients either changed once or went back and forth between preferences (Figure 2a and 2b). Changes in treatment preferences were seen in patients who initially expressed preferences for life-prolonging care, as well as in patients who initially expressed preferences for comfort care. For instance, two patients who expressed their preference for life-prolonging care at baseline, Month 1, and Month 2, changed their preference towards comfort care at Month 3. Another patient indicated a preference for comfort care at baseline, subsequently changed the preference toward life-prolonging care at

Month 1, returned to a preference for comfort care at Month 2, whereas settled with a preference for life-prolonging care at Month 3.

Table 1. Patient characteristics and preferences at baseline (N = 104)

	Stable preferences after Month I (n = 84)	Unstable preferences after Month 1 (n = 20)
Characteristics	mean (SD)	mean (SD)
Age in years	61.4 (8.2)	60.9 (10.7)
Education in years	14.8 (3.3)	14.9 (3.3)
Quality of life[1]	7.6 (1.6)	7.1 (1.7)
	n (%)	n (%)
Sex		
Male	27 (87.1)	4 (12.9)
Female	56 (77.8)	16 (22.2)
Race		
Other	13 (92.9)	1 (7.1)
White	70 (78.7)	19 (21.3)
Marital status		
Not married	31 (81.6)	7 (18.4)
Married	50 (82.0)	11 (18.0)
Insurance status		
Uninsured	19 (86.4)	3 (13.6)
Insured	64 (79.0)	17 (21.0)
Type of cancer		
Gastrointestinal cancer	39 (88.6)	5 (11.4)
Other cancer	32 (74.4)	11 (25.6)
Lung cancer	39 (88.6)	5 (11.4)
Currently receiving chemotherapy or radiation		
No	10 (90.9)	1 (9.1)
Yes	73 (80.2)	18 (19.8)
Description of the current health status		
Not terminally ill	34 (70.8)	14 (29.2)
Terminally ill nature	42 (87.5)	6 (12.5)
Treatment preference at baseline		
Life-prolonging care	44 (83.0)	9 (17.0)
Comfort care	40 (78.4)	11 (21.6)

[1] McGill Quality of Life Questionnaire (range 0-10), higher scores indicate better self-reported levels of quality of life.

Table 2. Stability of treatment preferences during follow-up (n=104)

	n (%)
Stable preference for life-prolonging care	36 (34.6)
Stable preference for comfort care	35 (33.7)
Unstable preferences	33 (31.7)

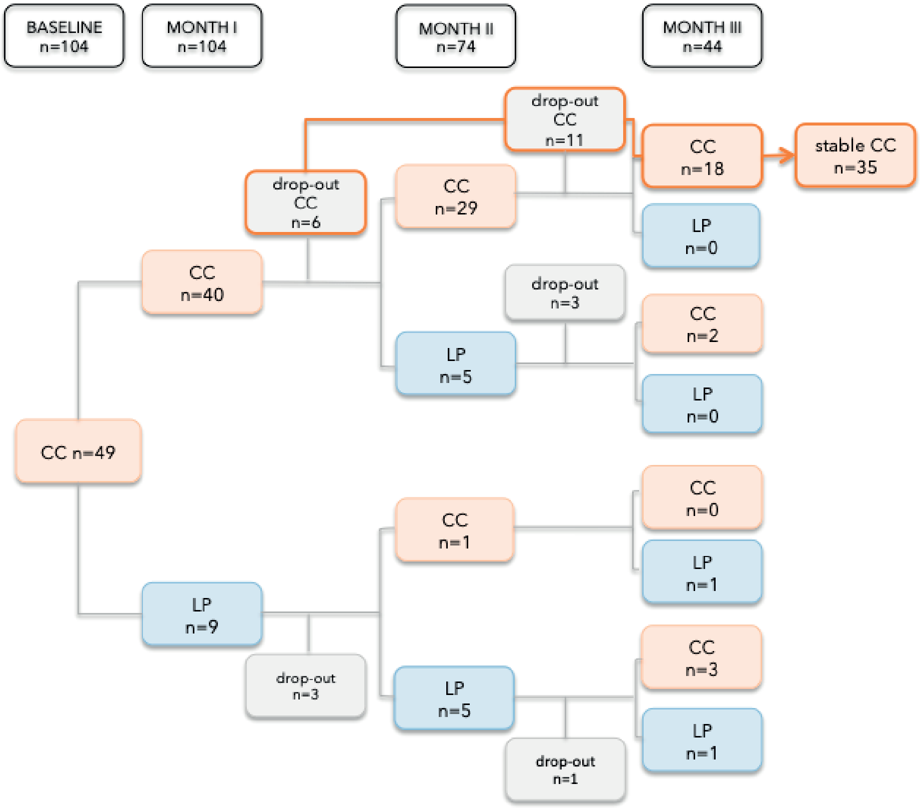

Figure 2a. Preferences over time, beginning with comfort care.
Abbreviations: CC=preference for comfort care; LP=preference for life-prolonging care; drop-out CC=stable preferences for comfort care until drop-out

Predictors of the stability of treatment preferences after one month of follow-up

Between baseline and Month 1, 84 patients (81%) had stable treatment preferences. Of 20 patients (19%) who changed their preference in this period, nine changed toward life-prolonging care (9%) and 1 changed toward comfort care (11%).

Patients' treatment preferences at baseline strongly predicted treatment preferences at Month 1 (OR = 17.8; CI = 6.7-47.3; *P* < .001).

Patients' sociodemographic and clinical characteristics, quality of life, and treatment preferences at baseline were not associated with stability of treatment preferences at Month 1 (Table 3). The association between the description of the current health status and stability of treatment preferences was significant (OR = 2.88; CI = 1.001-8.302; *P* = .05). Not describing the current health status as terminal was associated with unstable treatment preferences.

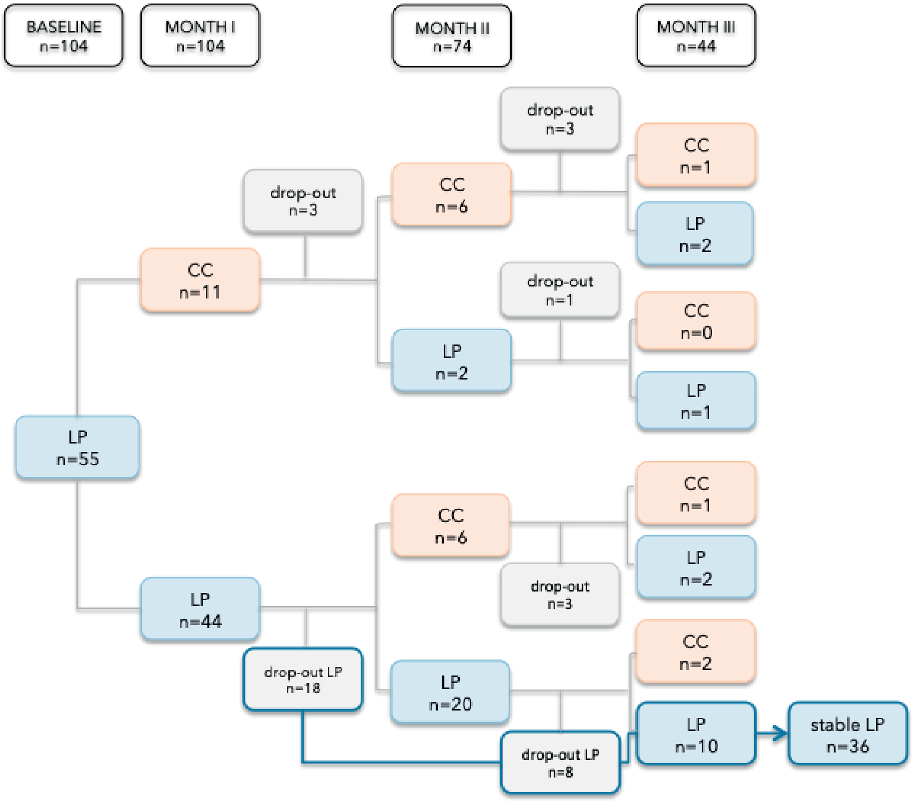

Figure 2b. Preferences over time, beginning with life-prolonging care.
Abbreviations: CC=preference for comfort care; LP=preference for life-prolonging care; drop-out LP=stable preferences for life-prolonging care until drop-out

DISCUSSION

We examined the stability of treatment preferences and predictors of stability in a cohort of patients with advanced cancer and an estimated life expectancy of six or fewer months. Most patients had stable treatment preferences during one to three months of follow-up. No patient characteristics, nor quality of life, predicted the stability of treatment preferences, except from the description of the current health status.

After discussing the most recent scan results during a clinical visit, 53% of patients preferred a course of treatment that focused as much as possible on prolonging life. The remaining 47% of patients preferred comfort care. Interestingly, previous studies found considerably lower rates (28% and 38%) of patients with advanced cancer wanting life-prolonging care.[12,16] The same applies to a study on attitudes of the Dutch general public towards the hypothetical scenario of becoming

Table 3. Predictors of stability of treatment preferences after one month of follow-up (n=104).

	Univariate OR	95% CI	*P*-value
Age (per year)	0.99	0.94-1.05	0.810
Education (per year)	1.01	0.87-1.18	0.887
Quality of life	0.82	0.57-1.16	0.263
Sex			
Male	0.52	0.16-1.70	0.279
Female	Ref		
Race			
Other	0.28	0.04-2.31	0.238
White	Ref		
Marital status			
Not married	1.03	0.36-2.93	0.961
Married	Ref		
Insurance status			
Uninsured	0.59	0.16-2.25	0.443
Insured	Ref		
Type of cancer			
Gastrointestinal cancer	0.37	0.12-1.19	0.373
Other cancer	0.90	0.24-3.33	0.869
Lung cancer	Ref		
Currently receiving chemotherapy or radiation			
No	0.41	0.05-3.38	0.404
Yes	Ref		
Description of the current health status			
Not terminally ill	2.88	1.00-8.30	0.050
Terminal ill	Ref		
Treatment preference at baseline			
Life-prolonging care	1.11	0.42-2.96	0.833
Comfort care	Ref		

Note:
OR: odds ratio, 95% CI: 95% confidence interval

seriously ill, which found 30% of people striving for life-prolonging care.[17] A potential explanation for the high proportion of patients in our study preferring life-prolonging care might be provided by Weeks et al.[13] They found that patients with metastatic cancer tend to overestimate their survival probabilities, which affected their treatment preferences.[13] Patients who thought that they would survive for at least six months were more prone to prefer life-prolonging care than patients who thought that they would survive less than six months.[13] Although the patients in our study had, according to their oncologist, an estimated life expectancy of six or fewer months, 50% of them did not describe their current health status as terminal, which might explain the large percentage of patients favoring life-prolonging treatment. In addition, the vast majority of patients in our study received chemotherapy or radiation at baseline. This might have led them to believe that they had longer survival than was the case, which would further make them want to remain on anti-cancer treatment. Throughout the follow-up period, which varied from one to three months, most patients (68%) had stable treatment preferences. This high proportion of patients with stable preferences is in accordance with a recent review on treatment preference stability in a variety of noncancer patient populations[10] and a study among Dutch patients with cancer who had a life-expectancy of less than two years.[12] Our study extends these findings towards a population of patients with advanced cancer and a life expectancy of six or fewer months, who de facto went through the process of having to make decisions on how to proceed.

Although most patients had stable preferences, one-third changed their preference at least once during follow-up. Some patients who initially repeatedly indicated a preference for comfort care subsequently changed toward life-prolonging care, whereas other patients changed their preference every month. Stability of treatment preferences was neither predicted by patient or clinical characteristics nor by quality of life. The OR for the description of the current health status was significant. The understanding of one's health status may thus play a role in the formation of preferences and patients who do not describe their health status as terminal might be more prone to change their treatment preferences. Besides, patients receiving chemotherapy are less likely to understand that they are terminal. Anticancer treatment may thus fuel a preference for more treatment. Overall, our findings extend and confirm the review by Auriemma et al., who found that the direction of changes in treatment preferences mostly seems inconsistent.[10] Although we did not detect such a difference, it is worth highlighting that patients may hold negative stereotypes towards palliative care/comfort care because these stereotypes (such as "giving up" or being "quitters") have been found in patients with cancer.[18,19] Taking the decision to stop life-prolonging care in favor of comfort care might be more challenging for patients to make. Health care professionals should be aware of this possible imbalance of treatment preferences during the decision-making process.

Our results highlight the need to view discussions of treatment preferences as a dynamic process. Despite guidelines highlighting the discussion of treatment preferences as an important component of high-quality patient care,[2] many physicians postpone these discussions with their patients with cancer who are incurably ill, but still free of symptoms.[20] It has been suggested that clinicians are uncertain as to how early and frequently they should discuss treatment preferences.[10] Our findings should encourage clinicians to engage in these conversations repeatedly because a considerable number of patients showed contradictory and fluctuating preferences as a part of their decision-making process. Clinicians therefore should be aware that preferences may change and that reevaluation of previously expressed treatment preferences during subsequent medical encounters is essential. This was also suggested in a recently published white paper on advance care planning, an increasingly used method that has been found to improve concordance between the care patients receive and the care they desire.[21,22] These repeated discussions may also help to overcome uncertainty with respect to the reliability of preferences of patients who have become incompetent. Because in that situation physicians cannot check the patient's actual preferences, they need to rely on the previously expressed ones. This will be easier to do when the physicians (and the family) have become convinced of the stability of the wishes, expressed at different moments by the then-competent patient. Following the recommendations of Rietjens et al.,[22] we would like to emphasize that advance care planning discussions should go beyond discussing treatment preferences alone and should be held in the context of assessing patients' illness understanding and discussing medical information, such as the diagnosis and prognosis. This is particularly important given the fact that half of the patients in our study did not describe their current health status as terminal and that low numbers of accurate illness understanding have been established elsewhere too.[23]

Our study is limited by the relatively small sample size and attrition of the sample during follow-up. Due to the restricted sample size at Months 2 and 3, we were only able to analyze the association between baseline treatment preferences and preferences at Month 1. Likewise, in-depth analyses on, for example, the impact of the description of the current health status on the change of treatment preferences could not be conducted because of a limited sample size and corresponding statistical power for multivariable analyses. Besides, we were unable to ascertain whether patients who dropped out thereafter had a change in treatment preferences. Because recruitment took place in academic hospitals, the patients were in treatment settings typically focused on aggressive cancer treatment.[24] Therefore, findings need to be confirmed in nonacademic oncology settings. The high attrition rate might have created a bias such that those with more stable illness were retained and those with more quickly advancing cancer dropped out. Based on findings of previous studies, in which stable disease was associated with stable preferences, this might have led to a possible overestimation of stability in our study. The preference question we used (i.e., care primarily aimed at life-prolongation vs. care primarily aimed at comfort) is a simplistic dichotomy of care options for patients near the end of life. We recommend more nuanced measures in future research, such as those used by Schubart et al.[11]

With these limitations in mind, our study provides evidence for the stability of treatment preferences of most patients with advanced cancer regarding life-prolonging versus comfort care in the last months of life. Our results suggest that early discussions about treatment preferences may be useful predictors for the type of treatment patients prefer when death approaches. It is however essential for clinicians to keep in mind that patients may change their treatment preferences and that continuous discussions about these preferences are crucial for the alignment of patients' preferences with the actual treatment.

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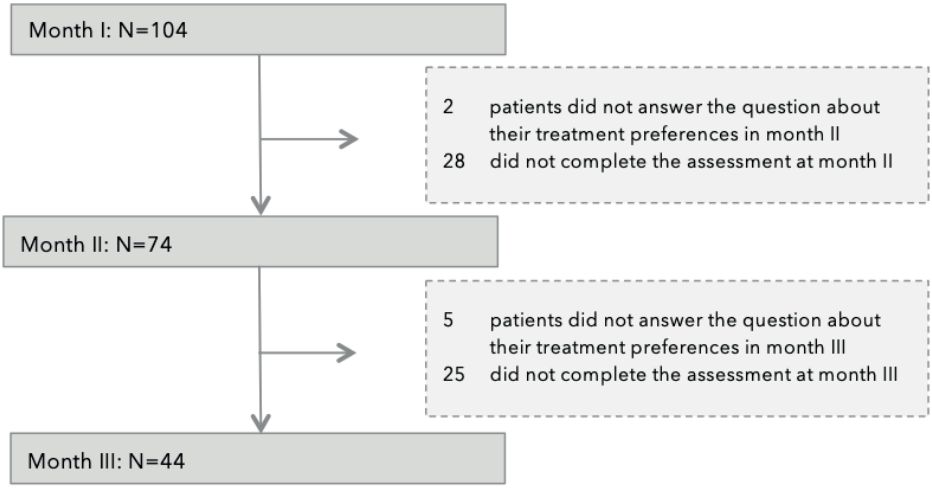
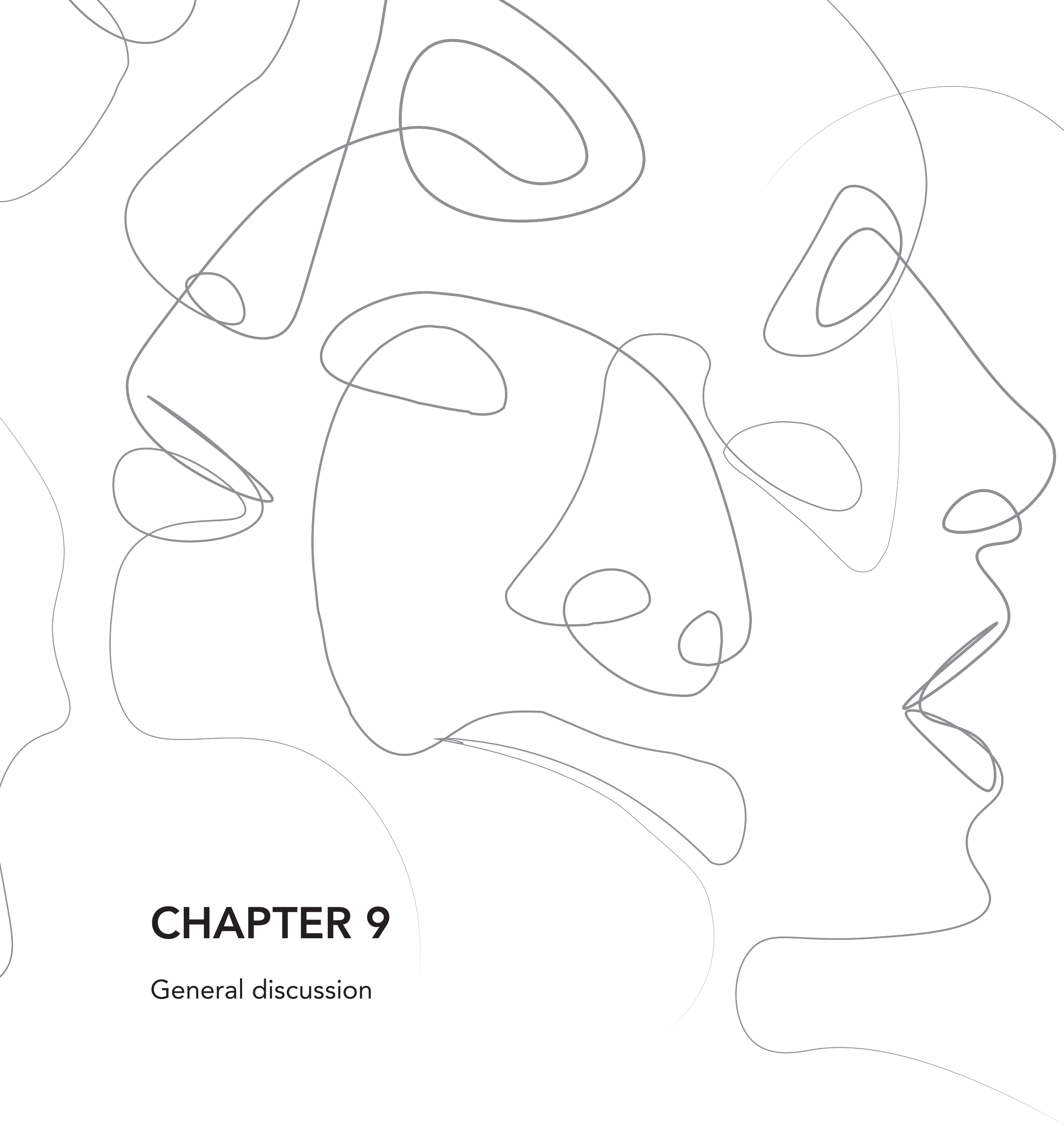
SUPPLEMENTARY MATERIAL



Supplementary Figure 1. Flow diagram of patients who completed the questions on treatment preferences throughout the follow-up period.



CHAPTER 9

General discussion

Following the developments in advance care planning for patients with an advanced, life-limiting disease, this thesis characterized patients' well-being and preferences near the end of life. This general discussion presents (1) an overview of the main findings of the conducted studies, (2) a brief discussion of methodological considerations and (3) a reflection on patient-centred care and advance care planning near the end of life.

SUMMARY OF THE MAIN FINDINGS

Patients' well-being near the end of life

Part I of this thesis aimed at describing patients' well-being and lived experience near the end of life through a characterization of patients' illness representations (chapter 3), coping (chapter 4) and quality of life (chapter 5).

We found that patients with advanced cancer who hold negative illness representations experience a worse quality of life (chapter 3). This association has previously been described in other patient groups,[1,2] but the underlying mechanisms were unclear. We were able to decompose this complex relationship and found that symptoms of anxiety and depression mediate the association between illness representations and quality of life (41-87% and 39-69%, respectively). Patients with negative illness representations were at increased risk of developing symptoms of depression and anxiety, which ultimately contributed to a worse quality of life. The mediating effect was stronger for some illness representations than for others. It was strongest for patients who feel that their illness has severe effects and outcomes on their life (illness representation 'Consequences'), for patients who (overly) attribute experienced symptoms to their illness ('Identity') and for patients who are very concerned about their situation ('Concern').

Eventually, patients' illness representations guide their coping efforts.[3,4] Across six European countries we found that patients with advanced cancer score higher on Acceptance and Problem-focused coping than on Denial (chapter 4). However, rather than using a single coping strategy, patients rely on several coping strategies, such as Acceptance in combination with Problem-focused coping or Problem-focused coping combined with Denial. We also found that the use of coping strategies differs between various sociodemographic and clinical subpopulations and between countries. Older patients tend to use Denial more than their younger counterparts, probably related to a higher tendency of keeping feelings to themselves.[5] Likewise, we found that patients in Italy and Denmark score higher on Denial than patients in the other countries, which we connected to a general reluctance to talk about death in these countries.[6] Furthermore, we found that higher educated patients use Acceptance more strongly than patients with lower education. Higher education has been linked to more communication and involvement in end of life decision-making[7] and we hypothesized that increased involvement in medical decision-making combined with presumably higher cognitive abilities may enable patients with higher education to manage the multiple demands of a terminal disease better, which contributes to the use of Acceptance. The WHO performance status was the only clinical variable that influenced coping strategies. Patients with a worse WHO performance status (1 or 2) score lower on Problem-focused coping that patients who are fully active and do not experience restrictions. We attributed this finding to the behavioral efforts that are linked to Problem-focused coping,[8] which might become more challenging when patients' physical abilities decline.

An often used outcome measure for the evaluation of healthcare interventions is quality of life.[9] We investigated an innovative way of measuring quality of life, using item banks (chapter 5). We found that using questionnaire items that are tailored to patients' individual characteristics gives a more precise and efficient estimate of patients' quality of life. Consequently, the customized questionnaire allows for a smaller sample size without reducing power.

Patients' preferences near the end of life

Part II of this thesis focused on the experiences of patients and healthcare professionals with advance care planning (chapters 6 and 7) and the stability of patients' treatment preferences (chapter 8).

We systematically searched electronic databases for studies on experiences with advance care planning of patients with a life-threatening or life-limiting disease (chapter 6). We found that patients often experience ambivalent feelings during advance care planning conversations. These feelings vary from being distressed and experiencing the conversations as difficult, to perceiving them as informative and helpful. Ambivalence was also observed in patients' level of readiness. While readiness is perceived to be a prerequisite for engaging in advance care planning, readiness has also been observed to increase throughout these conversations. We conclude that advance care planning can be a meaningful experience if patents feel comfortable to open up about their goals and preferences. Patients should feel encouraged to ask questions in order to plan for their current and future medical care.

Our second systematic review focused on advance care planning for patients with chronic respiratory diseases (chapter 7). We found that patients are generally interested in discussing end of life care preferences. Despite of healthcare professionals sharing this interest and seeing the added value of advance care planning, the uptake of advance care planning is low. In an effort to support healthcare professionals in engaging in advance care planning, we identified several barriers and facilitators. An essential, yet complex, factor is the identification of the right moment for having these conversations.

Related to this is the question of the stability of patients' treatment preferences (chapter 8). While we found that most patients with advanced cancer and a life-expectancy of ≤ 6 months have stable treatment preferences, a considerable group of patients change their preferences within a time interval of four months. Change in treatment preferences was not specific into a certain direction (life-prolonging care versus comfort care). Furthermore, change could not be predicted by sociodemographic and clinical characteristics or initial treatment preference. However, patients who do not describe their current health status as terminal were more prone of changing their treatment preferences.

METHODOLOGICAL CONSIDERATIONS

Throughout this thesis different methodologies were used to address the aims and objectives, among which the analysis of cross-sectional data collected through questionnaires, prospective observational data and systematic literature reviews. In the following paragraph considerations on these methods will be discussed. This brief discussion is supposed to be understood in addition to and extending the limitations and strengths discussed in the previous chapters.

In chapters 3, 4 and 5 we conducted secondary analyses of cross-sectional data. Secondary analyses refer to the analysis of data that were collected for another primary aim, which makes these analyses very efficient, both concerning time as well as resources.[10] Besides, using these data acknowledges the time and energy patients invested into filling out questionnaires. This is particularly important when conducting research near the end of life, a phase in which participation in research projects can be a burdening experience for patients with a fragile condition.[11] Secondary analyses are also socially valuable, considering that many research projects are financially supported by non-profit bodies, such as national governments or cancer societies. Thus, leaving as little unused data as possible through secondary analyses is a responsible and efficient way of increasing knowledge.

In this thesis, the secondary analyses were used to describe the patients' well-being (chapters 3, 4 and 5) and investigate underlying mechanisms (chapter 3). However, while cross-sectional data can provide an accurate and valuable description of certain outcomes, such as illness representations or coping, the main disadvantage is that these analyses do not allow drawing conclusions on causality. Particularly for the study on illness representations (chapter 3) longitudinal studies would enable researchers to extend the findings on observed associations towards causal relationships. We therefore would be interested to see if future research could replicate these findings with longitudinal data and verify the direction of the association we hypothesized. The same applies to the study on coping strategies (chapter 4), which would benefit from looking at the development of coping strategies over time and at coping strategies as an effect of interventions (e.g. on communication near the end of life). Similarly, longitudinal data would enable researchers to validate and extend the findings on the improved way of measuring quality of life (chapter 5) through comparing the questionnaire's ability of detecting changes in quality of life over time.

The study on the stability of treatment preferences (chapter 8) was based on secondary analyses of prospective observational data. One drawback of this study, possibly inherent to conducting research with patients nearing their end of life, is loss to follow-up due to deterioration of the disease and death.[12,13] High attrition rates can lead to selection bias and may limit the strength of evidence due to loss of power. Accounting for drop-out in power calculations and making realistic estimations of the response rates of patients is therefore important, particularly in trials with vulnerable patients.

The descriptions of patients' experiences with advance care planning (chapter 6) and practice of advance care planning in chronic respiratory diseases (chapter 7) were based on systematic reviews, supposedly the strongest form of medical evidence.[14] However, systematic reviews depend on the quality of their included studies and are therefore subject to the same biases as their included studies.[14] We tried to account for that by conducting thorough quality assessments of all included studies and highlight the quality of studies in the interpretation of the results. This hopefully aids the reader in forming his/ her own judgment on the strength of the presented evidence.

REFLECTION: CARE AND COMMUNICATION NEAR THE END OF LIFE

While death ultimately occurs due to the cessation of biological functions, dying is certainly not a strictly medical event.[15] A recurring theme during this thesis is the individual and multi-dimensional way patients experience their illness and the last phase of their life. To account for these individual experiences, the National Academy of Medicine recommends that high-quality care near the end of life should preeminently be patient-centered, acknowledging the medical, social, psychological and spiritual dimension of patients.[15]

Patient-centered medicine was preceded by disease-oriented medicine, a way of thinking that focused on the localization and diagnosis of a localizable disease.[16] Patient-centered medicine extended this approach towards studying and understanding the person and his or her complaints as a whole in order to reach an 'overall diagnosis'.[16] Related to this way of medical thinking is the biopsychosocial model, which includes interacting biological, psychological and social dimensions that are equally important and necessary for diagnosing and treating the patient.[17] Within the biopsychosocial model, the patient is seen as the expert on the own disease and symptoms.[17] The healthcare professional aims at understanding the patients' lived experience, including their values and preferences. At the same time the healthcare professional fulfills the role of the medical expert.[15] Ideally, the patient and healthcare professional combine their areas of expertise and jointly develop a customized and comprehensive care plan for the patient.[15]

While the paradigm of patient-centered care is not a strictly new way of medical thinking, it challenges healthcare professionals, since their training focuses on the biomedical aspects of care rather than psychosocial aspects.[18] Indeed, during consultations with patients newly diagnosed with breast cancer, 88% of all utterances by the oncologists were biomedical. The remaining 12% of utterances were equally divided between administrative and psychological notions.[18] If emotional concerns are not deliberately attended to, they may get lost since patients mainly express their concerns through indirect cues[19] and typically disclose just 40% of their emotional concerns.[20]

Advance care planning

Physicians are in a key position for communicating with patients about their values and well-being and can ensure that these topics are not undermined by biomedical aspects.[21] Advance care planning could provide a framework for healthcare professionals that can support them in engaging in conversations about patients' well-being and preferences. Instead of focusing on the disease and medical treatment options alone, advance care planning extends medical encounters towards the patient as a whole, with particular emphasis on the patients' concerns.[22] Due to its focus on the exploration of patients' health-related experiences, knowledge, concerns and personal values on the physical, psychological, social and spiritual domain,[22] advance care planning can be seen as a patient-centered care conversation.

The ideas and aims of advance care planning have received wide recognition. However, the form and methods of these conversations are not yet universally defined and there is no accepted standard on how and when to perform advance care planning. The right timing for engaging in these conversations also depends on the stability of treatment preferences.[23] We found that most patients with advanced cancer have stable treatment preferences, but for reasons we were unable to unravel some patients still change their preferences. The only influential factor we found was the description or understanding of the current health status (chapter 8). We therefore recommend to integrate questions on patients' illness understanding into advance care planning conversations. This might be even more important, since on average just 11 seconds (less than 1%) of the total patient-oncologist speaking time is spent on checking the patients' understanding of information on prognosis and biomedical issues.[24]

That being said, stable treatment preferences do not have to be a prerequisite for advance care planning. Most likely, (re)considering preferences and personal values in the light of (disease) progression is a natural and integral part of decision-making. Likewise, our review showed that ambivalence exists in attitudes towards advance care planning and readiness (chapter 6). Ideally, advance care planning is a dynamic and flexible process that creates a space in which patients can reflect openly on their values and preferences. Thinking about the own preferences and wishes may be new for patients and they might benefit from guidance and support during this process. Indeed, there is a discrepancy between feeling comfortable to discuss preferences and wishes and actual conversations; 70% of the general population in the United Kingdom say that they feel comfortable talking about death, however just about one in three respondents actually discusses their wishes.[25] Even though this number increases with age when conversations might become more relevant, still just 45% of 75+ years old people discussed their wishes and preferences.[25] In our review we found that patients generally preferred healthcare professionals to offer and open these advance care planning conversations (chapter 7). However, introducing advance care planning is a sensitive matter, since we found that patients with advanced, life-limiting diseases can also experience invitations for advance care planning interventions as confronting. In that case, questions and concerns about the severity of their situation and possible disease progression were triggered (chapter 6).

Based on these findings and in the light of patient-centered care, advance care planning might benefit from an approach which it is embedded in usual medical encounters. By doing so, advance care planning would adopt a process character with the goal of getting to know the patients' wishes and preferences through understanding their lived experience, instead of a distinct conversation focused on stating these wishes and preferences. This process approach would take away the barrier of having to start these conversations explicitly (chapter 7) and would allow for the development of and reflection upon individual (treatment) preferences.

Better care through better communication

Understanding advance care planning as a process that unfolds during medical encounters possibly requires a different style and focus of communication. Instead of an interview on preferences, an almost disease-oriented way of medical thinking, these encounters would be characterized by a focus on patients' concerns.[16] It is worthwhile to highlight the importance of this focus, given that fact that in only 28% of observed medical encounters patients were able to complete their initial statements of (health related) concerns towards their family physician.[26] The mean time for patients to express their concerns until the first physician redirection was 23 seconds.[26] Most redirections occurred after the first concern that was expressed by the patient.[26] Patients were mostly hindered from sharing their concerns by closed-ended questions of their physicians, absence of solicitation or physicians' statements (such as "that sounds serious").[26] Interestingly, completed and noncompleted patient statements took about the same time.[26]

The techniques of motivational interviewing might support healthcare professionals during their communication with patients near the end of life.[27] In the spirit of patient-centered medicine, the focus of healthcare professionals during motivational interviewing is to listen, rather than to intervene.[27] Carl Rogers, the inventor of this patient-centered approach, puts it as follows "*Real communication occurs, (…) when we listen with understanding. (…) It means to see the expressed idea and attitude from the other person's point of view, to sense how it feels for him, to achieve his frame of reference in regard to the thing he is talking about.*[28]

Motivational interviewing includes three principles.[27] The first principle is collaboration: healthcare professionals and patients work together as partners. The second principle is autonomy: healthcare professionals respect the patients' ability to make their own decisions. Patients are approached as autonomous human beings, with the freedom to make their own choices. The third principle is evocation: This principle includes the healthcare professionals' ability to support patients in reflecting on their internal motivations for a (treatment) preference.[27] Introducing these principles during medical encounters may stimulate patients in reflecting upon their wishes and preferences, and the underlying values, and could eventually inform healthcare professionals for developing and proposing a care plan that is consistent with the patients' values.

Acknowledging mortality

In our review on advance care planning in chronic respiratory diseases (chapter 7) healthcare professionals reported an ethos of 'cure at all costs' in medicine, which forms a barrier for them to engage in advance care planning.[29] Indeed, a recent comment of the Lancet Commission on the Value of Death pointed out that medicine continues to strive to keep patients with life-limiting illnesses alive, often beyond the point of benefit.[30] Similarly, healthcare professionals have been found to feel uncomfortable to discuss end of life care topics.[30] Two-thirds of general practitioners reported not feeling comfortable to talk to someone about their end of life wishes.[30] Interestingly, communication about end of life issues has not been found to be related to patients feeling more depressed or worried, neither to patients loosing hope, increased suffering or hastened death.[31]

Medical care strives for improvements in diagnostics and treatment and therefore acknowledging impending death in terminally ill patients might feel contradictory to these intensions. Acknowledging mortality could well be an essential element of successful end of life care and might take away one of the barriers for engagement in advance care planning (chapter 7). Philippe Ariès extensively reflected on the attitudes of people towards death throughout history.[32] He argued that death used to be generally accepted prior to the 17th century, when people were aware of their own death and prepared for it.[32] Throughout the years, the appreciation of death changed and by the end of the 20th century, society had adopted the concept of 'forbidden death', in which death is seen as something shameful and forbidden.[32] According to Ariès, we all seem to technically admit that we are mortal, however *"really, at heart we feel we are non-mortals"*.[32] In psychology, the so-called 'terror management theory' explains this arguable contradiction of knowing that we are mortal but not wanting to admit to it, by relating it to the basic psychological conflict of having a self-preservation instinct, whilst realizing that death is inevitable and cannot be controlled.[33]

Accepting the inevitable death of others and ourselves is therefore a complex matter.[33] Self-reflection can help to increase awareness of the personal mortality and mortality of patients. Eventually, this could help healthcare professionals to engage in conversations about treatment preferences in the last phase of life.[34]

CONCLUSION AND RECOMMENDATIONS

For clinical practice

Advance care planning has the potential to increase the accordance between patient preferences and actual care, and patients' satisfaction with care. We found that the patients' lived experience, their understanding of their illness and preferences are highly individual and dynamic. To account for these individual differences, advance care planning might be most efficient and patient-centered if understood as a process, embedded in medical encounters. We would recommend healthcare professionals to be alert for patients' emotional and health concerns, incorporate them in medical encounters and repeat these conversations regularly. We found that treatment preferences are not necessarily stable, therefore conversations and decision-making should account for this and allow preferences to develop throughout time. Physicians are in a good position to have advance care planning conversations and might benefit from additional communication skills that are focused on increasing self-reflection as well as a patient-centered way of communicating.

For research

The number of studies in the field of care and decision-making near the end of life has increased throughout the years and the field, both research and practice, has benefitted from many well-conducted projects. For future research, we recommend to invest in longitudinal studies on the development of psychological outcomes (such as illness representations and coping) throughout the illness trajectory. Ideally, outcome measures on the adaptiveness and impact of these psychological concepts are included in the studies. It would also be worthwhile to investigate how advance care planning can best be integrated into medical encounters. It is important to acknowledge and investigate the perspective of healthcare professionals, to focus on experienced facilitators and barriers, to understand the perspectives of patients and their loved ones during this process and to get insight in their needs and challenges.

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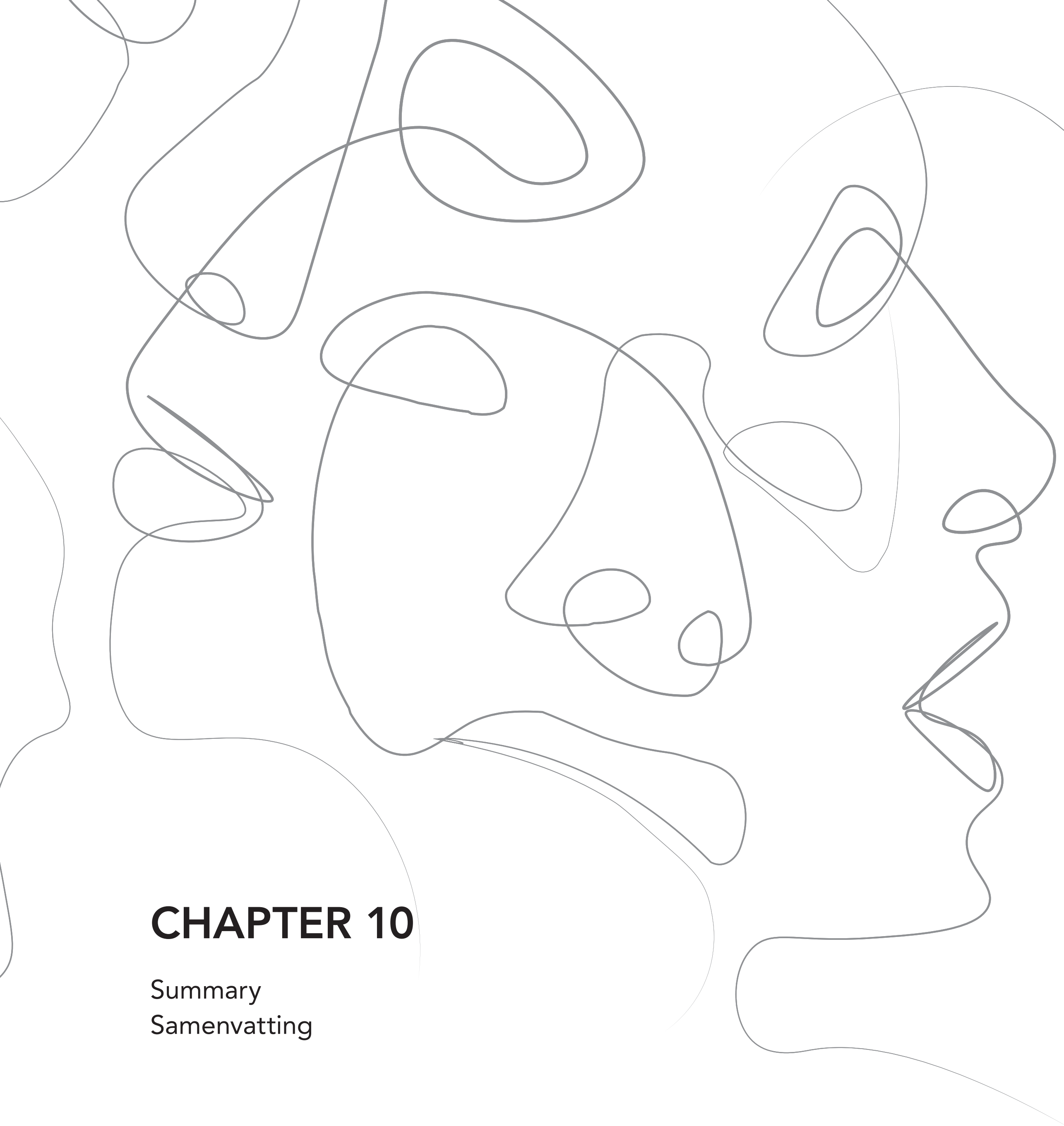


CHAPTER 10

Summary

Samenvatting

Chapter 1 outlines the background of this thesis. Due to advances in living conditions, diagnostics and treatment, the causes leading to death have changed. Nowadays, the end of life can often be anticipated and medical care can be planned in accordance with patients' preferences. These preferences are influenced by patients' lived experience. Three concepts of this lived experience were introduced, namely illness representations, coping and quality of life.

It has been suggested that the lived experience of patients influences medical decision-making. 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 was twofold:

To characterize 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 (Part I), and

To describe experiences of both patients and healthcare professionals with advance care planning. This includes an exploration of the stability of patients' treatment preferences (Part II).

Chapter 2 includes the study protocol of the ACTION study. This cluster randomised clinical trial investigated an advance care planning intervention in six European countries. In 2013 the ACTION trial started in Belgium, Denmark, Italy, the Netherlands, Slovenia and the United Kingdom. Between 2015 and 2018 patients with stage III or IV lung cancer and stage IV colorectal cancer were included in the trial. In the intervention hospitals, eligible patients were offered the ACTION Respecting Choices advance care planning intervention in addition to usual care. The scripted conversations were delivered by trained facilitators. In the control hospitals, patients received usual care. The primary endpoints were patients' emotional functioning and symptoms at 2.5 months post inclusion. Secondary endpoints included coping, patient satisfaction and shared decision-making. A complementary qualitative study was carried out to explore the lived experience of patients with the intervention. The ACTION trial is the first cluster randomised controlled trial on the effects of an advance care planning intervention in patients with advanced cancer in Europe.

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

Chapter 3 contains the results of secondary analyses of the PROFILES database, a registry for the study of the physical and psychosocial impact of cancer and its treatment in the Netherlands. We selected questionnaire data on illness representations, symptoms of anxiety and depression and quality of life of patients diagnosed with stage IV (non)Hodgkin lymphoma, colorectal cancer or thyroid cancer. We found that patients with negative illness representations, for instance patients who (overly) attribute their experienced symptoms to their illness (illness representation 'Identity') or patients who are very concerned about their illness ('Concern'), experience worse quality of life. We were able to decompose this association and found that symptoms of anxiety and depression mediate the association between illness representations and quality of life (41-87% and 39-69%, respectively). Thus, negative illness representations seemed to contribute to the development of symptoms of anxiety and depression, which are associated with worse quality of life. The strength of the association differed between illness representations. The effect was strongest when patients felt that their disease had severe negative effects and a strong negative influence on their life (illness representation ‘Consequences’), when patients (overly) attributed experienced symptoms to their disease (‘Identity’) and when patients were very concerned about their situation (‘Concern’). Based on these findings, we would like to encourage healthcare professionals to invest in getting to know patients’ illness representations, particularly because they can be in line with the patients’ actual medical situation, but may also involve a distorted interpretation of medical facts. We would also like to recommend that interventions aiming at improving the quality of life of patients with advanced cancer include psychotherapeutic elements and psychoeducation, interventions known to be effective in reducing symptoms of anxiety and depression in patients with advanced cancer.

Chapter 4 describes the results of a multilevel analysis based on a subset of the baseline data collected for the ACTION trial. We investigated Denial, Acceptance and Problem-focused coping and influencing factors in patients with stage III or IV lung cancer or stage IV colorectal cancer. We found that patients predominantly use Acceptance and Problem-focused coping. The coping strategies on dealing with advanced cancer do not seem to exclude each other, but are used simultaneously. The use of the individual coping strategies differs between various sociodemographic and clinical subpopulations and between countries. For instance, older patients tended to use Denial more than their younger counterparts, as did patients in Denmark and Italy in comparison to patients in the other countries. Higher educated patients were found to use Acceptance more than patients with lower education. The use of problem-focused coping was higher in patients with a WHO performance status of 1 or 2 than in patients with a WHO performance status of 0. We recommend taking these factors into account when developing tailored interventions to support patients’ coping strategies.

Chapter 5 includes the analyses of another subset of baseline data from the ACTION trial. We investigated a more efficient way of measuring emotional functioning of patients with advanced cancer. Using item banks, we constructed a questionnaire with tailored items to known characteristics of a certain patient group. We found that this customized questionnaire is a more efficient approach for measuring quality of life than using a generic questionnaire. The customized questionnaire showed a superior power to detect differences between groups. This allows for 20% to 34% smaller sample size to detect differences without reducing power.

Part II: Patients’ preferences near the end of life

Chapter 6 presents the results of a systematic review on the experiences with advance care planning of patients with a life-threatening or life-limiting illness. We identified 3555 possibly relevant articles and ultimately included 20 of them in our review. We found that advance care planning is a highly dynamic process. Patients are ambivalent about engaging in advance care planning, on the one hand, they feel reluctant to engage in the discussion of certain aspects, on the other hand they find the discussion of these aspects helpful. This ambivalence is also reflected in the readiness to engage in advance care planning. While a certain amount of patient readiness is necessary to start with advance care planning, readiness was also observed to increase during these conversations. In any case, for advance care planning to be a successful experience, patients need to feel comfortable to open up about their goals and preferences, which highlights the important position of healthcare professionals in creating this atmosphere.

Chapter 7 includes the results of a systematic review on advance care planning in patients with chronic respiratory diseases. We systematically searched 12 electronic databases for empirical studies on advance care planning in adults with chronic respiratory diseases. Of 2509 articles, 21 were eligible and included in the review. Despite of both patients and healthcare professionals being interested in advance care planning and seeing its added value, the uptake of these conversations was low. In an effort to support healthcare professionals in the engagement in advance care planning, we identified several barriers and facilitators related to the patient, the healthcare professional and the system. Barriers, among others, are the unpredictable disease course and difficult prognostication, a fear of taking away patients' hope and an ethos of 'cure at all costs'. Among the facilitating factors are patients' acceptance of their disease and continuity of care. An essential, yet complex, facilitating factor is to identify the right moment for having these conversations.

Chapter 8 describes the results of secondary analyses of the 'Coping with cancer 2' cohort study in the United States of America. We looked at the development of treatment preferences within a three month time interval of patients with advanced cancer and an oncologist estimated life-expectancy of ≤ 6 months. We found that most patients with advanced cancer have stable treatment preferences, still a considerable group of patients changes their preferences. The stability of treatment preferences could not be predicted by patient characteristics or quality of life. However, patients who do not describe their current health status as terminal seem to be more prone of changing their preferences. This brings us back to highlighting that advance care planning is indeed a dynamic process, in which the reconsideration of treatment preferences may naturally occur. We therefore recommend healthcare professionals to be aware of this process and therefore engage in these conversations timely, to allow patients to ponder over their treatment preferences and the implications thereof.

Chapter 9 contains the summary of the key findings of the conducted studies, a brief discussion of methodological considerations and a reflection on patient-centered care near the end of life. We conclude that dealing with an advanced, life-limiting disease is an individual and multi-dimensional process. Therefore, high-quality care near the end of life preferably integrates the medical, social, psychological and spiritual dimension and is preeminently be patient-centered. The conversation about preferences near the end of life can possibly benefit from merging with standard medical care. Consequently, these conversations would become a continuous process with the aim of getting to know the patient in all dimensions, rather than a one-time only event. A continuous process of conversations allows patients to form their preferences and to reconsider and share them with their healthcare professionals and loved ones. Self-reflection and coming to terms with one's own mortality can help healthcare professionals to overcome the barrier of introducing these conversations, particularly in a medical setting that may still be embedded in an ethos of ‘cure at all costs’.

NEDERLANDSE SAMENVATTING

Hoofdstuk 1 schetst de achtergrond van dit proefschrift. Door verbeteringen in de leefomstandigheden, diagnostiek en behandeling zijn de doodsoorzaken veranderd. Tegenwoordig kan het levenseinde vaak geanticipeerd worden, waardoor de medische zorg in overeenkomst met de voorkeuren van de patiënt gepland kan worden. Deze voorkeuren worden beïnvloed door de leefwereld van de patiënt. Drie concepten van deze leefwereld werden geïntroduceerd, namelijk ziekteperceptie, coping en kwaliteit van leven.

Het werd gesuggereerd dat de leefwereld van patiënten de medische besluitvorming beïnvloed. Voortbordurend op de ontwikkelingen in de vroegtijdige zorgplanning voor patiënten met een vergevorderde, levensbeperkende ziekte, en in een poging om gaten in onze kennis te dichten, was het doel van dit proefschrift tweeledig:

Het karakteriseren van de ziekteperceptie van patiënten, hun coping en kwaliteit van leven, in een poging om het welzijn van patiënten en hun leefwereld rond het levenseinde te begrijpen (Deel I), en

Het beschrijven van de ervaringen van zowel patiënten als ook zorgverleners met vroegtijdige zorgplanning. Dit houdt een verkenning van de stabiliteit van behandelvoorkeuren van patiënten in (Deel II).

Hoofdstuk 2 behoud het studie protocol van de ACTION studie. Deze cluster gerandomiseerde trial onderzoekt een vroegtijdige zorgplanningsinterventie in zes Europese landen. In 2013 is de ACTION trial in België, Denemarken, Italië, Nederland, Slovenië en het Verenigde Koningrijk gestart. Tussen 2015 en 2018 werden patiënten met stadium III of IV longkanker en stadium IV colorectale kanker in de trial geïncludeerd. In de interventie ziekenhuizen werd aan geschikte patiënten de ACTION *Respecting Choices* vroegtijdige zorgplanningsinterventie aangeboden, naast de gebruikelijke zorg. De gestructureerde gesprekken werden door getrainde gespreksondersteuners gegeven. In de controle ziekenhuizen ontvingen patiënten de gebruikelijke zorg. De primaire eindpunten waren het emotionele functioneren en de symptomen van patiënten na 2.5 maanden post-inclusie. Secundaire eindpunten hielden coping, patiëntentevredenheid en gedeeltelijke besluitvorming in. Een aanvullende kwalitatieve studie werd uitgevoerd om de leefwereld van patiënten met de interventie te verkennen. De ACTION trial is de eerste cluster gerandomiseerde gecontroleerde trial naar de effecten van een vroegtijdige zorgplanningsinterventie met patiënten met vergevorderde kanker in Europa.

Deel I: Het welzijn van patiënten rond het levenseinde

Hoofdstuk 3 bevat de resultaten van secundaire analyses van de PROFILES database, een register voor de studie van de fysieke en psychosociale invloed van kanker en de behandeling ervan in Nederland. We selecteerden vragenlijstdata over de ziekteperceptie, symptomen van angst en depressie en kwaliteit van leven van patiënten gediagnosticeerd met stadium IV (non)Hodgkin lymphoma, colorectale kanker en schildklierkanker. Wij vonden dat patiënten met een negatieve ziekteperceptie, bijvoorbeeld patiënten die (overmatig) hun ervaren symptomen aan hun ziekte toeschrijven (ziekteperceptie *'Identity'*) of patiënten die erg bezorgd zijn over hun ziekte (*'Concern'*), een slechtere kwaliteit van leven ervaren. Wij waren in staat om deze associatie te ontvlechten en ontdekten dat symptomen van angst en depressie de associatie tussen de ziektepercepties en kwaliteit van leven mediëren (respectievelijk 41-87% en 39-69%). Negatieve ziektepercepties lijken dus bij te dragen aan de ontwikkeling van symptomen van angst en depressie, hetgeen geassocieerd is met een slechtere kwaliteit van leven. De sterkte van de associatie verschilde tussen de ziektepercepties. Het effect was het sterkst wanneer patiënten van mening waren dat hun ziekte ernstige negatieve effecten en een sterke negatieve invloed op hun leven had (ziekteperceptie '*Consequences'*), wanneer patiënten ervaren symptomen (overmatig) aan hun ziekte toekenden ('*Identity'*) en wanneer patiënten erg bezorgd waren over hun situatie (*'Concern'*). Op basis van deze bevindingen willen wij zorgverleners aanmoedigen om te investeren in het bespreken van de ziektepercepties van patiënten, vooral omdat deze percepties in overeenstemming met de feitelijke medische situatie van de patiënt kunnen zijn, maar ook een vertekende interpretatie van medische feiten in kunnen houden. Wij willen ook aanbevelen dat interventies gericht op het verbeteren van de kwaliteit van leven van patiënten met vergevorderde kanker, psychotherapeutische elementen en psycho-educatie omvatten, interventies waarvan bekend is dat zij effectief zijn bij het verminderen van symptomen van angst en depressie bij patiënten met vergevorderde kanker.

Hoofdstuk 4 beschrijft de resultaten van een multilevel-analyse op basis van een subset van de baseline data die voor de ACTION-trial zijn verzameld. Wij onderzochten ontkenning, acceptatie en probleemgerichte coping en beïnvloedende factoren bij patiënten met stadium III of IV longkanker of stadium IV darmkanker. We ontdekten dat patiënten overwegend acceptatie en probleemgerichte coping gebruiken. De copingstrategieën voor het omgaan met vergevorderde kanker lijken elkaar niet uit te sluiten, maar worden tegelijkertijd gebruikt. Het gebruik van de individuele coping-strategieën verschilt tussen verschillende sociaal-demografische en klinische subpopulaties en tussen landen. Oudere patiënten neigden er bijvoorbeeld vaker toe om ontkenning te gebruiken dan jongere patiënten, hetzelfde gold voor patiënten in Denemarken en Italië in vergelijking met patiënten in de andere landen. Hoger opgeleide patiënten bleken acceptatie meer te gebruiken dan laagopgeleide patiënten. Het gebruik van probleemgerichte coping was hoger bij patiënten met een WHO performance status van 1 of 2 dan bij patiënten met een WHO performance status van 0. Wij adviseren om rekening te houden met deze factoren bij het ontwikkelen van interventies op maat die beogen de copingstrategieën van patiënten te ondersteunen.

Hoofdstuk 5 bevat de analyses van een andere subset van de baseline data uit de ACTION trial. Wij onderzochten een efficiëntere manier om het emotionele functioneren van patiënten met vergevorderde kanker te meten. Met behulp van *item banks* construeerden wij een vragenlijst met op maat gemaakte items gebaseerd op bekende kenmerken van een bepaalde patiëntengroep.

Wij vonden dat deze aangepaste vragenlijst een efficiëntere benadering is voor het meten van de kwaliteit van leven dan het gebruik van een generieke vragenlijst. De aangepaste vragenlijst toonde een superieur vermogen om verschillen tussen groepen te detecteren. Dit zorgt voor 20% tot 34% kleinere steekproefomvang om verschillen te detecteren zonder het verminderen van de statistische power.

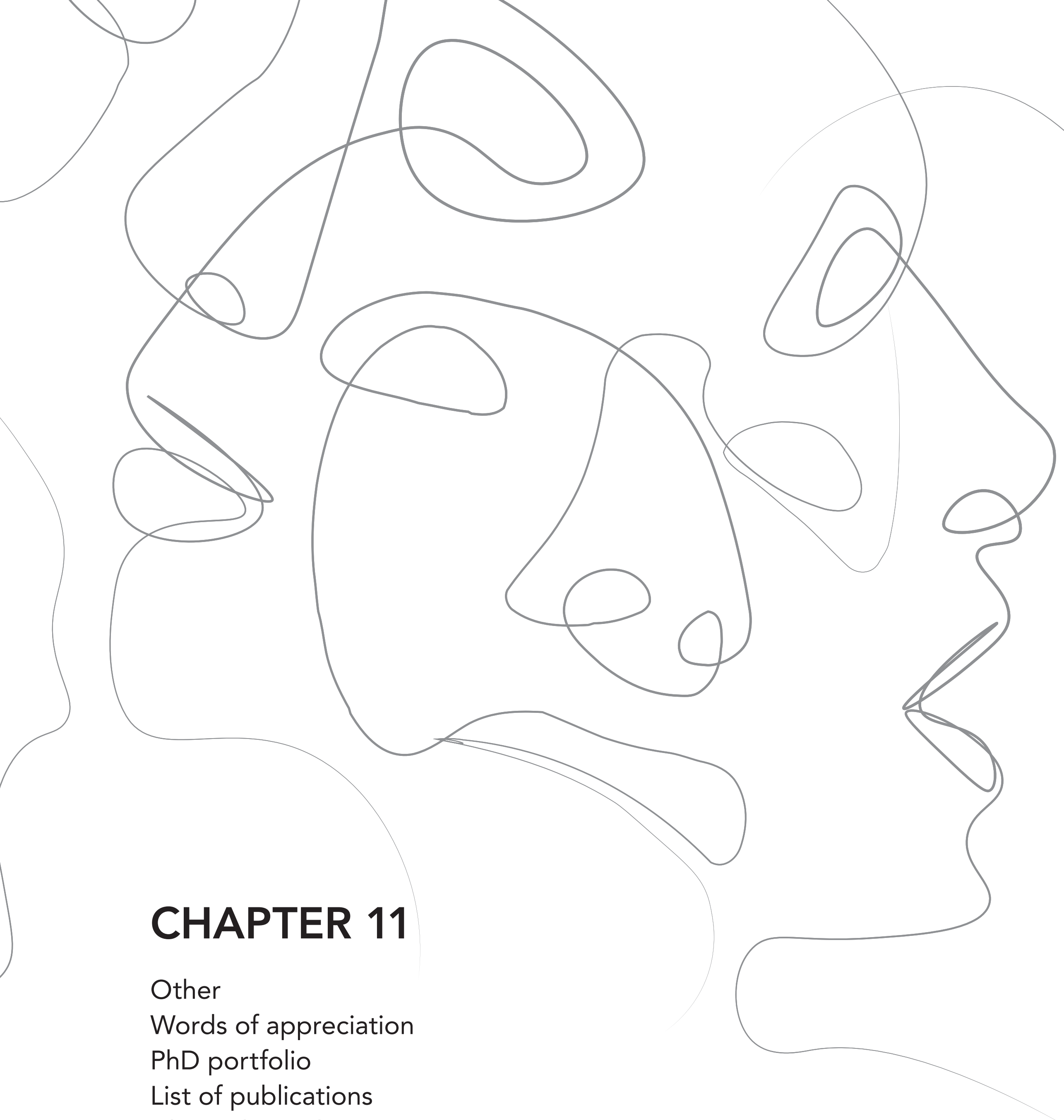
Deel II: De voorkeuren van patiënten rond het levenseinde

Hoofdstuk 6 presenteert de resultaten van een systematische review van de ervaringen met vroegtijdige zorgplanning bij patiënten met een levensbedreigende of levensbeperkende ziekte. Wij hebben 3555 mogelijk relevante artikelen geïdentificeerd en uiteindelijk 20 daarvan opgenomen in onze review. Wij vonden dat vroegtijdige zorgplanning een zeer dynamisch proces is. Patiënten zijn ambivalent tegenover vroegtijdige zorgplanning, aan de ene kant zijn zij terughoudend in het bespreken van bepaalde aspecten, aan de andere kant vinden zij een gesprek over deze aspecten nuttig. Deze ambivalentie wordt ook weerspiegeld in de bereidheid om deel te nemen aan vroegtijdige zorgplanning. Hoewel een zekere mate van bereidheid bij de patiënt noodzakelijk was om te beginnen met vroegtijdige zorgplanning, nam de bereidheid tijdens deze gesprekken ook toe. Om vroegtijdige zorgplanning een succesvolle ervaring te laten worden, moeten patiënten zich prettig voelen om open over hun doelen en voorkeuren te communiceren, wat de belangrijke positie van zorgverleners in het creëren van deze sfeer benadrukt.

Hoofdstuk 7 bevat de resultaten van een systematische review over vroegtijdige zorgplanning bij patiënten met chronische longziekten. Wij hebben 12 elektronische databanken systematisch doorzocht naar empirische studies naar vroegtijdige zorgplanning bij volwassenen met chronische longziekten. Van de 2509 artikelen kwamen 21 in aanmerking en werden opgenomen in de review. Ondanks het feit dat zowel patiënten als zorgverleners geïnteresseerd waren in vroegtijdige zorgplanning en de toegevoegde waarde ervan zagen, vonden deze gesprekken weinig plaats. In een poging om zorgverleners te ondersteunen bij vroegtijdige zorgplanning, hebben wij verschillende belemmerende en faciliterende factoren geïdentificeerd die betrekking hebben op de patiënt, de zorgverlener en het systeem. Belemmerende factoren zijn onder andere de onvoorspelbare ziekte en moeilijke prognose, een angst om de hoop van patiënten weg te nemen en een ethos van ‘genezing ten koste van alles’. Onder de faciliterende factoren zijn de acceptatie van de ziekte door patiënten en continuïteit van zorg. Een essentiële, maar complexe, faciliterende factor is het identificeren van het juiste moment om deze gesprekken te voeren.

Hoofdstuk 8 beschrijft de resultaten van secundaire analyses van de ‘*Coping with cancer 2*’cohort studie in de Verenigde Staten van Amerika. Wij keken naar de ontwikkeling van behandelvoorkeuren binnen een tijdsinterval van drie maanden bij patiënten met vergevorderde kanker en een door de oncoloog ingeschatte levensverwachting van minder dan 6 maanden. Wij vonden dat de meeste patiënten met vergevorderde kanker stabiele behandelvoorkeuren hebben, desondanks is er een aanzienlijke groep van patiënten die hun voorkeuren veranderen. De stabiliteit van behandelvoorkeuren kon niet voorspeld worden door patiëntenkenmerken of kwaliteit van leven. Echter, patiënten die hun huidige gezondheidstoestand niet als terminaal beschreven, waren vaker geneigd om hun voorkeuren aan te passen. Dat brengt ons terug bij het benadrukken dat vroegtijdige zorgplanning inderdaad een dynamisch proces is, waarbij het heroverwegen van behandelvoorkeuren een natuurlijk verschijnsel is. Wij raden zorgverleners daarom aan om zich bewust te zijn van dit proces en daarom deze gesprekken tijdig aan te gaan, zodat patiënten de tijd hebben om over hun behandelvoorkeuren en diens implicaties na te denken.

Hoofdstuk 9 houdt een samenvatting van de belangrijkste bevindingen van de uitgevoerde studies in, een korte discussie van methodologische overwegingen en een reflectie op patiëntgerichte zorg aan het levenseinde. Wij concluderen dat het omgaan met een vergevorderde, levensbeperkende ziekte een individueel en multidimensioneel proces is. Daarom is het wenselijk dat hoogwaardige zorg aan het levenseinde de medische, sociale, psychologische en spirituele dimensies integreert en, bij uitstek, patiëntgericht is. Het gesprek over voorkeuren aan het levenseinde zou er mogelijk van kunnen profiteren om ingebed te worden in de gewone medische zorg. Derhalve worden deze gesprekken een continu proces met het doel om de patiënt in al zijn of haar dimensies te leren kennen, in plaats van een eenmalig gesprek. Een continu proces van gesprekken geeft de patiënt de mogelijkheid om eigen voorkeuren te ontwikkelen en deze te heroverwegen en met hun zorgverleners en naasten te delen. Zelfreflectie en in het reine komen met de eigen mortaliteit kan zorgverleners helpen om de barrière te overkomen deze gesprekken te introduceren, met name in een medische setting die mogelijk nog steeds ingebed is in een ethos van “genezing ten koste van alles”.



CHAPTER 11

Other
Words of appreciation
PhD portfolio
List of publications
About the author

WORDS OF APPRECIATION

… and here we are. This little book just gives a glimpse of the work that has been invested and all the people who made an invaluable contribution to it. I will hold dear memories of all of them.

To start with, I hold a great gratitude towards all participants of our studies. Many of them were patients in the last months of their lives who invested their precious time and energy in our studies. Thank you so much.

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My ACTION buddy Marieke – you have achieved so much and can be very proud of your work. I will miss our calls, e-mails and your encouragements, and I am happy that our conversations will continue and have shifted from inclusion numbers and articles to review, to life in general and all its wonders.

Many thanks to the participating hospitals and all employees who did their very best for our study; special thanks to the facilitators who managed to squeeze this project into their busy schedules.

Thank you to Lia for spending so much time with me screening the patient lists. It is a pity that we realized I could actually do it alone, which was the end of our meetings – luckily not a definite one! I am glad our paths keep crossing and we continue to work together.

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The Erasmus MC is an inspiring environment and so are its employees. Tilleke, my Dutch mama, it was a privilege to learn from you. You truly are one of a kind; please never retire, every psychologist (every human being in fact!) should learn from you. Hanneke, thank you for being such a good colleague in the Psychiatry, I am happy we are still in touch.

My dear, dear lovely colleagues of the MBL group – what a great bunch of people you are! You have no idea what you all mean to me. I will always remember our meetings, social events, random talks on the corridor and your support throughout all this time. Anouk, we started together and it was so special to see you grow and succeed. Well done! Arianne, same for you, you work so hard and never forget to pay attention to the people around you. Cathy, thanks for New York and Lisbon (which was quite alright actually), Jet – Rotterdam's finest, Mirjam, Sophie and Veerle, you all mean so much to me!

Dear colleagues of MGZ, PhD life is not always easy, but as long as you were around, life was good! Many thanks to Valerie and David (for the support, sushi and *patat*!), Joost and Jeroen, Gianni, Marcel (a perfect day in St. Louis and everything since then), Leah (for being gym buddies, without ever going …), Jan (for all the walks through the park), Nikki, Hafez, Damir (not technically a MGZ-er but still; Paris, Paris – glad that you moved here!), Maryse (I loved seeing you grow and grow and grow, happy to have you as a friend), and many many more. Domino, Esther, Frank, Kevin, Suzette and Tiago, you were amazing roommates. The social committee, Farsia our very own leader, Rik, Veerle, Sophie, Branko, Erik – you are so much fun!

Thanks to my new colleagues at MPP and the pain department – every day I am looking forward to working with you! Special thanks to Jessica, who helped me with everything and was so welcoming and kind. Krishna, I couldn't be happier to have you as a colleague, please never start your residency so we can stay together forever!

The Persian group – thanks for all the lunches. Special thanks to Mohsen, Marzyeh and of course Amir and Yasaman. You are truly amazing.

One might forget, but there is a whole life outside of the EMC and particularly away from your loved ones, friends become your family. My girls, I am so proud of each and every one of you – I admire you all, the support and love you give, is amazing. I am looking forward to growing old with you. Jana – this PhD was worth it just because it brought us together! We went through a lot (getting lost in snow storms, sharing this US experience, champagne walks and so so many coffee meetings). I miss you a lot, your energy is radiant (Ps: could you please leave Germany and come back? Thanks). Kristina, you are the most humble, intelligent and stable person! I am happy that we started together in little Groningen and after many different places and countries we are neighbours again. I love your humour and no-nonsense point of view! Sasha, you are like my sister! I know I can always count on you, your energy and enthusiasm is contagious! You are so smart and hard working, you deserve the world.

Mahnaz and Azadeh, my Persian pearls, our coffee meetings and sharing the highs and lows of life was one of my most favourite parts of this journey. Nasim – my Persian better half on the other side of the world, I miss you! Minajoon, I am so proud of your journey, there is nothing you can't do! Nati, what was supposed to be a language exchange ended up in one of my most valuable friendships. You are one of a kind, I admire your passion and drive! I love how we stick together, through many different places and countries, and an eternal thanks to technology that lets us keep in touch no matter where we are. Florence, I have a lot of respect for how you juggle all demands in your life, you are amazing and so strong! And of course Jantje, my oldest friend, your friendship means the world to me. I admire your passion and strength, how you always seem to find a way for the impossible to work out and keep being sparkly, happy and optimistic.

My friends from my early Holland-days, Jorn and Jo-Janneke, I am so happy we are still in touch. Lianne, how special that we started in the cellars of the faculty building and look where we are now! You are doing amazingly. Vera, you inspire me and I cannot wait to start our very own practice.

Julian, for being there for me for so many years, thank you. Also many thanks to the familly Gretsch for being a second home. Thanks to my friends in Germany, die Jungs, particularly Heiko, Raphael, Steffen, Hauke and Kirill (for our *Brieffreundschaft*!). Ingeborg, for being so colourful and inspiring. Ana, you were the most amazing mentor, your friendship means a lot to me and Lisbon will forever be in my heart!

I am lucky to have two very special people as my paranymphs who brighten up my world. Farsia, you are the strongest, so smart and inspiring. The world would be boring and colourless without you! Thank you for your unconditional support, it means a lot to me! Rik, you are like my little brother, but foremost the most wonderful colleague and friend. Thank you for laughing about my jokes that are never funny. I love that we share the same passion for psychology. I am honoured to have you by my side.

Thank you to the Solano family, how beautiful to meet you and being greeted with so much love. Muchas gracias.

And then my own family – to start with those that always watch and guide me. Oma, maman bozorg, baba bozorg – like no one else you taught me unconditional love, to believe in yourself and see opportunities wherever you go. You showed me that cultures and languages do not matter and that we have to stick true to ourselves and never forget where we came from. You were, all in your own way, so inspiring and paved my way. I am looking up to you, I know you are there and I miss you every day. This one is for you.

My family - the bravest of them all, you are everything to me and I am nothing without you. Ahmad, your journey is very inspiring for me, as is your indestructible calmness (and I am well aware that I will never be able to reach your level). Cornelia, Katharina and Hannah, I love how creative, colourful and full of joy you are! Azi, you are so inspiring, so sharp and smart, I look up to you. Bega, same for you (but really, Bangkok? Wasn't there anything closer?). Susu, how could I possibly describe what you mean to me? You are so supportive, cool and smart. You have achieved so much and will always be a shining example for me. Torsten, you are so supportive and genuine, thank you for always sending me postcards and taking me along your journey! My little boys, Alexi and Leo, I have seen you grow up and now you are adults (life is crazy). I am so proud of you – go and discover the world (but don't go far, ok?)! Jan, my big brother, my rock, I always thought nothing could happen to me as long as you are around and it is still true even though we are far away from each other. Ich hab' dich lieb Jani! Tina, I am happy you are part of the family, you brought your very own (Badisch) light! And of course my parents, without them I would not be here. Thank you for you love and help, I know I can always rely on you. Mama, thank you for inspiring me and teaching me so much! You are amazing just the way you are. Baba, as a father, as a colleague, you mean everything to me. Your optimism is unique and your life philosophy tremendously inspiring. The world is a better place because of you.

And of course, Juan. Thank you for being there for me, for loving me the way I am and for sharing your precious time with me. You have this special capability of seeing the beauty in small things, never losing your sense of humour and supporting me unconditionally. The future is ours, te quiero mucho.

PHD PORTFOLIO

Name PhD student:	Lea Jasmina Jabbarian
Erasmus MC Department:	Public Health
Research school:	Netherlands Institute for Health Sciences (NIHES)
PhD period:	2013-2018
Promotors:	Prof.dr. A. van der Heide (Erasmus MC) Prof.dr. J.J.M. van Delden (UMC Utrecht)
Supervisors:	dr. I.J. Korfage (Erasmus MC) dr. J.A.C. Rietjens (Erasmus MC)

1. PhD training

General academic skills	Year	Workload
CPO course "Patient oriented research"	2014	0.2 ECTS
Systematic literature retrieval in PubMed	2014	0.2 ECTS
EndNote	2014	0.2 ECTS
Research integrity	2015	0.2 ECTS
Didactic training – part-qualification teaching, Erasmus MC	2015	0.2 ECTS
Time and project management course for PhD students	2016	1 ECTS
Basic course Rules and Organization for Clinical researchers (BROK ®)	2016	1.5 ECTS
Biomedical English writing and communication	2016	0.5 ECTS

Research skills	Year	Workload
Master of Science in Health Sciences, specialization epidemiology (NIHES) - In depth course: Suffering, death and palliative care	2014-2016	70 ECTS

Presentations	Year	Workload
Oral presentations		
Respecting Choices in the Netherlands, Symposium for junior researchers in proactive palliative care, Nijmegen, the Netherlands	2014	1 ECTS
The ACTION trial, ACP Research Networking Meeting, Calgary, Canada	2014	1 ECTS
Preferences and practices of patients with lung disease and their healthcare providers regarding advance care planning: a systematic review, Congress of the Society for Medical Decision Making, St. Louis, United States of America	2015	1 ECTS
The ACTION trial, Research meeting of the Department of Public health (Erasmus MC), Rotterdam, the Netherlands	2015	1 ECTS
The ACTION trial, Pre-congress seminar of the European Association for Palliative Care Research Network & European Palliative Care Research Centre, Dublin, Ireland	2016	1 ECTS
Advance care planning in pulmonology: a systematic review of preferences and practices, World research congress of the European Association for Palliative Care, Dublin, Ireland	2016	1 ECTS
Patients' experiences with advance care planning: a systematic review, World research congress of the European Association for Palliative Care, Dublin, Ireland	2016	1 ECTS
Advance care planning in pulmonology: a systematic review of preferences and practices, Research meeting of the Department of Public health (Erasmus MC), Rotterdam, the Netherlands	2016	1 ECTS

Advance care planning, 'Post-EAPC symposium', Utrecht, Netherlands	2016	1 ECTS
Illness representations, mental health and quality of life in patients with advanced cancer, IPOS World congress of Psycho-oncology, Berlin, Germany	2017	1 ECTS
Relatieve validiteit van de EORTC item bank voor emotioneel functioneren in de internationale ACTION studie, Nederlands-Vlaamse wetenschapsdagen palliative zorg, Amsterdam, the Netherlands	2017	1 ECTS
Challenges face during cross-cultural research, Infant, child and adolescent research group, Department of Public Health, Rotterdam, the Netherlands	2018	1 ECTS
Assessing emotional functioning with increased power, World research congress of the European Association for Palliative Care, Bern, Switzerland	2018	1 ECTS
The stability of treatment preferences among patients with advanced cancer, Advance Care Planning international conference, Rotterdam, the Netherlands	2019	1 ECTS
Coping strategies of patients with advanced lung or colorectal cancer in six European countries: Insights from the ACTION study, World congress of the European Association for Palliative Care, Berlin, Germany	2019	1 ECTS
Poster presentations		
Stability of treatment preferences of patients with advanced cancer, Congress of the Society for Medical Decision Making, Pittsburgh, United States of America	2017	0.3 ECTS
Multicenter cluster gerandomiseerde trial naar de effecten van een advance care planning interventie op de kwaliteit van leven van patiënten met kanker – de ACTION studie, Nederlands-Vlaamse wetenschapsdagen palliative zorg, Amsterdam, the Netherlands	2017	0.3 ECTS
The stability of treatment preferences among patients with advanced cancer, World research congress of the European Association for Palliative Care, Bern, Switzerland	2018	0.3 ECTS

Conferences, seminars and workshops	Year	Workload
Weekly research seminars of the Department of Public Health, Rotterdam, the Netherlands	2013-2018	3 ECTS
Biweekly meetings of the research group Medical Care and Decision-Making at the End of Life, Rotterdam, the Netherlands	2013-2018	1.5 ECTS
Symposium for junior researchers in proactive palliative care, Nijmegen, the Netherlands	2014	0.3 ECTS
ACP Research Networking Meeting, Calgary, Canada	2014	1.2 ECTS
Research meeting 'Expertisecentrum Palliatieve Zorg', Rotterdam, the Netherlands	2014	0.3 ECTS
Erasmus MC PhD Day	2014	0.3 ECTS
Nationaal Congres Palliatieve Zorg, Lunteren, the Netherlands	2014	0.9 ECTS
Research meeting on Elderly care, Rotterdam, the Netherlands	2015	0.3 ECTS
Congresses of the Society for Medical Decision Making	2015, 2017	2.4 ECTS
World congresses of the European Association for Palliative Care	2016, 2018, 2019	3.0 ECTS
IPOS World congress of Psycho-oncology	2017	1.2 ECTS
Weekly research seminars of the Center for Research on End-of-Life Care, Cornell University, New York City, United States of America	2017	2.4 ECTS
Advance Care Planning international conference	2019	0.9 ECTS

Grants		
Travel grant of the René Vogels Foundation (Dutch Society for Oncology)	2017	
Travel grants of the Stichting Erasmus Trustfonds	2015, 2017, 2018	

2. Teaching activities

Educational activities and lecturing	Year	Workload
Supervision of medical students – 'community projects', 3rd year curriculum Medicine, Erasmus MC	2015-2016	4 ECTS
Lecturer 'Lifestyle counselling and primary prevention' 3rd year curriculum Medicine, Erasmus MC	2015-2016	2 ECTS
Evaluating bachelor essays, 3rd year curriculum Medicine, Erasmus MC	2015-2016	4 ECTS

ABOUT THE AUTHOR

Lea Jasmina Jabbarian was born on the 18th of August 1989 in Lennestadt, Germany. After graduating from the Teletta-Gross-Gymnasium in Leer in 2009, she started studying Psychology at the Rijksuniversiteit in Groningen, the Netherlands. During her Bachelor programme she was selected for the *Honours College*. In 2011, she studied at the University of Lisbon, Portugal for 7 months during her Erasmus exchange programme.

In 2012 she started her Master in Clinical Psychology at the Erasmus University Rotterdam, which she finished in 2013, and was awarded the Thesis prize for the best master thesis in Psychology. In December 2013 she started her PhD at the Department of Public Health in the Erasmus MC under supervision of Prof.dr. Agnes van der Heide, Prof.dr. Hans van Delden, dr. Ida Korfage and dr. Judith Rietjens. The PhD was embedded in the international ACTION project, investigating an advance care planning intervention for patients with advanced cancer. During her PhD, she finished a Master in Health Sciences (Epidemiology) at the Netherlands Institute for Health Sciences. In 2017, she was awarded the René Vogels Travel Scholarship and worked for three months as a visiting researcher at the Center for Research at the End-of-Life at Cornell University in New York City, the United States of America, under supervision of Prof.dr. Holly Prigerson. In 2018, she worked two weeks at the University of Copenhagen, Denmark, under supervision of Prof.dr. Mogens Grønvold and dr. Anna Thit Johnsen.

In 2018 she started a new position in the Erasmus MC as a scientific lecturer at the Department of Medical Psychology and Psychotherapy and as a psychologist at the Center for Pain Medicine.

LIST OF PUBLICATIONS

This thesis

Rietjens JA, Korfage IJ, Dunleavy L, Preston NJ, **Jabbarian LJ**, Christensen CA, de Brito M, Bulli F, Caswell G, Červ B, van Delden J, Deliens L, Gorini G, Groenvold M, Houttekier D, Ingravallo F, Kars MC, Lunder U, Miccinesi G, Mimić A, Paci E, Payne S, Polinder S, Pollock K, Seymour J, Simonič A, Johnsen AT, Verkissen MN, de Vries E, Wilcock A, Zwakman M, van der Heide Pl A. Advance care planning--a multi-centre cluster randomised clinical trial: the research protocol of the ACTION study. BMC Cancer. 2016;16:264

Jabbarian LJ, Zwakman M, van der Heide A, Kars MC, Janssen DJA, van Delden JJ, Rietjens JAC, Korfage IJ. Advance care planning for patients with chronic respiratory diseases: a systematic review of preferences and practices. Thorax. 2018;73(3):222-230.

Zwakman M, **Jabbarian LJ**, van Delden J, van der Heide A, Korfage IJ, Pollock K, Rietjens J, Seymour J, Kars MC. Advance care planning: A systematic review about experiences of patients with a life-threatening or life-limiting illness. Palliat Med. 2018;32(8):1305-1321.

Jabbarian LJ, Groenvold M, Petersen MA, Christensen CA, Deliens L, van der Heide A, Kars MC, Miccinesi G, Payne S, Wilcock A, Korfage IJ; ACTION consortium. Assessing Emotional Functioning with Increased Power: Relative Validity of a Customized EORTC Short Form in the International ACTION Trial. Value Health. 2019;22(1):92-98.

Jabbarian LJ, Maciejewski RC, Maciejewski PK, Rietjens JA, Korfage IJ, van der Heide A, van Delden JJ, Prigerson HG. The Stability of Treatment Preferences among Patients with Advanced Cancer. J Pain Symptom Manage. 2019. pii: S0885-3924(19)30049-1.

Jabbarian LJ, Rietjens JAC, Mols, F, Oude Groeniger J, van der Heide A, Korfage IJ. Illness representations, mental health and quality of life in patients with advanced cancer. Submitted

Jabbarian LJ, Korfage IJ, Červ B, van Delden JJM, Deliens L, Miccinesi G, Payne S, Thit Johnsen A, Verkissen MN, Wilcock A, van der Heide A, Rietjens JAC, on behalf of the ACTION consortium. Coping strategies of patients with advanced lung or colorectal cancer in six European countries: Insights from the ACTION study. Under review

Other publications and manuscripts

Korfage IJ, Rietjens JA, Overbeek A, **Jabbarian LJ**, Billekens P, Hammes BJ, Hansen-van der Meer E, Polinder S, Severijnen J, Swart SJ, Witkamp FE, van der Heide A. A cluster randomized controlled trial on the effects and costs of advance care planning in elderly care: study protocol. BMC Geriatr. 2015;15:87

Overbeek A, Rietjens JAC, **Jabbarian LJ**, Severijnen J, Swart SJ, van der Heide A, Korfage IJ. Low patient activation levels in frail older adults: a cross-sectional study. BMC Geriatr. 2018;18(1):7.

Overbeek A, Korfage IJ, **Jabbarian LJ**, Billekens P, Hammes BJ, Polinder S, Severijnen J, Swart SJ, Witkamp FE, van der Heide A, Rietjens JAC. Advance Care Planning in Frail Older Adults: A Cluster Randomized Controlled Trial. J Am Geriatr Soc. 2018;66(6):1089-1095.

Korfage IJ, Carreras G, Arnfeldt C; Bramley L, Briggs L, Bulli F, Caswell G, Cerv B, van Delden J, Deliens L, Eecloo K, Gorini G, Groenvold M, Hammes B, Ingravallo F, **Jabbarian LJ**, Kars M, Kodba Čeh H, Lunder U, Miccinesi G, Mimic A, Ozbic P, Payne S, Polinder S, Pollock K, Preston N, Seymour J, Simonic A, Thit Johnsen A; Toccafondi A, Verkissen M, Wilcock A, Zwakman M, van der Heide A*, Rietjens J* Advance care planning in patients with advanced cancer: results from the European six country, cluster-randomized ACTION trial. *Submitted*

Zwakman M, van Delden JJM, Caswell G, Christensen CA, Deliens L, Ingravallo F, **Jabbarian LJ,** Johnsen AT, Korfage IJ, Mimic A, Preston NJ, Kars MC. Content analysis of Advance Directives completed by patients with advanced cancer as part of an Advance Care Planning intervention: insights gained from the ACTION trial. *Under review*

Zwakman M, Milota M, van der Heide A, **Jabbarian LJ**, Korfage IJ, Rietjens J, van Delden JJM, Kars MC. Patients' Readiness for Advance Care Planning Conversations: a Qualitative Study as part of the ACTION Study *Submitted*