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IN IT TOGETHER:

a dyadic approach to care experiences and quality of life
of patients with advanced cancer and their loved ones

Janneke van Roij



In it together:

a dyadic approach to care experiences and quality of life of
patients with advanced cancer and their loved ones

Proefschrift ter verkrijging van de graad van doctor aan Tilburg
University

op gezag van de rector magnificus, prof. dr. W.B.H.J. van de Donk, in
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CHAPTER 1

General introduction

GENERAL INTRODUCTION

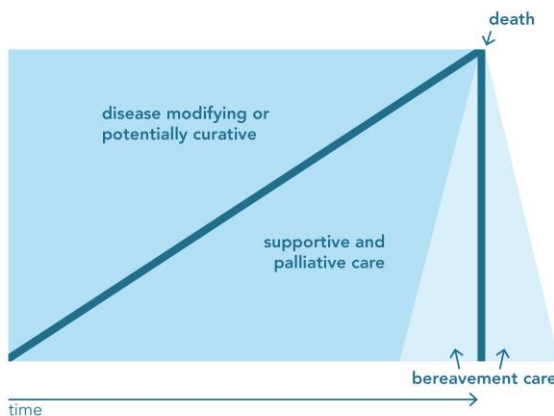
Each year, over 38.000 people are newly diagnosed with metastatic cancer in the Netherlands (1). In metastatic cancer, cancer cells travel from the primary tumor through blood or lymph nodes to distant organs or tissue to form a new tumor (i.e., stage IV cancer). Most patients with metastasized cancer are unlikely to be cured or controlled with treatment. Most of these incurable cancers are solid cancers that are spread to other parts of the body. Up to 65% of all newly diagnosed patients with cancer have to deal with metastasis during their disease trajectory (1) of whom 20% already have these (primary tumor) metastasis at time of diagnosis. Unfortunately, 50% of all patients with metastasis at time of diagnosis live six month or less after their diagnosis (1). Furthermore, the median survival of patients with metastatic cancer has increased just one month in the past ten years (1). However, there is much variation between cancer types. For instance, 84% of patients with metastasized prostate cancer is alive one year after diagnosis while only 8% of the patients with metastasized pancreatic cancer are. Despite all innovations within oncology, cancer is still one of the leading causes of death worldwide (2). In the Netherlands, more than 44.000 people die annually due to cancer (3). For patients with metastatic cancer, also referred to as 'advanced cancer' in the literature and in this thesis, palliative care is available.

Palliative care: a twin-track strategy

Palliative care is care for patients with an incurable illness and their relatives which aims to improve or maintain their quality of life (QoL) by focusing on reducing distress, symptoms, and discomfort and stimulation of wellbeing (4). Advanced cancer cannot be cured, but medical treatments may still be beneficial to slow down the growth of cancer cells and/or manage disease symptoms such as pain. Tumor directed

treatment and palliative care are initiated at the same time (Figure 1). The main focus of the treatment is initially on slowing down tumor growth and, as the disease progresses, gradually shifts towards supportive treatments with the aim to manage disease symptoms. Of all patients with advanced cancer who had metastasis at time of diagnosis in the Netherlands in 2018, more than half received systemic therapy (i.e., chemotherapy, hormone therapy, targeted therapy and/or immunotherapy). Most of the patients (35%) who received systemic therapy received chemotherapy, 22% of the patients received radiotherapy and targeted therapy or immunotherapy was applied in 16% of the patients. Finally, one third of the patients with advanced cancer at diagnosis did not receive tumor directed medical treatment at all (1). Besides medical treatments, patients or their relatives may also need help to cope with their illness and palliative care may be available for them. For relatives of patients with advanced cancer, bereavement care is available to support them before and after the death of the patient.

Figure 1. Integrated palliative care in oncology, adapted from Lynn and Adamson, 2003 (5)



Benefits of integrated palliative oncology care

Due to the gradual decline of disease modifying treatment, timely integration of palliative care in the illness trajectory of advanced cancer is essential. A wide body of research has underpinned the added value of early palliative care (6); a landmark study published in the New England Journal of Medicine demonstrated that early specialist palliative care (monthly consultations with a palliative care team) leads to better QoL in patients with metastatic non-small-cell lung cancer (7). The positive effects of palliative care on patient QoL and symptom burden have been confirmed and synthesized in a meta-analysis (8-18). Several studies have also demonstrated positive effects of palliative care on QoL in relatives of patients with advanced cancer (19-23). This growing recognition of palliative care as an essential integral aspect of standard oncology hospital care has prompted a range of national (24) and international guidelines to enhance the integration of palliative care in oncology (25, 26).

Integrated palliative oncology care in the Netherlands

In the Netherlands, palliative care is generalist care, meaning that all health care professionals are required to provide palliative care and are supported by specialist palliative care professionals if needed. In 2017 the Dutch Federation of Oncologic Specialties (SONCOS) came with a professional standard which stated that every hospital in the Netherlands has to have a Palliative Care team (27). This norm set by SONCOS also stated specific quality demands related to the formation and educational background of the team, the availability of the team for medical specialists and general practitioners and more. In 2018 the Dutch Quality Framework of Palliative Care was developed to provide guidelines for physicians regarding the organization and implementation of palliative care (24).

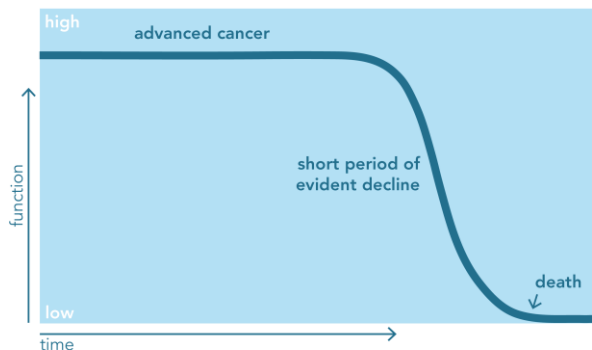
Despite this rapid development of guidelines and frameworks, palliative care is still often initiated relatively late. A survey among Dutch hospitals in 2018 showed that in hospitals palliative care is initiated only weeks before the death of the patient (28). For specialist palliative care (there is yet no consensus on the definition of specialist palliative care in the Netherlands), the availability of multidisciplinary specialist palliative care consultation teams (PCTs) are mandatory, but those are consulted too little and often too late for patients with incurable cancer and their relatives (29). Besides standards and guidelines, timely identification of patients or relatives with palliative care needs and will facilitate better integration of generalist palliative care into oncology (30).

Quality of life of patients with advanced cancer

Information regarding the impact of care on QoL of patients with advanced cancer in the Netherlands is lacking. For instance, it remains unclear which aspects of care are important for the QoL of patients and/or for their relatives. (31, 32). QoL is the "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." (12). QoL is a broad concept that includes physical, psychological, social, and spiritual wellbeing. The illness trajectory of patients with advanced cancer is best explained by a relative good physical health followed by a short period of evident decline and a foreseen death (Figure 2). During the course of their illness, patients with advanced cancer may experience symptoms such as pain, fatigue, dyspnea, loss of cognitive functioning, loss of appetite or nausea (32). Patients may also experience emotional distress (34-36) or depressive symptoms (37, 38). Distress due to prognostic uncertainty (39), preparatory grief (40), and death anxiety (41) are also common in patients with advanced cancer (42, 43). Traditionally, patients are the main focus

in clinical practice and research. This is unfortunate as patients cannot be fully understood without taking their social context into account.

Figure 2. Illness trajectory of advanced cancer, adapted from Lynn and Adamson, 2003 (5)



Relatives: having cancer together

Relatives are also a focus of palliative care because the patients' diagnosis of advanced cancer is also distressing for them. Care for patients with advanced cancer is predominantly placed on their relatives. Relatives are often involved in the practical care of the patients and may participate in conversations with the patient and health care professionals about treatment and medical decisions. Informal caregiving can lead to feelings of worth, purpose, emotional closeness and satisfaction in relatives (44, 45). Relatives often also provide emotional support to the patient and may have concerns about the loss of their spouse and life thereafter themselves (46, 47). Research shows that spousal caregivers often fail to address their own needs and feelings while providing support for the patient (48-50). Other research also shows that relatives are at risk for psychological, physical, and social morbidities due to their caregiving role and increasing caregiving demands throughout the cancer trajectory (51-

54). Research has also shown that distress experienced by patients and relatives is interdependent, meaning that the distress of the patient may spill over to the relative and vice versa (55, 56). The relational interaction may especially be present in patients and their partners due to their (marital) adjustment to advanced cancer (57, 58). For instance, a previous study found that the anxiety towards death, dysfunctional attitudes, and QoL were interdependent between patients with advanced cancer and their partners (59). Large studies that include both the patient and relative perspective and assess their interdependence are scarce. Patients and relatives coping with advanced cancer face many challenges together and we need to further unravel their interdependent relation in order to provide optimal palliative care.

Aims and outline of this thesis

The central goal of this thesis is to gain a better understanding of the experiences of patients with advanced cancer and that of their relatives in the Netherlands and their interdependent relationship regarding quality of care and QoL. The three aims were:

- 1) To explore care experiences and QoL of patients with advanced cancer and that of their relatives.
- 2) To assess the interdependent relationship between patients' and relatives' care experiences and QoL.
- 3) To assess relational aspects of couples coping with advanced cancer.

Increasing our knowledge about their experienced quality of care and life including their interdependence will ultimately provide opportunities to optimize care and improve QoL in patients with advanced cancer and their relatives.

The outline of the thesis is categorized in three parts: 1) Quality of care and life concept inventory, 2) Assessing quality of life and care experiences, and 3) a dyadic perspective among couples.

Part 1: Quality of care and life concept inventory

The starting point of this thesis is a qualitative study to explore what patients with advanced cancer and their informal caregivers find important regarding health care and their QoL. Results from this qualitative study are described in chapter 2 and 3. Chapter 4 shows results from a systematic literature review that was conducted to assess how QoL is best measured in patients with advanced cancer. The qualitative study and systematic literature review are preparatory work leading to the study protocol of a quantitative study presented in the following chapter.

Part 2: Assessing quality of life and care experiences

Chapter 5 presents the study protocol of the eQuiPe study: a prospective longitudinal multicenter observational study that is conducted to assess experiences of patients with advanced cancer and their relatives on health care and QoL in the Netherlands. Chapter 6 provides an overview on how patients and their relatives experience care and shows which aspects of care are related to their own emotional functioning or their relatives' emotional functioning. Chapter 7 shows whether self-care and resilience in relatives of patients with advanced cancer may be related to the amount of caregiver burden they experience.

Part 3: A dyadic perspective among couples

Chapter 8 describes the dyadic coping of patients with advanced cancer and their partners. This chapter also shows to what extent satisfaction with coping as a couple in patients and partners is associated with their emotional functioning. Chapter 9 presents how sexuality and feelings of

closeness among couples is related while taking each other's perspective into account.

References

1. IKNL. Uitgezaaide kanker in beeld. 2020.
2. WHO. Leading cause of death. <http://www.who.int/mediacentre/factsheets/fs297/en/> Last accessed 4 August 2020.
3. kanker Co. Deceased after cancer. www.cijfersoverkankernl.nl. Last accessed 4 August 2020.
4. WHO. Definition palliative care. <http://www.who.int/cancer/palliative/definition/en/> . Last accessed November 23 2016. 2002.
5. Lynn J, Adamson DM. Living well at the end of life. Adapting health care to serious chronic illness in old age. Washington: Rand Health, 2003.
6. Kaasa S, Loge JH, Aapro M, Albrecht T, Anderson R, Bruera E, et al. Integration of oncology and palliative care: a Lancet Oncology Commission. *Lancet Oncol*. 2018;19(11):e588-e653.
7. Temel JS, Greer JA, Muzikansky A, Gallagher ER, Admane S, Jackson VA, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med*. 2010;363(8):733-42.
8. Temel JS, Greer JA, El-Jawahri A, Pirl WF, Park ER, Jackson VA, et al. Effects of Early Integrated Palliative Care in Patients With Lung and GI Cancer: A Randomized Clinical Trial. *J Clin Oncol*. 2017;35(8):834-41.
9. Zimmermann C, Swami N, Krzyzanowska M, Hannon B, Leigh N, Oza A, et al. Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. *Lancet*. 2014;383(9930):1721-30.
10. Bakitas MA, Tosteson TD, Li Z, Lyons KD, Hull JG, Li Z, et al. Early Versus Delayed Initiation of Concurrent Palliative Oncology Care: Patient Outcomes in the ENABLE III Randomized Controlled Trial. *J Clin Oncol*. 2015;33(13):1438-45.
11. Maltoni M, Scarpi E, Dall'Agata M, Schiavon S, Biasini C, Codeca C, et al. Systematic versus on-demand early palliative care: A

- randomised clinical trial assessing quality of care and treatment aggressiveness near the end of life. *Eur J Cancer*. 2016;69:110-8.
12. Groenvold M, Petersen MA, Damkier A, Neergaard MA, Nielsen JB, Pedersen L, et al. Randomised clinical trial of early specialist palliative care plus standard care versus standard care alone in patients with advanced cancer: The Danish Palliative Care Trial. *Palliat Med*. 2017;31(9):814-24.
 13. Vanbutsele G, Van Belle S, Surmont V, De Laat M, Colman R, Eecloo K, et al. The effect of early and systematic integration of palliative care in oncology on quality of life and health care use near the end of life: A randomised controlled trial. *Eur J Cancer*. 2020;124:186-93.
 14. El-Jawahri A, Greer JA, Temel JS. Does palliative care improve outcomes for patients with incurable illness? A review of the evidence. *J Support Oncol*. 2011;9(3):87-94.
 15. Davis MP, Temel JS, Balboni T, Glare P. A review of the trials which examine early integration of outpatient and home palliative care for patients with serious illnesses. *Ann Palliat Med*. 2015;4(3):99-121.
 16. Haun MW, Estel S, Rucker G, Friederich HC, Villalobos M, Thomas M, et al. Early palliative care for adults with advanced cancer. *Cochrane Database Syst Rev*. 2017;6:CD011129.
 17. Gaertner J, Siemens W, Meerpohl JJ, Antes G, Meffert C, Xander C, et al. Effect of specialist palliative care services on quality of life in adults with advanced incurable illness in hospital, hospice, or community settings: systematic review and meta-analysis. *BMJ*. 2017;357:j2925.
 18. Fulton JJ, LeBlanc TW, Cutson TM, Porter Starr KN, Kamal A, Ramos K, et al. Integrated outpatient palliative care for patients with advanced cancer: A systematic review and meta-analysis. *Palliat Med*. 2019;33(2):123-34.
 19. Kavalieratos D, Corbelli J, Zhang D, Dionne-Odom JN, Ernecoff NC, Hanmer J, et al. Association Between Palliative Care and Patient and Caregiver Outcomes: A Systematic Review and Meta-analysis. *JAMA*. 2016;316(20):2104-14.

20. El-Jawahri A, Greer JA, Pirl WF, Park ER, Jackson VA, Back AL, et al. Effects of Early Integrated Palliative Care on Caregivers of Patients with Lung and Gastrointestinal Cancer: A Randomized Clinical Trial. *Oncologist*. 2017;22(12):1528-34.
21. McDonald J, Swami N, Hannon B, Lo C, Pope A, Oza A, et al. Impact of early palliative care on caregivers of patients with advanced cancer: cluster randomised trial. *Ann Oncol*. 2017;28(1):163-8.
22. Dionne-Odom JN, Azuero A, Lyons KD, Hull JG, Tosteson T, Li Z, et al. Benefits of Early Versus Delayed Palliative Care to Informal Family Caregivers of Patients With Advanced Cancer: Outcomes From the ENABLE III Randomized Controlled Trial. *J Clin Oncol*. 2015;33(13):1446-52.
23. O'Hara RE, Hull JG, Lyons KD, Bakitas M, Hegel MT, Li Z, et al. Impact on caregiver burden of a patient-focused palliative care intervention for patients with advanced cancer. *Palliat Support Care*. 2010;8(4):395-404.
24. Palliatief TNCCOI. Kwaliteitskader palliatieve zorg Nederland. 2017.
25. Ferrell BR, Temel JS, Temin S, Alesi ER, Balboni TA, Basch EM, et al. Integration of Palliative Care Into Standard Oncology Care: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol*. 2017;35(1):96-112.
26. Jordan K, Aapro M, Kaasa S, Ripamonti CI, Scotte F, Strasser F, et al. European Society for Medical Oncology (ESMO) position paper on supportive and palliative care. *Ann Oncol*. 2018;29(1):36-43.
27. (SONCOS) SOS. Multidisciplinaire normering Oncologische Zorg in Nederland - SONCOS normeringsrapport versie 2 www.soncos.org. 2014.
28. PZNL. Palliatieve zorg in Nederlandse ziekenhuizen www.palliaweb.nl. 2019.
29. Brinkman-Stoppelenburg A, Witkamp FE, van Zuylen L, van der Rijt CCD, van der Heide A. Palliative care team consultation and quality of death and dying in a university hospital: A secondary analysis of a prospective study. *PLoS One*. 2018;13(8):e0201191.

30. Kamal AH, Bausewein C, Casarett DJ, Currow DC, Dudgeon DJ, Higginson IJ. Standards, Guidelines, and Quality Measures for Successful Specialty Palliative Care Integration Into Oncology: Current Approaches and Future Directions. *J Clin Oncol*. 2020;38(9):987-94.
31. Kim Y, Baker F, Spillers RL. Cancer caregivers' quality of life: effects of gender, relationship, and appraisal. *J Pain Symptom Manage*. 2007;34(3):294-304.
32. Northouse LL, Mood D, Templin T, Mellon S, George T. Couples' patterns of adjustment to colon cancer. *Soc Sci Med*. 2000;50(2):271-84.
33. Raijmakers NJH, Zijlstra M, van Roij J, Husson O, Oerlemans S, van de Poll-Franse LV. Health-related quality of life among cancer patients in their last year of life: results from the PROFILES registry. *Support Care Cancer*. 2018;26(10):3397-404.
34. Kissane DW, Clarke DM, Street AF. Demoralization syndrome--a relevant psychiatric diagnosis for palliative care. *J Palliat Care*. 2001;17(1):12-21.
35. Mitchell AJ, Chan M, Bhatti H, Halton M, Grassi L, Johansen C, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *Lancet Oncol*. 2011;12(2):160-74.
36. Singer S, Das-Munshi J, Brahler E. Prevalence of mental health conditions in cancer patients in acute care--a meta-analysis. *Ann Oncol*. 2010;21(5):925-30.
37. Pirl WF. Evidence report on the occurrence, assessment, and treatment of depression in cancer patients. *J Natl Cancer Inst Monogr*. 2004(32):32-9.
38. Stark D, Kiely M, Smith A, Velikova G, House A, Selby P. Anxiety disorders in cancer patients: their nature, associations, and relation to quality of life. *J Clin Oncol*. 2002;20(14):3137-48.

39. Medicine) Ilo. Dying in America: Improving quality and honoring individual preferences near the end of life. Washington, DC: The National Academies Press. 2015.
40. Periyakoil VS, Kraemer HC, Noda A, Moos R, Hallenbeck J, Webster M, et al. The development and initial validation of the Terminally Ill Grief or Depression Scale (TIGDS). *Int J Methods Psychiatr Res.* 2005;14(4):202-12.
41. Neel C, Lo C, Rydall A, Hales S, Rodin G. Determinants of death anxiety in patients with advanced cancer. *BMJ Support Palliat Care.* 2015;5(4):373-80.
42. Hotopf M, Chidgey J, Addington-Hall J, Ly KL. Depression in advanced disease: a systematic review Part 1. Prevalence and case finding. *Palliat Med.* 2002;16(2):81-97.
43. Delgado-Guay MO, Parsons HA, Li Z, Palmer LJ, Bruera E. Symptom distress, interventions, and outcomes of intensive care unit cancer patients referred to a palliative care consult team. *Cancer.* 2009;115(2):437-45.
44. Anderson EW, White KM. "It Has Changed My Life": An Exploration of Caregiver Experiences in Serious Illness. *Am J Hosp Palliat Care.* 2018;35(2):266-74.
45. LeSeure P, Chongkham-Ang S. The Experience of Caregivers Living with Cancer Patients: A Systematic Review and Meta-Synthesis. *J Pers Med.* 2015;5(4):406-39.
46. Thomas C, Morris SM, Harman JC. Companions through cancer: the care given by informal carers in cancer contexts. *Soc Sci Med.* 2002;54(4):529-44.
47. Maughan K, Heyman B, Matthews M. In the shadow of risk. How men cope with a partner's gynaecological cancer. *Int J Nurs Stud.* 2002;39(1):27-34.
48. Chung C, Hwang E. Couples' experiences of breast cancer in Korea: a descriptive qualitative study. *Cancer Nurs.* 2012;35(3):211-20.
49. Foster C, Myall M, Scott I, Sayers M, Brindle L, Cotterell P, et al. 'You can't say, "what about me?" I'm not the one with cancer':

- information and support needs of relatives. *Psychooncology*. 2015;24(6):705-11.
50. Lopez V, Copp G, Molassiotis A. Male caregivers of patients with breast and gynecologic cancer: experiences from caring for their spouses and partners. *Cancer Nurs*. 2012;35(6):402-10.
 51. Stenberg U, Ruland CM, Miaskowski C. Review of the literature on the effects of caring for a patient with cancer. *Psychooncology*. 2010;19(10):1013-25.
 52. Haley WE, LaMonde LA, Han B, Narramore S, Schonwetter R. Family caregiving in hospice: effects on psychological and health functioning among spousal caregivers of hospice patients with lung cancer or dementia. *Hosp J*. 2001;15(4):1-18.
 53. Kim Y, Carver CS, Shaffer KM, Gansler T, Cannady RS. Cancer caregiving predicts physical impairments: roles of earlier caregiving stress and being a spousal caregiver. *Cancer*. 2015;121(2):302-10.
 54. Li QP, Mak YW, Loke AY. Spouses' experience of caregiving for cancer patients: a literature review. *Int Nurs Rev*. 2013;60(2):178-87.
 55. Jacobs JM, Shaffer KM, Nipp RD, Fishbein JN, MacDonald J, El-Jawahri A, et al. Distress is Interdependent in Patients and Caregivers with Newly Diagnosed Incurable Cancers. *Ann Behav Med*. 2017;51(4):519-31.
 56. Streck BP, Wardell DW, LoBiondo-Wood G, Beauchamp JES. Interdependence of physical and psychological morbidity among patients with cancer and family caregivers: Review of the literature. *Psychooncology*. 2020;29(6):974-89.
 57. S DMP. What's Love Got to Do with It? *Journal of Couple & Relationship Therapy*. 2007;6(1-2):31-43.
 58. Traa MJ, De Vries J, Bodenmann G, Den Ouden BL. Dyadic coping and relationship functioning in couples coping with cancer: a systematic review. *Br J Health Psychol*. 2015;20(1):85-114.
 59. Lau BH, Wong DFK, Fung YL, Zhou J, Chan CLW, Chow AYM. Facing death alone or together? Investigating the interdependence of death anxiety, dysfunctional attitudes, and quality of life in patient-

caregiver dyads confronting lung cancer. *Psychooncology*. 2018;27(8):2045-51.

PART 1

Quality of care and life concept inventory

CHAPTER 2

Social consequences of advanced cancer in patients and their informal caregivers: a qualitative study

van Roij J, Brom L, Youssef-El Soud M, van de Poll-Franse L, Raijmakers
N

Supportive Care in Cancer 2019; 27: 1187–1195

Abstract

Purpose: Cancer threatens the social well-being of patients and their informal caregivers. Social life is even more profoundly affected in advanced diseases, but research on social consequences of advanced cancer is scarce. This study aims to explore social consequences of advanced cancer as experienced by patients and their informal caregivers.

Methods: Seven focus groups and seven in-depth semi-structured interviews with patients (n = 18) suffering from advanced cancer and their informal caregivers (n = 15) were conducted. Audiotapes were transcribed verbatim and open coded using a thematic analysis approach.

Results: Social consequences were categorized in three themes: "social engagement", "social identity", and "social network". Regarding social engagement, patients and informal caregivers said that they strive for normality by continuing their life as prior to the diagnosis, but experienced barriers in doing so. Regarding social identity, patients and informal caregivers reported feelings of social isolation. The social network became more transparent, and the value of social relations had increased since the diagnosis. Many experienced positive and negative shifts in the quantity and quality of their social relations.

Conclusions: Social consequences of advanced cancer are substantial. There appears to be a great risk of social isolation in which responses from social relations play an important role. Empowering patients and informal caregivers to discuss their experienced social consequences is beneficial. Creating awareness among healthcare professionals is essential as they provide social support and anticipate on social problems. Finally, educating social relations regarding the impact of advanced cancer and effective support methods may empower social support systems and reduce feelings of isolation.

Introduction

Maintaining or improving quality of life (QoL) is a crucial outcome of palliative care. There is much attention for the physical domain of QoL, but the other domains (i.e., emotional, spiritual, and social well-being) receive less attention [1]. Social well-being is important for overall QoL because we are social creatures; people have an innate need to feel connected to other people [2–4]. This connection is the essence of social well-being. Cancer and its treatment can seriously threaten social well-being [5, 6]. Pooled data from multiple studies showed that 45% of cancer patients reported high levels of social difficulty [7] such as problems in social relationships and support [6], feelings of social isolation [8], restriction in social activities [9], challenges in work [10], and responsibilities outside work [11]. Wright and colleagues [12] identified 32 social problems experienced by cancer patients in the following categories: managing at home, health and welfare services, finances, employment, legal matters, relationships, sexuality and body image, and recreation.

Cancer does not only affect patients, but also their social relations such as partners, friends, and family members. Social relations of patients, who often act as informal caregivers, can help patients cope with the illness' consequences. Providing informal care is a meaningful task, but it can also be burdensome [13]. Informal caregivers often experience social consequences as a result of their caring activities [14–16]. Moreover, they find it challenging to communicate about the cancer with their social relations [15, 16] and experience negative responses from social relations [14, 17]. Furthermore, informal caregivers appear to participate less in social activities [18, 19] due to feelings of guilt or worry when they are separated from the patient [20]. A recent review showed that informal caregivers also experience positive social consequences of caring for

someone with cancer such as an enhanced relationship with the patient [21].

A body of research on social consequences of cancer focused on cancer patients undergoing curative treatment or on cancer survivors. Patients with advanced cancer have received less attention. This is surprising because social life is even more affected in advanced cancer [7]. Patients with advanced cancer and their informal caregivers are confronted with proximity to death that often changes their perspective on life and influences their social life [22]. Advanced cancer may seriously threaten the social well-being of patients and informal caregivers. However, knowledge on social consequences of advanced cancer including the perspective of patients and their informal caregivers simultaneously is lacking. Therefore, this study aims to explore the social consequences of advanced cancer in patients and their informal caregivers.

Methods

Study design

This qualitative focus group study was embedded within a larger study on quality of life and quality of care as experienced by patients with advanced cancer and their informal caregivers (eQuiPe study (NTR6584)), conducted in the Netherlands.

Study population

Patients were eligible for inclusion if they were diagnosed with colorectal cancer (stage IV and at least two metastasis in liver, peritoneum or lung), lung cancer (stage IV), breast cancer (stage IV with at least visceral or brain metastasis), prostate cancer (stage IV and castration resistant), nonresectable pancreatic cancer, or nonresectable esophageal cancer. Both patients and informal caregivers were eligible if they were 18 years or older and understood the objective of the study. An informal caregiver

could participate regardless of patient participation and vice versa. Patients and informal caregivers were not eligible for inclusion if they had a poor expression of the Dutch language, they suffered from dementia, or they had a history of severe psychiatric illness.

Recruitment

Patients with advanced cancer and their informal caregivers were informed about the study by their treating physician to participate between January 2017 and June 2017 in six Dutch hospitals. The physician asked permission for a research team member to call the patient to give detailed information about the study, address questions, and invite them to participate. Subsequently, when patients and/or informal caregivers agreed to participate, they were invited for a focus group.

Study procedure

Participants were assigned to a focus group based on their availability, and patients and informal caregivers participated in separate focus groups to minimize response bias. A focus group was approximately 90 min and was facilitated by two researchers (JvR and LB). A moderator (JvR) asked the questions, probed, and made sure that all participants were heard, and an observer (LB) listed the proceedings during each focus group (supplement 1). Consecutively, all participants completed a self-administered questionnaire regarding socio-demographics. If participants were not willing to participate in a focus group, an individual interview was offered. Interviews were also conducted separately for patients and informal caregivers. Two patients only wanted to participate with their informal caregiver present during the interview. All focus groups and interviews were audiotaped. After data saturation was reached, no additional focus groups and interviews were organized.

Data analysis

All focus groups and interviews have been transcribed verbatim and

analyzed with content analysis using Atlas.ti version 7.5.15. Two researchers (NR and JvR) independently coded a randomly selected transcript and compared results to evaluate consensus. Transcripts were coded by the qualitative thematic analysis approach [23, 24]. Data was analyzed by the open coding procedure [25]. The procedure to confirm uniformity across researchers was repeated four times during data analysis phase. Quotes reflecting social consequences as experienced by patients and informal caregivers were included in the further analysis. Two researchers (JvR and NR) clustered the subcategories to identify main themes. To illustrate important results from the analysis, quotes have been presented followed by an alphanumeric code in brackets where P = patient, C = informal caregiver, FG = focus group, and IV = interview.

Results

In total, 18 patients and 15 informal caregivers participated in a focus group (n = 23) or in an interview (n = 10) (Fig. 1). Most patients had lung or colorectal cancer and informal caregivers were most often the patients' partners (Table 1).

Figure 1. Flowchart inclusion process

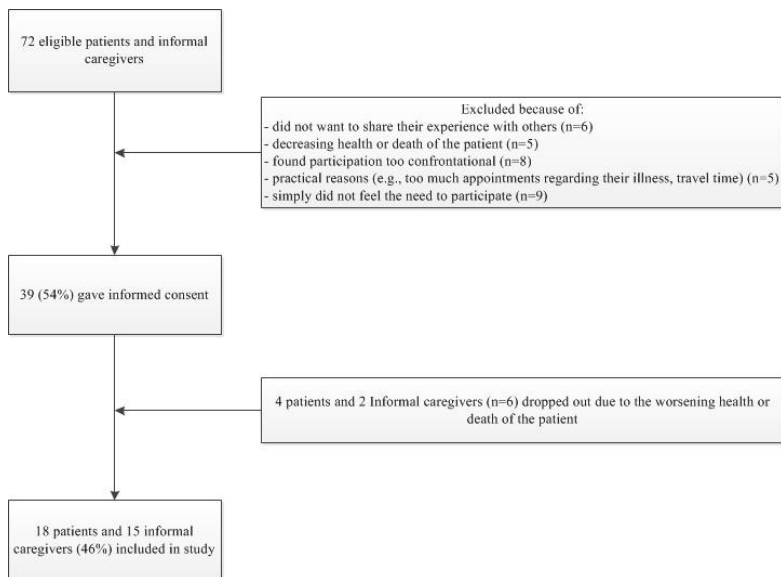


Table 1. Sociodemographic characteristics of the participants

	Patients with advanced cancer (n=18)	Informal caregivers (n=15)
Gender		
Male	9 (50%)	6 (40%)
Age		
Mean (range)	59 years (38-76)	58 years (40-76)
Education		
Low education	2 (11%)	4 (27%)
Middle education	6 (33%)	8 (53%)
High education	9 (50%)	3 (20%)
Missing	1 (6%)	-
Ethnicity		
Dutch	15 (83%)	15 (100%)
French	1 (6%)	-
Religious beliefs		
None	3 (17%)	5 (33%)
Protestants Christian, active	2 (11%)	-
Protestants Christian, not active	1 (6%)	1 (7%)
Roman Catholic, active	3 (17%)	1 (7%)
Roman Catholic, not active	9 (50%)	7 (47%)
Other, atheist	-	1 (7%)
Primary cancer site in patients		
Lung	8 (44%)	11 (73%)
Colorectal	6 (33%)	1 (7%)
Breast	2 (11%)	2 (13%)
Oesophagus	1 (6%)	1 (7%)
Prostate	1 (6%)	-
Time since patient's diagnosis		
1 year	5 (28%)	6 (40%)
2 years	6 (33%)	4 (27%)
≥3 years	5 (28%)	3 (20%)
missing	2 (11%)	2 (13%)
Relation with patient		
Partner	-	12 (80%)
Daughter		2 (13%)
Friend		1 (7%)

^a Low educational level = no education or primary school (e.g., LBO, VBO, LTS, LHNO, VMBO, MBO1), Intermediate educational level = lower general secondary education, vocational training or equivalent (e.g., MAVO, VMBO-t, MBO-kort, MBO, MTS, MEAO, HAVO, VWO), High educational level = pre-university education, high vocational training, university. (e.g., Hbo-bachelor, Hbo-master, wo-bachelor, wo-master, doctor).

"I have never been prepared for the social consequences. I found them much bigger and much more serious – so much more all-encompassing than I could ever have imagined". (P7-IV).

Social consequences of advanced cancer mentioned by patients and informal caregivers were categorized in three main themes: "social engagement", "social identity", and "social network" (Table 2).

Table 2. Social consequences of advanced cancer

Main theme	Subtheme	Category	Mentioned by ^a
Social engagement	Struggle to proceed as normal	Focus on continuing life prior to cancer	p, c
		More fun activities	p, c
		Caregiving role	c
	Missing out	Missing out on social events	p, c
		Consequences of missing out	p
		Work consequences	p, c
	Value of social activities	Daily social activities	p
		Personal social activities	c
Social identity	Cancer is central	Public possession	p
		One of them	c
		Social talk	p, c
		Seeking anonymity	c
	Being confronted with assumptions	Appearances	p, c
		Treated differently	p, c
		Isolation	p
		Stigma	c
Social network	Value of social relations	Meaning in life	p, c
		Instrumental	p
	Changes in the network	Loss of ties	p, c
		New ties	p, c
		Quality existing ties	p, c

	Perceived social support	Decreased support over time	p
		Delayed support	c
		Lack of emotional support	p, c
		Positive support	c

^a p=patients, c=informal caregivers.

Consequences for social engagement

Struggle to proceed with social life as normal

Both patients and informal caregivers emphasized the importance of continuing life prior the cancer diagnosis as much as possible; to strive for normality. “What it means to me is that I want to live my life just as I used to. And I want to make as few concessions as I possibly can to changing the way of life that I had. [...].The only thing I would want to change about my former life, is to fit more nice things into the way I live now”. (P3-IV). Patients explained that normality distracts them from the dominant feeling of being a patient. Being able to do the same things also gave them a feeling of control, satisfaction, meaning, and social embeddedness. Many patients mentioned adding more fun activities to their life as a consequence of prioritizing and the urge to escape from the situation. However, some informal caregivers mentioned that patients interpreted going on holiday with their children as a farewell because the reason for initiating this activity was their advanced cancer.

Many informal caregivers were aware that they would outlive the patient, and some informal caregivers felt the need to invest in a life after the patients’ death. Informal caregivers often explained how hard it was to combine their caregiving role with other responsibilities such as work and social activities: “At that time I made a conscious decision to continue playing golf; it is something that enables me to clear my head, and that is extremely important to me. But it is difficult, because you are away for

four or five hours at a time which is often rather too long for [PATIENT] [...]. At the beginning you stop going for a while. But I realise that if I don't go..., you really need to make some time for yourself. You can't be joined at the hip 24/7". (C7-IV).

Missing out

Patients' diagnosis and treatments interfered with their social life by physical or psychological complaints and medical appointments, and they often missed out on social events and resigned or reduced their job. Patients also explained how society is rushing by, while they were struggling with the uncertainty regarding their limited life expectation. Some patients planned social events ahead regardless of their condition, while others put their social life on hold, as illustrated here: "And even if it is just a weekend away or something like that... but I do find it difficult, everything is difficult actually, we are now planning a few things... you do try some things, but I can't promise anything because I don't know where I will be up to after the end of March". (P24-FG). Missing out on social events made patients feel socially excluded, as well as missing out on conversations about these events.

For informal caregivers, there were also major social consequences. Some resigned their job to spend as much time as possible with the patient, while others kept working as long as possible. Reasons for informal caregivers to continue working were financial pressure, satisfaction, and distraction. Many working informal caregivers mentioned that their career was on hold and that their professional functioning was negatively affected because their situation pushed them to their limits. Many found it difficult to continue work because they felt to be of more use at home. Others also mentioned that social relations were sometimes judgmental about continuing work.

The value of social activities

Many patients explained how daily activities in life gained value, the cancer diagnosis appeared to change the perspective on daily activities: "Do you know what you never do any more when you are as sick as I am? You don't just pop out to the shops on your own, or have a rummage in the bargain basement of a department store and end up buying a lipstick that you don't really need. I miss that". (P7-IV). One patient called it the "noise" or "playfulness" of life.

Some informal caregivers emphasized the increased value of social activities. However, most informal caregivers spend less time on social activities for multiple reasons: lack of time and energy due to the experienced caregiving burden, difficult to leave the patient due to feelings of selfishness, shame, worries, or being judged by others. Some also explained that social activities did not result in positive energy as it used to do. They explained how their current life did not feel as their own, and social activities became associated with freedom and self-control. Most patients stimulated their caregivers to engage in social activities: "It is very important to me that she continues to live her own life as far as possible. We do a lot of things together, but you don't have to do everything together. If she fancies going to town to buy a new dress or if she wants to have lunch with a friend, although actually she doesn't really want to go out and leave me. But I push her to go, I'm fine staying at home". (P21-IV).

Consequences for social identity

Cancer is central

Patients and informal caregivers often explained how cancer has become central to their social identity. Conversations with social relations were often focused on the illness and its treatments: "It got to the point where I was beginning to find it rather strange to be the focus of so much

attention, I felt like a freak or something; all of a sudden everyone wanted to know all about how things were going". (P39-FG). Some patients were also troubled when random people would ask them intimate questions about their health status.

Informal caregivers emphasized that many social relations feel uncomfortable to address the patient directly. Informal caregivers received many cancer-related questions from social relations that were tiresome. Some mentioned that social events were often a burden to them because of the confrontation with people asking questions about their situation. "I don't want to be the main attraction. Of course people look at you, and they do look at you. Or ask you things [...]. There is always a moment of hesitation, although not with the inner circle if you know what I mean. It is more with those people who aren't quite so close. There comes a time when you don't feel always feel comfortable with it, or strong enough. Or you really don't want to discuss it. You perceive it differently. It is a very serious business, not some light-hearted social occasion". (C32-IV). As a consequence, some informal caregivers mentioned that going on holiday would temporarily relieve them from their new social identity because they would be anonymous there.

Being confronted with assumptions regarding cancer patients

Many patients and informal caregivers emphasized that the patient's appearance can be misleading because people often assume you feel good when you look good. Many patients and informal caregivers found it confronting when people complimented the appearance of the patient or spoke negatively about it. Some informal caregivers mentioned that patients were keeping up appearances, because patients did not want to feel like a burden to others. According to informal caregivers, this behavior of the patient misrepresented their situation and made informal caregivers feel misunderstood by social relations.

Many patients found it difficult that their social identity changed due to cancer. Some informal caregivers also said that they were treated differently by social relations since the cancer diagnosis. "I've noticed that most people, my really good friends, find it difficult to disagree with me. Do you know what I mean? They treat you with kid gloves. And I am the type who always says 'Come on then! If you have a different opinion - come on, let's talk about it! But nowadays they are very guarded, and not happy with me tackling things head on. It isn't really helpful to me. So I invite them over and do it anyway". (C32-IV). Many patients also mentioned feelings of isolation due to exclusion from conversations about events. "And people just don't tell you things any more. Like accidentally discovering that your brother has been to Italy. Then you ask them why they didn't tell you, and they reply because you can't go on holiday anymore and they thought it might upset you". (P7-IV). Most informal caregivers mentioned that they helped their social relations to stop avoiding the patient and instruct them how to treat the patient and themselves. Some informal caregivers were very accepting towards socially awkward responses of their social relations, while others could not grasp the misconception of others.

Consequences for social network

The value of social relations

Most patients and informal caregivers spoke about an increased importance of social relationships. For patients, social connectedness has been giving meaning to their lives and brought support and enjoyment, but this was hindered by experienced social exclusion. "My friend has been to Spain recently and I told her how much I enjoy hearing her stories about it. And she said, I know you do but I find it difficult – us enjoying ourselves sitting in the sun enjoying a drink in Malaga. I feel so bad for you because you can't. And I told how upsetting it is when people just

don't tell you things any more. I can't go anywhere myself any more, but at least I can enjoy it through you". (P7-IV).

Changes in the network

Most patients and informal caregivers mentioned that they had lost social relations and that their social network also unexpectedly had expanded simultaneously by new social contacts and re-establishing contacts. "They have eaten here, they have drunk here, they have got drunk here, they have partied – they did it all, and now it's over. OK, if that's the way you want it, that's the way you'll get it. Then again, I have been back in contact with my brother for the past two years, not every day though". (P22-IV). Some informal caregivers said that they had less time to invest in relationships and to attend social events what has led to the loss of social relations. Both patients and informal caregivers also mentioned a decreased interest in superficial relations. Many patient and informal caregivers appreciated the increased transparency of their social network. They also mentioned an increased quality of certain relationships, supportive relations with healthcare professionals, and positive and negative changes in the relation between the patient and informal caregivers.

Perceived social support

Most patients experienced more support than they had anticipated. Patients and informal caregivers experienced mainly practical support, and emotional support was less available. "I used to be able to do everything, clean the whole house. Unfortunately those days are over. But two friends come every week to clean, they have set up a cleaning club especially for the purpose". (P4-FG). Many patients experienced a decrease in support over time. Contrary, most informal caregivers experienced an increase in support over time. "More people are beginning to ask me how I am, my colleagues too. The first three or four

months nobody bothers to ask. Because the person who is ill gets all the attention". (C19-FG).

Visits from social relations were sometimes burdensome, while other times, they were helpful. This depended on how social relations approached the situation. "I had a friend with cancer, I used to go and see her often and she always used to say that I came in full of life and ideas about we could do that day... it wasn't always immediately gloom and misery. She said, she didn't need anyone reminding her about that. It was so much better for her if someone suggested going out to lunch, or going for a walk or invited her over to eat with the family that evening. For people like her, these are definitely the best reactions to the situation". (C21-IV). Some patients appreciated peer support, while others found it confronting because it made them feel like a patient. Many informal caregivers informed social relations about the patient's status and instructed them how to treat the patient. Most informal caregivers mentioned that their mediating role was important for maintaining the patient's supportive social network. Most informal caregivers also provided support to their social relations regarding the situation.

Discussion

This qualitative study shows that social consequences are substantial for patients with advanced cancer and their informal caregivers. Major consequences have been found regarding social engagement, social identity, and social network. Several findings deserve particular attention. Firstly, patients and informal caregivers often mentioned their struggle to proceed with social life as prior to cancer, with an increased focus on fun activities. However, our study also reveals that patients and informal caregivers experience barriers in doing so. This coincides with Hasegawa et al.'s [26] findings that the top unmet need in advanced cancer patients

was not being able to do the usual things. Patients in our study mentioned symptom burden and lack of time due to medical appointments as barriers. This coincides with previous research showing that the diagnosis of advanced colorectal cancer takes a big part of life, leaving little time for patients to continue normal life activities [27].

Secondly, informal caregivers experienced less joy from social activities, and both patients and informal caregivers felt socially excluded to some extent. Knox et al. showed that young adults with advanced cancer became socially isolated because they felt misunderstood and alienated from the rest of the world [8]. In our study, patients, but especially caregivers, often provided instructions to social relations to reduce feelings of social isolation.

Thirdly, both patients and informal caregivers emphasized that the illness had become central in their social life. The social identification process appeared to be influenced by the strive for normality and social isolation. Many patients and informal caregivers resisted self-identification with cancer because they do not want to be treated differently by others and strive for normality. When patients and informal caregivers failed to reach normality, it appeared to be more likely that they are viewed and treated as cancer patients by their social network. Consequently, this further enhanced the self-identification with cancer. Harwood and Sparks [28] suggested that cancer identification also may have positive effects, such as the cognitive representation of a cancer patient as a strong and positive person [28]. However, such positive associations were not found in our study.

Fourth, patients and informal caregivers experienced structural changes in their social network. Mosher et al. [29] also described similar social network changes among patients with advanced colorectal cancer and their informal caregiver, including closer relationships, greater

appreciation for life, and clarified priorities. In our study, the perceived support was greater than anticipated. However, patients also reported a decrease in experienced support over time, while informal caregivers experienced the opposite. It is known that the absence of a supportive context has negative health consequences for patients [30] and informal caregivers [31] and that social support also has beneficial effects in patients with advanced cancer [32, 33] and informal caregivers [34]. However, it is important to differentiate between types of social support as in our study patients, and informal caregivers reported sufficient practical support but a lack of emotional support.

Lastly, our study shows that many social consequences were partly equivalent to experiences of other cancer patients or cancer survivors [6, 8–10]. Some similarities in social consequences are changes in social relations, problems with social support, and feelings of social isolation. However, some social consequences appear to be specific for advanced cancer; patients in our study worried greatly about leaving behind their loved ones. This affected them more than worries regarding their illness or impending death. Patients were worried about the emotional impact of their death and about the financial consequences for their loved ones. Many patients were also worried about being a burden to others. Previous research found that the perception of being a burden to others can have negative health effects [35]. Social consequences specific for informal caregivers of advanced cancer patients were the struggle to combine the caregiving role with normal life activities due to an increased responsibility regarding their own and, sometimes, their children's future after the patient's death. They also feel less supported, because the patient already checked-out of life which made them feel less supported.

A strength of this study is that both advanced cancer patients and their informal caregivers were included. Nevertheless, our study has some

limitations. First, selection bias is present because most participants were highly educated and no non-western patients participated in the study. It is known that there are barriers in including minorities in studies [36, 37]. Due to this selection bias, cultural and educational differences regarding beliefs about cancer may be absent, while it is known that these differences exist [38–40]. Second, the focus groups were smaller than anticipated (two to six participants per focus group), mainly due to death or decreasing health. Guidelines advise at least six participants in a focus group, because it may be difficult to get the group conversation going [41]. However, considering our vulnerable study population, our participants felt more comfortable to discuss private topics in a smaller group with plenty opportunity to contribute to the conversation. Furthermore, this number of participants appeared to have provided sufficient variation in experiences.

Practical implications

It is ironic that cancer is able to undermine the powerful resource of social relationships to cope with the illness, which may actually cause additional distress [42]. Empowering patients and their informal caregivers to discuss their feelings regarding social consequences may be beneficial. Suggestions to empower patients and their informal caregivers are via psychological support and by increasing societal awareness, via national campaigns or websites. Also, creating awareness among healthcare professionals regarding the social impact of advanced cancer is essential as they are able to address the topic, anticipate on social problems, and provide social support. Also, informing social relations regarding the impact of advanced cancer and effective support methods may empower social support systems and reduce feelings of isolation. Furthermore, a quantitative study should map the extent of social consequences among these patients and their informal caregivers.

Conclusions

Our results suggest that advanced cancer has substantial impact on social engagement, social identity, and social networks. Many patients and their informal caregivers engage less in social activities, their social identity shifts towards the disease, and they perceive many changes in their social network. Feelings of social exclusion appear to be inevitable.

References

1. Kamal AH, Gradison M, Maguire JM, Taylor D, Abernethy AP (2014) Quality measures for palliative care in patients with cancer: a systematic review. *J Oncol Pract* 10(4):281–287
2. Maslow AH (1943) A theory of human motivation. *Psychol Rev* 50(4):370–396
3. Baumeister RF, Leary MR (1995) The need to belong: desire for interpersonal attachments as a fundamental human motivation. *Psychol Bull* 117(3):497–529
4. Bowlby J (1969) Attachment and Loss. Volume 1, Attachment. Hogarth Press New York: Basic Books, London
5. Catt S, Starkings R, Shilling V, Fallowfield L (2017) Patient reported outcome measures of the impact of cancer on patients' everyday lives: a systematic review. *J Cancer Surviv* 11(2):211–232
6. Warner EL, Kent EE, Trevino KM, Parsons HM, Zebrack BJ, Kirchhoff AC (2016) Social well-being among adolescents and young adults with cancer: a systematic review. *Cancer* 122(7): 1029–1037
7. Wright P, Smith A, Booth L, Winterbottom A, Kiely M, Velikova G, Selby P (2005) Psychosocial difficulties, deprivation, and cancer: three questionnaire studies involving 609 cancer patients. *Brit J Cancer* 93(6):622–626
8. Knox MK, Hales S, Nissim R, Jung J, Lo C, Zimmermann C, Rodin G (2017) Lost and stranded: the experience of younger adults with advanced cancer. *Support Care Cancer* 25(2):399–407
9. Sodergren SC, Husson O, Robinson J et al (2017) Systematic review of the health-related quality of life issues facing adolescents and young adults with cancer. *Qual Life Res* 26(7):1659–1672
10. Malone M, Harris AL, Luscombe DK (1994) Assessment of the impact of cancer on work, recreation, home management and sleep using a general health status measure. *J R Soc Med* 87(7):386–389
11. Mackenzie CR (2014) 'It is hard for mums to put themselves first': how mothers diagnosed with breast cancer manage the sociological

boundaries between paid work, family and caring for the self. *Soc Sci Med* 117:96–106

12. Wright EP, Kiely MA, Lynch P, Cull A, Selby PJ (2002) Social problems in oncology. *Br J Cancer* 87(10):1099–1104
13. Kim Y, Schulz R (2008) Family caregivers' strains: comparative analysis of cancer caregiving with dementia, diabetes, and frail elderly caregiving. *J Aging Health* 20(5):483–503
14. Balfe M, Keohane K, O'Brien K et al (2016) Social networks, social support and social negativity: a qualitative study of head and neck cancer caregivers' experiences. *Eur J Cancer Care* 26(6)
15. Ewing G, Ngwenya N, Benson J, Gilligan D, Bailey S, Seymour J, Farquhar M (2016) Sharing news of a lung cancer diagnosis with adult family members and friends: a qualitative study to inform a supportive intervention. *Patient Educ Couns* 99(3):378–385
16. Wittenberg E, Borneman T, Koczywas M et al (2017) Cancer communication and family caregiver quality of life. *Behav Sci* 7(1):1–8
17. Litzelman K, Kent EE, Rowland JH (2016) Social factors in informal cancer caregivers: the interrelationships among social stressors, relationship quality, and family functioning in the CanCORS data set. *Cancer* 122(2):278–286
18. Mosher CE, Bakas T, Champion VL (2013) Physical health, mental health, and life changes among family caregivers of patients with lung cancer. *Oncol Nurs Forum* 40(1):53–61
19. Longo CJ, Fitch M, Deber RB, Williams AP (2006) Financial and family burden associated with cancer treatment in Ontario, Canada. *Support Care Cancer* 14(11):1077–1085
20. Girgis A, Lambert S, Johnson C, Waller A, Currow D (2013) Physical, psychosocial, relationship, and economic burden of caring for people with cancer: a review. *J Oncol Pract* 9(4):197–202
21. Li Q, Loke AY (2013) The positive aspects of caregiving for cancer patients: a critical review of the literature and directions for future research. *Psychooncology* 22(11):2399–2407

22. Shilling VM, Starkings R, Jenkins VA, Fallowfield L (2017) Uncertainty about the future for patients with advanced cancer and their informal caregivers: a qualitative view. *J Clin Oncol* 35(5):218
23. Braun V, Clarke V (2006) Using thematic analysis in psychology. *Qual Res Psychol* 3(2):77–101
24. Rennie DL (2012) Qualitative research as methodical hermeneutics. *Psychol Methods* 17(3):385–398
25. Strauss AL (1998) Basics of qualitative research: techniques and procedures for developing grounded theory. Sage, Thousand Oaks
26. Hasegawa T, Goto N, Matsumoto N, Sasaki Y, Ishiguro T, Kuzuya N, Sugiyama Y (2016) Prevalence of unmet needs and correlated factors in advanced-stage cancer patients receiving rehabilitation. *Support Care Cancer* 24(11):4761–4767
27. Sjövall K, Gunnars B, Olsson H, Thomé B (2011) Experiences of living with advanced colorectal cancer from two perspectives: inside and outside. *Eur J Oncol Nurs* 15(5):390–397
28. Harwood J, Sparks L (2003) Social identity and health: an intergroup communication approach to cancer. *Health Commun* 15(2): 145–159
29. Mosher CE, Adams RN, Helft PR, O’Neil BH, Shahda S, Rattray NA, Champion VL (2017) Positive changes among patients with advanced colorectal cancer and their family caregivers: a qualitative analysis. *Psychol Health* 32(1):94–109
30. Akechi T, Okuyama T, Sugawara Y, Nakano T, Shima Y, Uchitomi Y (2004) Major depression, adjustment disorders, and posttraumatic stress disorder in terminally ill cancer patients: associated and predictive factors. *J Clin Oncol* 22(10):1957–1965
31. Adelman RD, Tmanova LL, Delgado D, Dion S, Lachs MS (2014) Caregiver burden: a clinical review. *JAMA* 311(10):1052–1060
32. Colloca G, Colloca P (2016) The effects of social support on health related quality of life of patients with metastatic prostate cancer. *J Cancer Educ* 31(2):244–252

33. Dobrikova P, Pcolkova D, AlTurabi LK et al (2015) The effect of social support and meaning of life on the quality-of-life care for terminally ill patients. *Am J Hosp Palliat Care* 32(7):767–771
34. Goldstein NE, Concato J, Fried TR, Kasl SV, Johnson-Hurzeler R, Bradley EH (2004) Factors associated with caregiver burden among caregivers of terminally ill patients with cancer. *J Palliat Care* 20(1): 38–43
35. Tang ST, Chang WC, Chen JS, Su PJ, Hsieh CH, Chou WC (2014) Trajectory and predictors of quality of life during the dying process: roles of perceived sense of burden to others and posttraumatic growth. *Support Care Cancer* 22(11):2957–2964
36. Hudson SV, Momperousse D, Leventhal H (2005) Physician perspectives on cancer clinical trials and barriers to minority recruitment. *Cancer Control* 12(2):93–96
37. Ford JG, Howerton MW, Lai GY, Gary TL, Bolen S, Gibbons MC, Tilburt J, Baffi C, Tanpitukpongse TP, Wilson RF, Powe NR, Bass EB (2008) Barriers to recruiting underrepresented populations to cancer clinical trials: a systematic review. *Cancer* 112(2):228–242
38. Patel-Kerai G, Harcourt D, Rumsey N, Naqvi H, White P (2017) The psychosocial experiences of breast cancer amongst Black, South Asian and White survivors: do differences exist between ethnic groups? *Psycho-Oncology* 26(4):515–522
39. Vrinten C, Wardle J, Marlow LA (2016) Cancer fear and fatalism among ethnic minority women in the United Kingdom. *Br J Cancer* 114(5):597–604
40. Marcu A, Black G, Vedsted P, Lyratzopoulos G, Whitaker KL (2017) Educational differences in responses to breast cancer symptoms: a qualitative comparative study. *Br J Health Psychol* 22(1): 26–41
41. Raats I. Handleiding Focusgroepen. PGO Support. Raats voor mensgerichte zorg, 2017. Available at:<https://www.participatiekompas.nl/sites/default/files/Handleiding%20Focusgroepen%202017%20nov.pdf> . Accessed 31 Aug 2018
42. Wortman CB (1984) Social support and the cancer patient. Conceptual and methodologic issues. *Cancer* 53(10):2339–2362

Supplement 1. An abbreviated guideline of the focus group / interview

INTRODUCTION

Welcome (10 minutes)

- What to expect
- Confidentiality
- Tape recording

PART 1: GET TO KNOW EACH OTHER (20 minutes)

Before we start with our group discussion I would like to invite everyone to introduce themselves briefly.

Prompts:

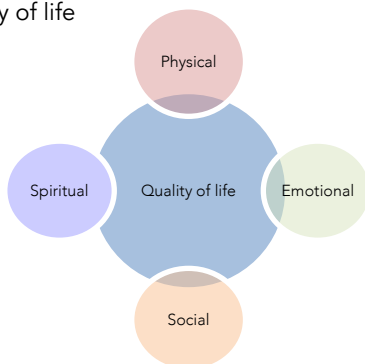
- What can you tell us about your personal situation?

PART 2: QUALITY OF LIFE (25 minutes, followed by a short break)

We would like to start talking with you about how you are doing now and how you experience your own quality of life at this moment. In this figure you can see that quality of life contains multiple domains, namely physical wellbeing, emotional wellbeing, social wellbeing, and spiritual wellbeing (show figure).

Regarding physical wellbeing you can think for example of physical functioning, regarding emotional wellbeing you can think of emotional responses such as for example anxiety or sadness, but also joy and happiness. Regarding social wellbeing you can think of for example the relation you have with other people such as friends, family, and colleagues. Regarding spiritual wellbeing you can think of for example of meaning in life, religion, and transcendence.

Figure. Quality of life



Prompts:

- Can you describe, in your own words, what quality of life is to you?
- What determines your quality of life? What is important to you?

Optional:

- What makes you feel good?
- How has your quality of life changed since the diagnosis (of your relative)?

PART 3: QUALITY OF CARE (25 minutes)

Next, we would like to discuss quality of care. It is important health care that is provided meet the needs of the care receiver. Therefore, we would like to know what is important to you and what your health care needs are. I would like to point out again that everything that is discussed here will not be communicated to your health care professionals.

Prompts:

- Can you describe to us, in your own words, what good care is to you?
- What is important to you regarding health care?

Optional:

- What are your health care needs? What do you need from health care professionals?

PART 4: ROUND OFF AND THANKS (10 minutes)

We would like to round off this discussion. Are there any important topics that have not been discussed but you find important to point out to us? Are there any questions at this moment? I would like to thank everyone for participating in this focus group.

CHAPTER 3

Shared Perspectives of Patients With Advanced Cancer and Their Informal Caregivers on Essential Aspects of Health Care: A Qualitative Study

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Abstract

Objective: The aim of this study is to explore the essential aspects of health care according to patients with advanced cancer and their informal caregivers by using a dyadic approach.

Methods: Seven focus groups and 7 in-depth semi-structured interviews were conducted. Patients with advanced cancer and informal caregivers were recruited between January 2017 and June 2017 in 6 Dutch hospitals. All interviews were audiotaped, transcribed verbatim, and open coded using a thematic analysis approach. For this analysis Atlas.ti was used.

Results: There was congruence between the aspects mentioned by patients and their informal caregiver. Two essential aspects of quality of care arose: "relation" and "organization of care." Regarding relation, patients and informal caregivers found it essential that health care professionals were personally engaged and provided support and compassion. Regarding organization of care, patients and informal caregivers expressed the importance of supportive care being offered multiple times during the disease trajectory, continuity of care, and well-organized logistics tailored to their needs.

Conclusion: This study generates awareness among health care professionals that patients with advanced cancer and their relatives have similar perspectives on essential aspects of care and may increase anticipation to meet health care preferences to optimize care.

Introduction

Patients with advanced cancer live longer after their diagnosis due to advances in health care technologies [1, 2]. Therefore, the number of patients who live with metastatic cancer has increased and the duration of the period of having potential palliative care needs has been stretched. Furthermore, health care needs of both patients and their informal caregivers are increasingly complex because advanced cancer is more often experienced as coping with a chronic illness [3] followed by an inevitable death. Tough decisions with trade-offs regarding treatment continuation and maintaining a good quality of life are common in patients with advanced cancer and their informal caregivers. Palliative care aims to improve quality of life of patients with life-threatening illness and their informal caregivers [4]. Early palliative care can significantly improve quality of life in patients with advanced cancer and their informal caregivers and may positively impact patients' survival [5-9]. Furthermore, early palliative care also can increase satisfaction with care among informal caregivers of patients with advanced cancer [10].

Despite a large body of research there is no uniform definition of high quality palliative care in medical literature. Moreover, there are great differences in perceptions of health care providers, patients, and informal caregivers regarding quality of care [11, 12], underscoring the importance to assess health care needs from the recipients of care perspective. Unfortunately, patients receiving palliative care [13-16] and informal caregivers of patients with advanced cancer [17] experience unmet health care needs. Qualitative research on palliative care preferences of patients and informal caregivers simultaneously is limited [11], although it is evident that the cancer experience of patient and informal caregivers are intertwined [18]. Knowledge on contemporary health care preferences of patients with advanced cancer and their informal caregivers can guide

health care professionals in providing the best individualized care for an increasing number of patients and informal caregivers with potential palliative care needs.

Research on quality of palliative care that includes the perspectives of patients with advanced cancer and their informal caregivers simultaneously is scarce. Only a few studies focused on the perspectives of patients [5, 11, 19, 20] or their informal caregivers [5, 11, 20, 21]. By including both perspectives simultaneously, we may detect differences and/or similarities in how dyads perceive health care while being confronted with the same cancer situation. It is crucial to examine essential aspects of health care from a dyadic perspective in order to improve current palliative care practice. Therefore, the aim of this study is to gain a deeper understanding of the essential aspects of health care according to patients with advanced cancer and their informal caregivers by using a dyadic approach.

Methods

Study Design

This qualitative focus group study was embedded within a larger prospective longitudinal observational cohort study with the aim to assess quality of care and quality of life as experienced by patients with advanced cancer and their informal caregivers (eQuiPe study (NTR6584)), conducted in the Netherlands.

Study Population

Patients were eligible for inclusion if they were diagnosed with colorectal cancer (stage IV and at least 2 metastasis in liver, peritoneum or lung), lung cancer (stage IV), breast cancer (stage IV with at least visceral or brain metastasis), prostate cancer (stage IV and castration resistant), non-resectable pancreatic cancer, or non-resectable esophageal cancer.

Patients were asked whether they had an informal caregiver who wanted to participate in the study, after which the identified informal caregiver was contacted by phone. An informal caregiver could participate regardless of patient participation and vice versa. Both patients and informal caregivers were eligible if they were 18 years or older, and understood the objective of the study. Patients and informal caregivers were not eligible for inclusion if they had a poor expression of the Dutch language, suffered from dementia or had a history of severe psychiatric illness.

Recruitment

Patients with advanced cancer and their informal caregivers were informed about the study by their treating physician between January 2017 and June 2017 in 6 Dutch hospitals. The physician asked the patients' permission for a research team member to call the patient to provide detailed information about the study, address questions, and invite them to participate. Subsequently, when patients and/or informal caregivers agreed to participate, they were invited for a focus group meeting.

Study Procedure

Participants were assigned to a focus group based on their availability, and patients and informal caregivers participated in separate focus groups to minimize response-bias. A focus group meeting lasted approximately 90 minutes and was facilitated by 2 researchers (JvR and LB). The focus groups were organized at The Netherlands Comprehensive Cancer Organization(IKNL) and one at the Antoni van Leeuwenhoek hospital. A moderator (JvR) asked the questions, probed, and made sure that all participants were heard and an observer (LB) listed the proceedings during each focus group (see supplement). Consecutively, all participants completed a self-administered questionnaire regarding

socio-demographics. If participants were not willing to participate in a focus group an individual interview was offered. Interviews were held at the preferred place of the interviewee, at home or The Netherlands Comprehensive Cancer Organization. Interviews were also conducted separately. Two patients only wanted to participate with their informal caregiver present during the interview. All focus groups and interviews were audiotaped. After data saturation was reached, no additional focus groups and interviews were organized. In total, 7 focus groups and 7 in-depth semi-structured interviews were conducted.

Data Analysis

All focus groups and interviews have been transcribed verbatim and analyzed with content analysis using Atlas.ti version 7.5.15. Transcripts of the focus groups and interviews were coded independently by 2 researchers (JvR and BdZ) according to the qualitative thematic analysis approach [22, 23]. Data was analyzed by the open coding procedure.²⁴ In the Netherlands, all healthcare professionals should provide generalist palliative care to patients with a life-threatening illness, and they will be supported by palliative care specialists when necessary. Therefore, quotes reflecting essential aspects of care in general as experienced by patients and informal caregivers were included in the further analysis. Codes were discussed during the analysis phase among 3 researchers (JvR, LB, and BdZ) until consensus was reached. The codes were clustered to identify main themes. To illustrate essential results from the analysis, quotes have been presented followed by an alphanumeric code in brackets where P = patient, C = informal caregiver, FG = focus group, and IV = interview.

Ethical Considerations

The study is conducted according to the declaration of Helsinki. The study protocol has been reviewed by the Medical Ethical Committee of the

Dutch Cancer Institute (NKI) in Amsterdam, the Netherlands METC16.2050). The METC has exempted this observational research from ethical review, accordingly to the Dutch Medical Research Involving Human Subjects Act (WMO). Informed consent was obtained from all participants. Furthermore, in data collection and analyses procedures the Dutch Personal Data Protection Act was followed.

Results

In total 18 patients and 15 informal caregivers participated in a focus group ($n = 23$) or in an interview ($n = 10$) (Figure 1). Most patients had lung or colorectal cancer and informal caregivers were most often the patients' partners. Patients and informal caregivers had a mean age of 58 and 59 years respectively and had a middle or high educational level (Table 1).

Figure 1. Flowchart inclusion process

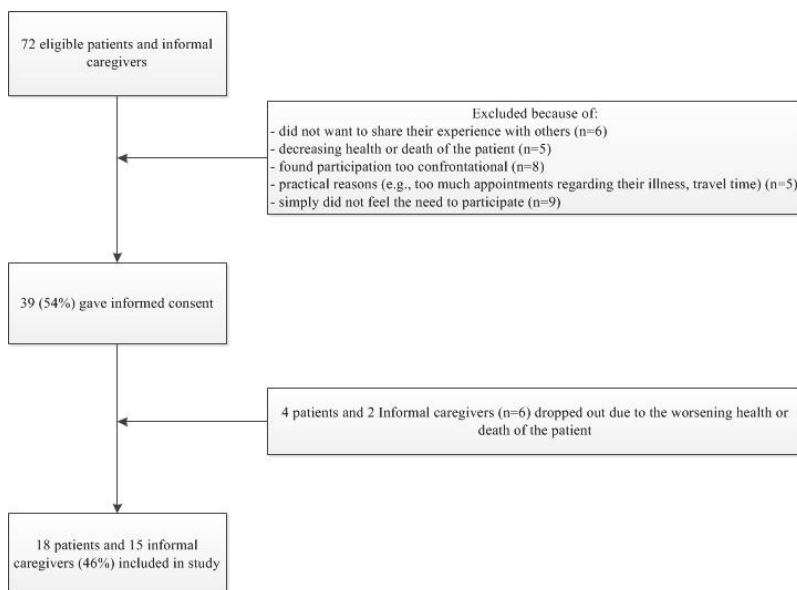


Table 1. Sociodemographic characteristics of the participants

	Patients with advanced cancer (n=18)	Informal caregivers (n=15)
Gender		
Male	9 (50%)	6 (40%)
Age		
Mean (range)	59 years (38-76)	58 years (40-76)
Education*		
Low education	2 (11%)	4 (27%)
Middle education	6 (33%)	8 (53%)
High education	9 (50%)	3 (20%)
Missing	1 (6%)	-
Ethnicity		
Dutch	17 (94%)	15 (100%)
French	1 (6%)	-
Religious beliefs		
None	3 (17%)	5 (33%)
Protestants Christian, active	2 (11%)	-
Protestants Christian, not active	1 (6%)	1 (7%)
Roman Catholic, active	3 (17%)	1 (7%)
Roman Catholic, not active	9 (50%)	7 (47%)
Other, atheist	-	1 (7%)
Primary cancer site in patients		
Lung	8 (44%)	11 (73%)
Colorectal	6 (33%)	1 (7%)
Breast	2 (11%)	2 (13%)
Oesophagus	1 (6%)	1 (7%)
Prostate	1 (6%)	-
Time since patient's diagnosis		
1 year	5 (28%)	6 (40%)
2 years	6 (33%)	4 (27%)
≥3 years	5 (28%)	3 (20%)
missing	2 (11%)	2 (13%)
Relation with patient	-	12 (80%)
Partner		2 (13%)
Daughter		1 (7%)
Friend		

* Low educational level = no education or primary school (e.g., LBO, VBO, LTS, LHNO, VMBO, MBO1), Intermediate educational level = lower general secondary education, vocational training or equivalent (e.g., MAVO, VMBO-t, MBO-kort, MBO, MTS, MEAO, HAVO, VWO), High educational level = pre-university education, high vocational training, university. (e.g., Hbo-bachelor, Hbo-master, wo-bachelor, wo-master, doctor).

Essential Aspects of Care

Two domains related to quality of care for both patients and informal caregivers were identified (Table 2): “relation” and “organization of care.” The main domains and its subthemes are described in more depth below.

Table 2. Themes regarding quality of care

Main domain	Subtheme	Category	Mentioned by
Relation	Personal engagement	Patient-physician match	p, c
		Feeling unique	p
		Inventory of mood	c
	Prerequisites of good communication	Empathic delivery of prognostics	p, c
		Understand concept of hope	p, c
		Empower via humour	p, c
		Discuss involvement in decision making	p, c
Organization of care	Patient-centred logistics	Predictability regarding schedules & procedures	p
		Take personal preferences into account	p, c
	Continuity of care	Who is in charge?	p, c
		Need for a care coordinator	p, c
		Readily availability of health care professionals	p, c
	Monitoring supportive care needs	Attention for psychological aspects of disease	p, c
		Accessibility	p, c

* p=patients, c=informal caregivers.

Relation

Personal Engagement

Patients and informal caregivers spoke about the importance of a personal match with their treating physician. Besides medical expertise patients found trust, mutual engagement, and understanding in their relation with their physician important. “and it’s important that you get on

with the doctor, I mean you are going to be seeing quite a lot of each other in the future and you need to have confidence in them.” (C3-IV). Solely patients found it important to be treated as a unique person and not being perceived as a common disease: “of course it’s been said a thousand times before, but really try to see the person and not the disease.” (P7-IV). Patients and informal caregivers spoke about the importance of physicians being empathic and said they experienced stress when this personal characteristic was absent “Yes, but in a situation like ours, you really need an empathetic doctor who understands how you are feeling, has a real interest in you and is there for you when you need them.” (P4-FG). Patients appreciated it when physicians were subtle in bringing bad news: “He always took a bit of an inventory first. Because you know, if you have some news to give that will have a direct effect on someone’s mood. Yes, I always liked that about him, a real point in his favour”. (C32-IV).

When a good relation was established, they preferred to be seen by their own physician because they valued the relation. Other patients preferred a more formal relationship with their physician and wanted the communication to be focused on treatment of the disease “I’ve got what you might call a business-like relationship with my physician; he is the mechanic and I am the car. Can you fix it or can’t you fix it? What do we need to do?” (P29-FG).

Prerequisites of Good Communication

Informal caregivers appreciated it when physicians started their consult with an inventory of their mood and sense how to communicate: “We [me and my partner] immediately laid our cards on the table about how we wanted to be treated. He asked us about it too. We were soon communicating on the same level because it appeared we both knew what we wanted”. (C32-IV).

Patients and informal caregivers also found it important that physicians take sufficient time for them “He took his time and he remained calm; it meant that the appointment overran but it didn’t matter and that was pleasing. I really appreciated that.” (P6-IV). Patients and informal caregivers also found transparency important when a mistake was made during the diagnostic process “He could at least have said that they hadn’t seen it, and said sorry for the way things went. That would have made a very different impression.” (C19-FG). Informal caregivers preferred transparent and realistic prognostic communication by the physician, said this was crucial to prevent existence of false hope: “I think it is very important that they [health care professionals] tell people, that they are open with you and tell you what is going on, however bad it may be. It is no use at all if they talk all around the subject first, it is better that you know what you are dealing with because then you can start to work on it yourself. Know what I mean?” (C30-FG).

However, patients and informal caregivers found it important that clear and realistic prognostic information is communicated carefully and with empathy. Also, patients and informal caregivers really appreciated humor in communication with health care professionals to make the illness trajectory bearable “yes, that sense of humour. I think it is the doctor’s sense of humour that has helped him (the patient) to get through the last five years.” (C20-FG). For patients it was important that their physicians respected their need for hope and empowered them when they decided to continue treatment.

Patients differed in the way they wanted to be involved in treatment decision making. Some patients followed the doctors advise and only started a discussion if they had different ideas: “Of course we always listen to the advice from the doctors, they know their business and naturally we

follow it as far as possible. But if we get the idea that it would be better to do things in a different way, then we discuss it". (C3-IV).

Others believed in the equality of their relation and wanted to be able to understand the physician: "I go to the doctor and I try to understand before I get into a discussion. So I want to know what the complicating factors are and which results are abnormal and what the results should be . . . - when I go to see the doctor I want to talk on equal terms, not as a patient. [...] He does his best. He makes an assessment and looks at the scans and the bloods and all the other things, but it is my body after all and I can feel things that he can't feel". (P31-FG).

Organization of Care

Monitoring Supportive Care Needs

Patients and informal caregivers found it important that there was attention for psychological support. Patients and informal caregivers mentioned that it was important for healthcare professionals to ask regularly questions regarding the psychosocial aspects of their illness. "What I have noticed is that, all the conversations with, er, doctors and the others, they concentrate mostly on the body and that, actually. And then I think, I mean, now and again I think well they don't ask much how, how are things at home or with you, or do you need some spiritual or . . . er. Yep. That is not automatic with them. Or with your partner, or your work or – I don't know". (P39-FG).

Also, according to patients there is a need for long term psychological support for informal caregivers who take care of patients with a chronic illness such as cancer: "I think the partners become exhausted, and I don't think the care system is flexible enough about it. It is the chronic strain, it goes on for years and really takes a lot out of a family like that. Because it

isn't . . . it isn't the biggest things that you can no longer do, but you still need help with everything". (P7-IV).

Patients and informal caregivers both said that it is important that information and access regarding supportive care is readily available. They explained that it should be offered explicitly and at multiple times during the disease trajectory. Some patients said they trusted their physician to start about supportive care when they would need it. Other patients said it was important to have the opportunity to receive supportive care such as a referral to a medical psychologist or home care. Patients found information regarding supportive options essential. Others also explained how they received a great amount of information at their diagnosis, but the timing did not match their need: "I was once asked if I wanted to talk to someone, if I needed further help with anything at all. But it never really came to anything much. And sometimes I think to myself, maybe it should be now, now that I have got things all straight in my mind, maybe they should offer it again". (P3-IV).

Continuity of Care

Patients and informal caregivers expressed a strong need for clarity regarding the health care professional who was leading their medical care: "Yes, it was hectic time when the diagnosis was made and I was sent from pillar to post, from one doctor to another, and every time you are new to the doctor with a new story to tell." (P4-FG). Patients and informal caregivers also expressed a need for a care coordinator or case manager because the communication between different health care professionals from separate departments within the same hospital, or communication between healthcare professionals from different hospitals and communication between the general practitioner and the medical specialist can be challenging: "Because you are undergoing an operation, they discover that all that chemo has made you develop a heart rhythm

disorder, so you end up in the cardiac circuit, then the urological circuit, then the neurology circuit, then the oncological circuit. You need someone who knows everything about you. And you try to tell the GP about it, but they don't have enough information". (P31-FG).

They explained that they had many appointments and had difficulty coordinating these appointments but also felt a need for someone who was up-to-date about their treatments and (medical) situation: "It would be very handy if someone just kept track of everything that is happening to you . . . , (and I could give you a few examples) . . . an overview of your physical state and all that sort of thing, so that you didn't have to keep a check on things yourself every time". (P24-FG).

Also, patients and informal caregivers mentioned that they found it important that health care professionals or a supportive staff member are readily available for support, also outside office hours.

Patient-Centered Logistics

Patients found predictability of care important. For instance, if a clear schedule was lacking, it made them feel distressed: "Yes, I believe that completely, and I also believe that if I had been treated at a smaller hospital that everything could have been planned much more easily and quickly, but on the other hand, I have also chosen a hospital with more expertise. But that doesn't mean that other things should be worse all of a sudden, they should be the same, the quality for me". (P3-IV).

Also procedures such as logistics around chemotherapy should be clear. Changes in their schedule generates anxiety: "yes but even if you knew, things could still change on the day that you came. Someone's chemo could have finished earlier and then that chair would have been free, so you could have got started, instead of in that room on that bed. [. . .] I understood that. But it does give you more peace of mind, because there

are so many other things to think about, then it gives you more peace of mind because you don't have to think about it". (P3-IV).

Patients and informal caregivers found it important that personal preferences about appointments were taken into account. For instance, patients with young children preferred to have their appointments while their children were at school in order to maintain their daily life as normal as possible. Other patients mentioned that they did not appreciate reminders of appointments via phone or mail because this confronted them with their illness when trying to enjoy their regular social activities.

Discussion

This qualitative study showed high congruence between the essential aspects of health care mentioned by patients and informal caregivers indicative for a shared perspective. Two essential aspect of care arose from the data: 1) the relation with health care professionals and 2) organization of care. Patients and their informal caregivers found it crucial that health care professionals are personally engaged and responsive to their unique experiences and impact of the disease. Furthermore, both patients and informal caregivers found attention for supportive care needs over time, continuity of care, and patient-centered logistics essential elements of organization of care. It appears to be essential for patients and informal caregivers that health care professionals take the time and effort to explore their unique needs, preferences, and expectations.

The importance and the role of communication, both verbal and nonverbal, in the relation between physicians and patients has been established frequently in the last decades [25-30]. Communication of the physician not only has the ability to improve satisfaction with care [31] but can also improve psychological [32] and clinical outcomes in patients with

cancer [33]. The process of communication in health care has changed over time. Firstly, nowadays shared decision making is the golden standard. Shared decision making is the process in which a health care professional and patient make decisions regarding diagnostics and treatment together while taking into account scientific knowledge, clinical experience, and the preferences and values of the patient [34]. Furthermore, nowadays in communication, more attention for family members and/or informal caregivers of patients is present. Health care is increasingly focused on the social system that surrounds the patient making the health care context more complex and dynamic for health care professionals. Especially in palliative care, where the social context of patients is perceived as a target population for care [4]. Clearly, the rise of shared decision making and focus on the social system perspective requires adequate interpersonal skills of health care professionals. Adequate communication is both more challenging and crucial in the experience of high quality oncological care for both patients and informal caregivers.

Regarding organization of care 3 essential aspects deserve attention: monitoring supportive care needs over time, continuity of care, and patient-centered logistics. Supportive care needs are important to monitor because patients with advanced cancer and their informal caregivers are at risk of developing psychological problems [35]. For instance, many patients and informal caregivers in our study pointed out that they experienced an unmet need in (information regarding) supportive care which is in line with previous research [36-38]. Despite the decrease of taboo about receiving psychological care nowadays, our study suggests that psychosocial support is only limitedly offered to patients with advanced cancer or their informal caregivers. However, research suggests that discussing psychological distress with a health care

professional may already be effective in reducing distress [39]. Unfortunately, integration of palliative care in oncological daily practice is still in its infancy. Therefore, it seems to be crucial that health care professionals are aware of the importance of providing (information on) supportive care and monitor supportive care needs of patients and their informal caregivers over time because their needs may change during the illness trajectory. Integrated palliative care in oncological practice has the potential to improve outcomes in patients and informal caregivers [7, 10, 40].

Providing continuity of care is challenging because health care for patients is increasingly complex. Psychological problems in patients with advanced cancer are common [41] and polypharmacy [42] and comorbidities are also often present in patients with advanced cancer [43]. Because many healthcare professionals from different hospital departments and organizations are involved in the care of these patients, it may become unclear for patients who is in charge of their care. It also becomes more challenging for health care professionals to guarantee continuity of care as health care becomes more fragmented. Patients and their informal caregivers in our study mentioned they would greatly benefit from a coordinator who can guide them in their "web of care."

The organization of health care on a macro level is highly supply-oriented. To make efficient use of available care supply, daily clinical practice has to be efficiently organized. Unfortunately, highly organized health care may come with a price as patients in our study underscored the importance of flexibility in delivering care to meet patient specific unique needs. Flexibility in organization of care may positively contribute to the feeling of receiving patient-centered care as patients' preferences are met. Therefore, a more demand focused organization of care may

contribute to patient-centered health care and increase satisfaction in health care receivers.

Strengths and Limitations

A strength of this study is that both advanced cancer patients and their informal caregivers participated. A wide range of hospitals (academic and general hospitals, geographically spread) participated in this study to gather a diverse sample. Some limitations of this study also should be mentioned. First, selection bias is present because most participants were highly educated and no non-western patients participated in the study. It is known that there are barriers in including minorities in studies [44, 45]. Due to this selection bias, cultural and educational differences regarding beliefs about quality of cancer care may be absent. Second, due to decreasing health or death of participants, focus groups were smaller than anticipated (2-6 participants per focus group). However, the number of participants appeared to have provided sufficient variation in experiences.

What This Study Adds

This study shows that the patients with advanced cancer and their informal caregivers have a shared perspective on health care. It is essential for patients and informal caregivers that health care professionals are personally engaged and their supportive care needs are monitored over time. Also, health care should be patient-centered coordinated. To optimize quality of care, it is essential that health care professionals know their patient and the patients' context and possess adequate interpersonal skills. Furthermore, awareness among health care professionals about the burden of care coordination for patients and informal caregivers, and the value of predictability for patients may be beneficial. It may increase anticipation in health care professionals to meet health care preferences of patients and informal caregivers within

current organization structures. Future research should point out whether implementation of health care preferences mentioned in our study lead to improved (clinical) outcomes in patients and informal caregivers. Furthermore, it is also valuable to gain a deeper understanding of the relative importance of the health care preferences of patients and informal caregivers to prioritize the implementation of preferences.

References

1. Haylock PJ. Advanced cancer: emergence of a new survivor population. *Semin Oncol Nurs*. 2010;26(3):144-150.
2. Lage A, Crombet T. Control of advanced cancer: the road to chronicity. *Int J Environ Res Public Health*. 2011;8(3):683-697.
3. Harrison JD, Young JM, Price MA, Butow PN, Solomon MJ. What are the unmet supportive care needs of people with cancer? A systematic review. *Support Care Cancer*. 2009;17(8): 1117-1128.
4. World Health Organization. Definition palliative care. WHO website. <http://www.who.int/cancer/palliative/definition/en/>. Accessed November 23, 2016.
5. Lorenz KA, Lynn J, Dy SM, et al. Evidence for improving palliative care at the end of life: a systematic review. *Ann Intern Med*. 2008;148(2):147-159.
6. El-Jawahri A, Greer JA, Temel JS. Does palliative care improve outcomes for patients with incurable illness? A review of the evidence. *J Support Oncol*. 2011;9(3):87-94.
7. El-Jawahri A, Greer JA, Pirl WF, et al. Effects of early integrated palliative care on caregivers of patients with lung and gastrointestinal cancer: a randomized clinical trial. *Oncologist*. 2017; 22(12):1528-1534.
8. Haun MW, Estel S, Rucker G, et al. Early palliative care for adults with advanced cancer. *Cochrane Database Syst Rev*. 2017;6: CD011129.
9. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med*. 2010;363(8):733-742.
10. McDonald J, Swami N, Hannon B, et al. Impact of early palliative care on caregivers of patients with advanced cancer: cluster randomized trial. *Ann Oncol*. 2017;28(1):163-168.
11. Vedel I, Ghadi V, Lapointe L, Routelous C, Aegerter P, Guirimand F. Patients', family caregivers', and professionals' perspectives on

- quality of palliative care: a qualitative study. *Palliat Med.* 2014;28(9):1128-1138.
12. Snyder CF, Dy SM, Hendricks DE, et al. Asking the right questions: investigating needs assessments and health-related quality-of-life questionnaires for use in oncology clinical practice. *Support Care Cancer.* 2007;15(9):1075-1085.
 13. Konstantinidis TISG, Sarafis P, Philalithis A. Assessment of needs of hospitalized cancer patients with advanced cancer. *Global Journal of Health Science.* 2016;9(6):184.
 14. Israel KB, Solis S. Psychosocial needs and their determinants among patients with cancer. *SPMC J Health Care Servi.* 2016; 2(1):1.
 15. Ventura AD, Burney S, Brooker J, Fletcher J, Ricciardelli L. Home-based palliative care: a systematic literature review of the self-reported unmet needs of patients and carers. *Palliat Med.* 2014;28(5):391-402.
 16. Husson O, Thong MS, Mols F, Smilde TJ, Creemers GJ, van de Poll-Franse LV. Information provision and patient reported outcomes in patients with metastasized colorectal cancer: results from the PROFILES registry. *J Palliat Med.* 2013;16(3):281-288.
 17. Butow PN, Price MA, Bell ML, et al. Caring for women with ovarian cancer in the last year of life: a longitudinal study of caregiver quality of life, distress and unmet needs. *Gynecol Oncol.* 2014;132(3):690-697.
 18. Shaffer KM, Jacobs JM, Nipp RD, et al. Mental and physical health correlates among family caregivers of patients with newly-diagnosed incurable cancer: a hierarchical linear regression analysis. *Support Care Cancer.* 2017;25(3):965-971.
 19. Stefanou N, Faircloth S. Exploring the concept of quality care for the person who is dying. *Br J Community Nurs.* 2010;15(12): 588-593.
 20. Nelson JE, Puntillo KA, Pronovost PJ, et al. In their own words: patients and families define high-quality palliative care in the intensive care unit. *Crit Care Med.* 2010;38(3):808-818.

21. Bakitas M, Ahles TA, Skalla K, et al. Proxy perspectives regarding end-of-life care for persons with cancer. *Cancer*. 2008;112(8): 1854-1861.
22. Braun V CV. Using thematic analysis in psychology. *Qual Res Psychol*. 2006;3(2):77-101.
23. Rennie DL. Qualitative research as methodical hermeneutics. *Psychol Methods*. 2012;17(3):385-398.
24. Strauss AL. *Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory*. Sage; 1998.
25. Steward WP, Dunlop DJ. New drugs in the treatment of non-small cell lung cancer. *Ann Oncol*. 1995;6(Suppl 1):49-54.
26. Kruijver IP, Kerkstra A, Bensing JM, van de Wiel HB. Nurse-patient communication in cancer care. A review of the literature. *Cancer Nurs*. 2000;23(1):20-31.
27. Parker SM, Clayton JM, Hancock K, et al. A systematic review of prognostic/end-of-life communication with adults in the advanced stages of a life-limiting illness: patient/caregiver preferences for the content, style, and timing of information. *J Pain Symptom Manage*. 2007;34(1):81-93.
28. De Vries AM, de Roten Y, Meystre C, Passchier J, Despland JN, Stiefel F. Clinician characteristics, communication, and patient outcome in oncology: a systematic review. *Psychooncology*. 2014;23(4):375-381.
29. Yang LY, Manhas DS, Howard AF, Olson RA. Patient-reported outcome use in oncology: a systematic review of the impact on patient-clinician communication. *Support Care Cancer*. 2018; 26(1):41-60.
30. Prip A, Moller KA, Nielsen DL, Jarden M, Olsen MH, Danielsen AK. The patient-healthcare professional relationship and communication in the oncology outpatient setting: a systematic review. *Cancer Nurs*. 2018;41(5):E11-E22.
31. Ong LM, Visser MR, Lammes FB, de Haes JC. Doctor-patient communication and cancer patients' quality of life and satisfaction. *Patient Educ Couns*. 2000;41(2):145-156.

32. Fallowfield LJ, Hall A, Maguire GP, Baum M. Psychological outcomes of different treatment policies in women with early breast cancer outside a clinical trial. *BMJ*. 1990;301(6752): 575-580.
33. Spiegel D, Giese-Davis J. Depression and cancer: mechanisms and disease progression. *Biol Psychiatry*. 2003;54(3):269-282.
34. Elwyn G, Frosch D, Thomson R, et al. Shared decision making: a model for clinical practice. *J Gen Intern Med*. 2012;27(10): 1361-1367.
35. Trevino KM, Prigerson HG, Maciejewski PK. Advanced cancer caregiving as a risk for major depressive episodes and generalized anxiety disorder. *Psychooncology*. 2018;27(1):243-249.
36. Voogt E, van Leeuwen AF, Visser AP, van der Heide A, van der Maas PJ. Information needs of patients with incurable cancer. *Support Care Cancer*. 2005;13(11):943-948.
37. Stegmann ME, Geerse OP, Tange D, et al. Experiences and needs of patients with incurable cancer regarding advance care planning: results from a national cross-sectional survey. *Support Care Cancer*. 2020;28(9):4211-4217.
38. Aranda S, Schofield P, Weih L, et al. Mapping the quality of life and unmet needs of urban women with metastatic breast cancer. *Eur J Cancer Care (Engl)*. 2005;14(3):211-222.
39. Schuurhuizen CSEW, Braamse AMJ, Beekman ATF, et al. Screening and stepped care targeting psychological distress in patients with metastatic colorectal cancer: the TES cluster randomized trial. *J Clin Oncol*. 2018;36(15):3560.
40. Bakitas MA, Tosteson TD, Li Z, et al. Early versus delayed initiation of concurrent palliative oncology care: patient outcomes in the ENABLE III randomized controlled trial. *J Clin Oncol*. 2015; 33(13):1438-1445.
41. Miovic M, Block S. Psychiatric disorders in advanced cancer. *Cancer*. 2007;110(8):1665-1676.

42. LeBlanc TW, McNeil MJ, Kamal AH, Currow DC, Abernethy AP. Polypharmacy in patients with advanced cancer and the role of medication discontinuation. *Lancet Oncol.* 2015;16(7): e333-e341.
43. Sogaard M, Thomsen RW, Bossen KS, Sorensen HT, Norgaard M. The impact of comorbidity on cancer survival: a review. *Clin Epidemiol.* 2013;5(Suppl 1):3-29.
44. Hudson SV, Momperousse D, Leventhal H. Physician perspectives on cancer clinical trials and barriers to minority recruitment. *Cancer Control.* 2005;12(Suppl 2):93-96.
45. Ford JG, Howerton MW, Lai GY, et al. Barriers to recruiting underrepresented populations to cancer clinical trials: a systematic review. *Cancer.* 2008;112(2):228-242.

Supplement 1. An abbreviated guideline of the focus group / interview

INTRODUCTION

Welcome (10 minutes)

- What to expect
- Confidentiality
- Tape recording

PART 1: GET TO KNOW EACH OTHER (20 minutes)

Before we start with our group discussion I would like to invite everyone to introduce themselves briefly.

Prompts:

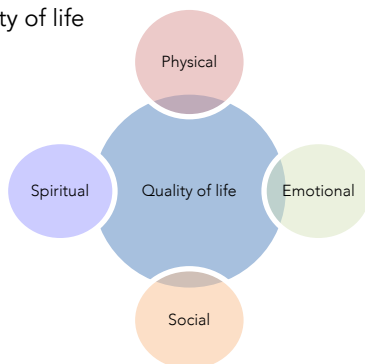
- What can you tell us about your personal situation?

PART 2: QUALITY OF LIFE (25 minutes, followed by a short break)

We would like to start talking with you about how you are doing now and how you experience your own quality of life at this moment. In this figure you can see that quality of life contains multiple domains, namely physical wellbeing, emotional wellbeing, social wellbeing, and spiritual wellbeing (show figure).

Regarding physical wellbeing you can think for example of physical functioning, regarding emotional wellbeing you can think of emotional responses such as for example anxiety or sadness, but also joy and happiness. Regarding social wellbeing you can think of for example the relation you have with other people such as friends, family, and colleagues. Regarding spiritual wellbeing you can think of for example of meaning in life, religion, and transcendence.

Figure. Quality of life



Prompts:

- Can you describe, in your own words, what quality of life is to you?
- What determines your quality of life? What is important to you?

Optional:

- What makes you feel good?
- How has your quality of life changed since the diagnosis (of your relative)?

PART 3: QUALITY OF CARE (25 minutes)

Next, we would like to discuss quality of care. It is important health care that is provided meet the needs of the care receiver. Therefore, we would like to know what is important to you and what your health care needs are. I would like to point out again that everything that is discussed here will not be communicated to your health care professionals.

Prompts:

- Can you describe to us, in your own words, what good care is to you?
- What is important to you regarding health care?

Optional:

- What are your health care needs? What do you need from health care professionals?

PART 4: ROUND OFF AND THANKS (10 minutes)

We would like to round off this discussion. Are there any important topics that have not been discussed but you find important to point out to us? Are there any questions at this moment? I would like to thank everyone for participating in this focus group.

CHAPTER 4

Measuring health-related quality of life in patients with advanced cancer: a systematic review of self-administered measurement instruments

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Quality of Life Research 2018; 27: 1937–1955

Abstract

Purpose: Patient-reported outcome measures (PROMs) are becoming increasingly important in clinical practice. The implementation of PROMS in routine practice is challenging because information regarding psychometric quality of measurement instruments is fragmented and standardization is lacking. The aim of this study is to evaluate the quality of self-administered HRQoL measurement instruments for use in patients with advanced cancer in clinical practice.

Methods: A systematic literature search was performed in PubMed, Embase, PsycINFO, and CINAHL to identify studies concerning self-administered HRQoL measurement instruments in patients with advanced cancer between January 1990 and September 2016. Quality of the measurement instruments was assessed by predefined criteria derived from the COSMIN checklist.

Results: Sixty-nine articles relating to 39 measurement instruments met the inclusion criteria. Information regarding important measurement properties was often incomplete. None of the instruments performed sufficient on all measurement properties. Considering available information, the EORTC QLQ-C15-PAL appeared to have adequate psychometric properties, together with the EORTC QLQ-BM22.

Conclusions: Many of the existing HRQoL measurement instruments have not yet been evaluated in an adequate manner. Validation of self-administered HRQoL measurement instruments is an ongoing development and should be prioritized. This review contributes to improved clarity regarding the availability and quality of HRQoL measurement instruments for patients with advanced cancer and supports health care professionals in an adequate selection of suitable PROMs in clinical practice.

Introduction

Integration of palliative care in oncology is recommended by European Society for Medical Oncology (ESMO) and American Society of Clinical Oncology (ASCO) as oncological palliative care will enhance quality of life (QoL), and may also positively influence the course of illness [1]. In their landmark paper, Temel et al. showed that early palliative care in fact leads to significant improvements in both health related quality of life (HRQoL) and mood [2]. For high-quality oncological palliative care in advanced cancer patients it is essential to monitor HRQoL in clinical practice in a suitable manner [3]. HRQoL generally consists of four domains: physical well-being, psychological well-being, social wellbeing, and spiritual well-being. Especially the spiritual wellbeing is important in patients with advanced cancer due to the confrontation with death [4–12]. Monitoring symptoms and HRQoL is extremely important in advanced cancer care, because it increases awareness among health care professionals to better anticipate on patients' changing needs [13,14] and improves clinical outcomes (i.e. fewer emergency room visits, fewer hospitalizations, a longer duration of palliative chemotherapy, and superior quality-adjusted survival), as recently demonstrated by Basch et al. [14].

The best method to monitor HRQoL in patients is to ask patients themselves, as asking health professionals or relatives is considered a less accurate method for estimating the HRQoL of a patient [15]. Inclusion of patient-reported outcome measures (PROMs) in routine clinical practice is, beside clinical benefits, also associated with improvements in discussion of patient outcomes during consultations and patient satisfaction [16–18]. However, the implementation of PROMS in routine practice is challenging because information regarding psychometric quality of measurement instruments is fragmented and standardization is lacking [19].

Earlier reviews have identified a variety of HRQoL measurement instruments that were appropriate for use in oncological palliative care [20–27]. However, none of these reviews could serve as a guide for an adequate and comprehensive choice of a measurement instrument for routine clinical practice because none used explicit criteria assessing measurement properties. For this reason, in 2010 Albers et al. [28] made an inventory of available HRQoL measurement instruments that were suitable for the use in palliative care and assessed the quality of these instruments. This review identified 29 different measurement instruments and showed a wide variety in measurement aim, content, target population, method (e.g. interview, questionnaire), completion time/length, and clinimetric quality [28]. In the last six years, a growing body of research has been published on the quality of existing HRQoL measurement instruments and also the development of new instruments is ongoing. It remains unclear what PROMs are most suitable for advanced cancer patients, receiving oncological palliative care nowadays.

Because the measurement of HRQoL in advanced cancer patients is a rapidly evolving field and the importance of PROMs in clinical practice is growing, an updated review on HRQoL measurement instruments seems appropriate. The aim of this study is to evaluate the quality of selfadministered instruments measuring HRQoL of patients with advanced cancer for use in oncological palliative care nowadays. The methodological quality of the measurement instruments is described in terms of measurement properties and measurement quality. This review aims to contribute to more clarity regarding the availability and quality of selfadministered HRQoL measurement instruments for patients with advanced cancer and to support health care professionals in an adequate selection of suitable PROMs in advanced cancer patients in clinical practice.

Methods

Search strategy

An electronic search of the database PubMed, Embase, PsycInfo, and CINAHL was performed to identify papers about instruments to measure HRQoL in advanced cancer patients that were published in English or Dutch between January 1990 and September 2016. Non-validation studies (article type) were excluded. A search strategy was developed for finding relevant publications in electronic literature databases, based on the search strategy of Albers et al. [28]. The computerized search was conducted using a search strategy to find studies on HRQoL measurement instruments in oncological palliative care: 'palliative', 'instruments', and 'QoL'. A detailed description of the MeSH-terms and keywords used in the search can be found in Supplement 1. The search string was initially developed in PubMed and later adapted for the other databases. Additionally, all Validation Studies (article type) of the 29 identified HRQoL measurement instruments of the review of Albers et al. [28] were added. In addition, the reference lists of selected articles were screened to retrieve relevant publications which had not been found in the computerized search.

Study selection process

Two reviewers (NR and HF) used a stepwise procedure to identify relevant studies. Firstly, all papers' titles and abstracts were assessed for relevance by one of the reviewers (NR) to see if the study describes the development or validation of a measurement instrument and whether the study involves (at least two domains of) HRQoL as outcome measurement. Irrelevant titles were excluded. Secondly, abstracts were screened by two reviewers (NR and HF) on the following inclusion criteria: (i) the study concerned the development or validation of a self-administered measurement instrument; (ii) non-primary tumour-specific HRQoL (and at least two of its

domains) was a primary or secondary objective of the study; (iii) the target population of the study included adult patients (i.e. ≥ 18 years old) with advanced or metastatic cancer; (iv) the measurement instrument used in the study was provided in Dutch or English language; (v) only full-text English or Dutch reports were included. Consensus regarding exclusion based on these exclusion criteria was reached after a consensus meeting. Of all the studies that did not pass the selection process, the reasons for exclusion were listed. Full-text papers were also assessed on the above-mentioned criteria and conference abstracts were excluded.

Data extraction procedure

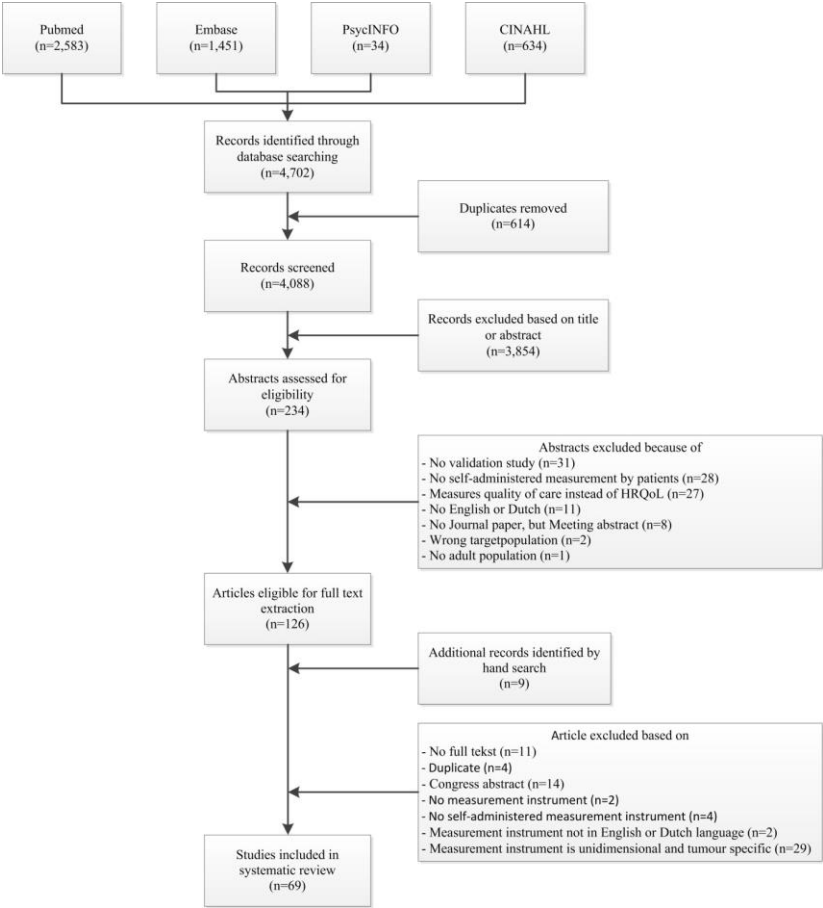
Two reviewers (NR and JvR) independently reviewed five randomly selected papers using a standard data extraction sheet and compared results to evaluate uniformity. Then, all papers were divided between the two researchers (NR and JvR) for data extraction. The procedure to confirm uniformity was repeated three times during the data extraction phase. The methodological quality of included validation studies was assessed using the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) checklist devised by Mokkink et al. [29]. Supplement 2 gives an overview and a description of the criteria used to assess quality. The assessment for the methodological quality of studies on measurement properties of health status measurements instruments covers nine topics: internal consistency, reliability, measurement error, content validity, construct validity (i.e. structural validity, hypotheses testing, and cross-cultural validity), criterion validity, and responsiveness. The methodological quality of the selected publications was assessed by two researchers (NR and JvR). The quality assessment was evaluated in the same manner as described earlier.

Results

Selection of papers

A flowchart of the selection process is presented in Fig. 1. In total, 4088 articles were identified from the different electronic databases, excluding duplicates. Initially, 3854 papers were excluded based on screening of relevance of title and abstract. The abstracts of the remaining 234 articles were assessed in depth for eligibility by two researchers (NR and HF). Finally, 126 studies were suitable for fulltext assessment. During full-text assessment, 37 studies were excluded. A number of studies ($n = 11$) were excluded because no full text was available after multiple attempts to retrieve the paper by contacting the author via Research gate or Email. Of these 11 papers, three were published more than 10 years ago, six were published in low-impact journals (impact factor < 2), which were often less accessible and two were untraceable. Other papers were excluded if they were a congress abstract ($n = 14$), the measurement instrument used in the study was in a language other than Dutch or English ($n = 2$), it was a duplicate ($n = 4$), it was not a self-administered measurement instrument ($n = 4$), it was not an measurement instrument ($n = 2$), or the measurement instrument was unidimensional or disease specific ($n = 29$). After checking reference lists of the selected articles, nine additional articles were identified. In total, 69 papers were included in this systematic review.

Figure 1. Flowchart study process



Study characteristics

The selected studies had between 10 and 3282 participants (21,077 participants in total) of whom 22–99% were men. Across studies, the average age of participants ranged from 51 to 79 years. Twenty percent of the studies included palliative patients suffering from various life-threatening illnesses (e.g. heart failure, end-stage lung disease, advanced renal disease, late-stage Parkinson disease, cancer), with the majority suffering from advanced cancer. Other studies focused on cancer patients of which most studies (67%) included a mixed cancer population (i.e. various primary cancer sites). The remaining studies (13%) selected one specific primary cancer site: 4% patients with lung cancer, 3% women with breast cancer, 3% patients with brain tumours, 1% men with prostate cancer, and 1% patients with colorectal cancer.

Health-related quality of life measurement instruments

Table 1 gives an overview of all the measurement instruments that were included in this review including the full form of the used acronyms. Across studies 39 measurement instruments were identified. Instruments were originally developed between 1972 (General Health Questionnaire -12) and 2013 [European Organisation of Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ)—Social Well-being 36]. The EORTC QLQ Core 30 (EORTC QLQ-C30) was most popular because ten studies (14%) validated this measure and seven studies (10%) administered a module of the EORTC (i.e. QLQ-Bone Metastases module 22 (QLQ-BM22), QLQ-Brain module 20 (QLQ-BN20), QLQ-Oral Health 17 (QLQ-OH17), and QLQ-SWB36). Nine studies (13%) validated the Edmonton Symptom Assessment Scale (ESAS) (or a modified or revised version of the ESAS), seven studies (10%) used the McGill Quality of Life Questionnaire (MQOL) (or the revised version), and four (6%) studies validated the Palliative care Outcome Scale (POS). For the majority of the

measurement instruments (58%) they measure (HR)QoL, eight instruments (11%) with symptom assessment or the impact of symptoms on daily functioning. For other measurement instruments it is argued that they assess spiritual well-being or spiritual distress (14%), psychological disorders or depressive symptoms (5%), core concerns and palliative needs (2%), or parenting concerns for adults with cancer (2%).

The number of items the measurement instruments contained ranged between one [Minimal Documentation System (MIDOS) and Quality of Life in Life-Threatening Illness-Patient version (QOLLI-P)] and 106 [Resident Assessment Instrument for Palliative Care (RAI-PC)]. The scoring of the measurement instruments was most often calculated as a total score and a subscale score (44%) or merely subscale scores (19%) or only a total score (14%). Other measurement instruments used single-item scores (5%), or a combination of single (visual analogue scale) items, subscale, and a total score (12%). One measurement instrument (2%) used content analysis to analyse responses.

Eight measurement instruments (19%) focused on the general population or patients in general, nine (21%) were targeted at palliative patients, nine (21%) at patients with cancer, and eight (19%) at patients with advanced cancer in specific. The target population of four measurement instruments (9%) were patients with brain tumours or brain metastases in specific. The remaining measurement instruments (12%) focused on bone or spina metastases, chest malignancies in cancer patients, and anorexia or cachexia. Most measurement instruments (33%) had a recall time of one week or had no recall time (14%). Others used a recall time of three days (7%), two weeks (2%), one month (2%), or one day (2%). The completion time of seven measurement instruments (16%) was reported. The completion time ranged between three [Patient-Evaluated Problem Scores (PEPS)] to 30 min (MQOL).

Table 1. Overview of the included measurement instruments

Name	Acronym	Purpose of measurement	HRQL domains	Year of development	Target population	#Items	Scoring	Recall time	Completion time
Assessment of Quality of life at the End of Life [30]	AQOL	Quality of life	All domains	1999	Patients in palliative care	20	Subscale	Last week	Not reported
Brain Symptom and Impact Questionnaire [31]	BASIQ	Symptom severity and impact on daily functional activities	PHW, PSW	Not reported	Patients with brain metastases	18	Subscale and total	Last 24 hours	Not reported
Condensed Memorial Symptom Assessment Scale [32]	CMSAS	Symptom assessment	PHW, PSW	2004	Patients	32	Subscale	Past 7 days	Not reported
European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Bone Metastases module [33-36]	EORTC QLQ-BM22	Health related quality of life	All domains	2009	cancer patients with bone metastases	22	Subscale and total	Not reported	<15min (72% of the patients)
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Brain module [37]	EORTC QLQ-BN20	Quality of life	PHW, PSW	2011	Patients with brain metastases	20	Subscale and total	Not reported	Not reported
European Organisation for research and Treatment of cancer Quality of Life Core 15 palliative questionnaire [38, 39]	EORTC QLQ-C15-PAL	Physical and psychosocial symptoms and functioning	PHW, PSW	2006	Patients with advanced, incurable, and symptomatic cancer	15	Subscale and total	One week	Not reported
European Organisation for Research and Treatment of cancer Quality of Life Questionnaire Core 30 [40-49]	EORTC QLQ-C30 (and a shortened version)	Health-related quality of life	PHW, PSW, SOW	1993, 2004	Cancer patients	30, shortened version 12	Single items, subscale and total	Last week	11-12 minutes

European Organisation for Research and Treatment of Cancer Core Questionnaire Oral Health [50]	EORTC QLQ-OH17	Oral and dental problems that may impact on quality of life	PHW, PSW	2012	Cancer patients	17	Subscale and total	Past week and present	Not reported
European Organisation for Research and Treatment of Cancer measure of Spiritual Wellbeing [51]	EORTC QLQ-SWB36	Spiritual wellbeing	PSW, SOW, SPW	2013	Palliative care patients with cancer	36	Subscale and total	Not reported	Not reported
Edmonton Symptom Assessment System [47, 52-58]	ESAS (ESAS-r, M-ESAS, ESAS-WB)	Commonly encountered symptoms in palliative care (ESAS-WB: feeling of well-being)	PHW, PSW	1991, modified version in 2000	Patients receiving palliative care	9 (modified version: 10 VAS-items)	Total (ESAS-WB: single item)	Present	Not reported
EQ-5D [59]	EQ-5D	Generic health-related quality of life (especially used to conduct economic evaluations)	PHW, PSW, SOW	Not reported	Not reported	5 and VAS-item	Total and VAS score	Present	Not reported
Functional Assessment of Anorexia Cachexia Therapy [60, 61]	FAACT	General aspects of quality of life and anorexia/cachexia-related concerns	PHW, PSW, SPW	1997	Patients suffering from anorexia/cachexia	18	Subscale and total	Not reported	Not reported
Functional Assessment of Cancer Therapy General [48]	FACT-G	Cancer specific quality of life	All domains	1993	Patients with cancer	34	Subscale and total	Not reported	Not reported
Functional assessment of Cancer Therapy - Brain [62]	FACT-Br	Quality of life	PHW, PSW	Not reported	Patients with primary brain tumours	50	Total	Not reported Last 7 days	Not reported
Functional Assessment of Chronic Illness Treatment [49]	FACT-G	Quality of life	All domains	1993	Cancer patients	27	Subscale and total	Last week	Not reported
Functional Assessment of Chronic Illness Therapy-Palliative Care [63, 64]	FACT-Pal	Health-related quality of life	All domains	2009	Palliative care patients	19	Subscales	Not reported	Not reported

General Health Questionnaire [65, 66]	GHQ-12	Psychological disorders	PSW, SOW, SPW	1972	Patients	12	Factors	Not reported	Not reported
Hospice Quality of Life Index [67, 68]	HQLI	Quality of life	All domains	1994, revised version in 1996	Hospice patients	25, revised version 28	Total, revised four factor scores	Present	Not reported
Hospital Anxiety and Depression Scale [66, 69]	HADS	Focus on the core depressive symptom of anhedonia	PHW, PSW	1983	Medically ill population	14	Subscale and total	Preceding week	<5 min
Linear Analog Scale Assessments [70]	LASAs	Quality of life	PHW, PSW, SPW	1999	Neuro oncology patients	5	Items	Past week	Not reported
McGill Quality of Life Questionnaire [47, 71-76]	MQOL, revised version, Cardiff Short form (MQOL-CSF)	Quality of life	All domains	1995, revised version in 1997	Patients with a life-threatening illness	17, revised version 1, short form 8	Subscale and total	Past two days	10-30 min, 15-35 min when verbally supervised
Memorial Symptom Assessment Scale [47, 77]	MSAS-(SF)	Physical and psychological symptom burden	PHW, PSW	1994, short form in 2000	Advanced cancer patients	32	Subscale and total	Previous week	Not reported
Minimal Documentation System [42]	MIDOS	Quality of life	All domains	2000	Cancer patients	1	Total	Current day	Not reported
Missoula-VITAS Quality of Life index [78, 79]	MVQOLI	Quality of life with a focus on the terminal phase of illness	All domains	2012, revised version in 2005	Patients in the terminal phase of illness	25	Subscale and total	Not reported	Not reported
National Institutes of Health Patient-Reported Outcomes Measurement Information System [80, 81]	NIH PROMIS	Quality of life	All domains	2007	Patients and relatives	Not fixed	Subscales	Past week	Not reported

Palliative Outcome Scale [47, 82-84]	POS	Core concern and palliative needs	All domains	1999	Patients with advanced cancer and their families	10	Items and total	Three days	≤10 minutes, mean completion time 6.9 minutes
Parenting Concerns Questionnaire [85]	PCQ	Parenting concerns	PHW, PSW, SOW	2012	Adults with cancer who have children ≤18 years old	15	Not reported	Not reported	Not reported
Patient Dignity Inventory [86, 87]	PDI	Dignity related distress	All domains	2002	Patients nearing the end of life	25	Subscale and total	Not reported	Not reported
Peace, Equanimity, and Acceptance in the Cancer Experience [88]	PEACE	Acceptance and struggle with terminal illness	PSW, SPW	2008	Terminally ill patients with cancer	12	Subscale and total	Present	Not reported
Patient Evaluated Problem Scores [71]	PEPS	Quality of life	All domains	Not reported	Patients	2 parts	Items	Not reported	3-8 minutes
Quality of Life and Health Questionnaire [89]	QLHQ	Health related quality of life	PHW, PSW, SOW	Not reported	Not reported	4	Dimensions and VAS score	One week	Not reported
Quality of life at the End of life [90-92]	QUAL-E (revised version: QUAL-EC)	Quality of life and quality of care at the end of life.	All domains	2002	Patients nearing the end of life	31, QUAL-EC has 17	Subscale and total	Last month and one week	Not reported
Quality of Life Index [48]	QLI	Cancer specific quality of life	All domains	1981	Patients with cancer	5	Total	Not reported	Not reported
Quality of Life in Life-Threatening Illness—Patient version [93]	QOLTLI-P	Quality of life	All domains	2010	Terminally ill cancer patients	1	Content analysis of the open-ended question	Two weeks	Not reported
Resident Assessment Instrument for Palliative Care [94]	RAI-PC	Palliative care needs and patient characteristics	All domains	2003	Palliative elder care	106	Domains	Last three days	Not reported

Measurement properties

None of the measurement instruments were adequately assessed for all measurement properties (Table 2). Information about the content validity (94%) was most often reported and in most cases adequate (58%). Information on the construct validity was reported by the majority of the studies (70%). However, compared to other measurement properties, the construct validity was most often inadequately tested (30%). Furthermore, information about the absolute measurement error, responsiveness, and interpretability was often incomplete (6, 22, and 51% respectively) or completely missing (88, 74, and 46% respectively).

Considering the available information on measurement properties, the EORTC QLQ Core 15 palliative questionnaire (QLQ-C15-PAL) showed best results. For instance, the EORTC QLQ-C15-PAL showed good content and construct validity, and the absolute measurement error and interpretability was also good. Other measurement properties had not been tested for the EORTC QLQ-C15-PAL. Equivalently, the EORTC QLQ-BM22 also appeared to have adequate psychometric properties because it appeared to have a good content and construct validity and the measurement instrument is reliable and responsive.

The ESAS showed good content validity, and the absolute measurement error and interpretability was good. However, information was lacking on other measurement properties. Other measurement instruments that had reasonable psychometric properties were the Assessment of Quality of life at the End of Life (AQOL), Quality of life at the End of life (QUAL-EC), and the Spiritual Attitude and Involvement List (SAIL). They had good content and construct validity, the internal consistency was good, but other information on measurement properties was lacking or missing.

The EORTC QLQ-C30 had undergone the most validation studies compared to other instruments but the studies did not adequately

evaluate some important fundamental psychometric properties. The content validity, construct validity, and absolute measurement error of the EORTC QLQ-C30 was good. Evidence on other psychometrics characteristics of the EORTC QLQ-C30 was unclear.

The POS, QUAL-E, and MQOL were also tested by multiple studies. The POS had good content validity and construct validity, but the internal consistency was inadequate. Information on other measurement properties was lacking or missing. The QUAL-E showed a good content validity and construct validity. However, the internal consistency and reliability was inadequately tested and information on other measurement properties was incomplete. The revised version of the QUAL-E (QUAL-EC) showed improved measurement properties. The MQOL had adequate content validity, but inadequate construct validity. There was conflicting evidence regarding the internal consistency of the MQOL, and other measurement properties were inadequately tested.

There was consensus across two studies that the Hospice Quality of Life Index (HQLI) had inadequate construct validity. Results about the content validity were inconsistent, the internal consistency of the measurement instrument was good, and other psychometric information was lacking. For the EORTC QLQ-SWB36 and the QOLLI-P, information on any of the measurement properties was absent. Other measurement instruments such as the EORTC QLQ-BN20, EQ-5D, Functional Assessment of Chronic Illness Treatment (FACIT-G), MIDOS, GHQ-12, Hospital Anxiety and Depression Scale (HADS), Rotterdam Symptom Checklist (RSCL), PEPS, Memorial Symptom Assessment Scale (MSAS-SF), and the RAI-PC were inadequately assessed because information on the measurement properties was incomplete or missing.

Table 2. Rating of Measurement Properties of the Instruments

Measurement instrument	Author	Population	Sample size	Content validity	Construct validity	Internal consistency	Reliability	Absolute measurement error	Responsiveness	Interpretability
AOOL	Henoch, L., et al. (2010)	Patients with lung cancer	106	+	+	+	0	0	0	?
BASIQ	Thavarajah, N., et al. (2015)	Patients with brain metastases	40	+	?	0	?	0	?	?
CMSAS	Chang, V. T., et al. (2004)	Cancer patients, terminal cancer patients and patients with severe cancer pain	479	?	+	?	0	0	0	0
	Chow, E., et al. (2009)	Cancer patients with bone metastases	170	+	0	0	0	0	0	0
	Chow, E., et al. (2012)	Cancer patients with bone metastases	400	+	+	?	+	0	+	?
	Zeng, L., et al. (2012)	Patients with bone metastases	93	+	+	0	0	?	0	?
EORTC QLQ-BM22	Zeng, L., et al. (2012)	Patients with bone metastases	79	?	0	0	0	0	0	?
EORTC QLQ-BN20	Wong, E., et al. (2015)	Patients with brain metastases	99	?	?	0	0	?	0	?
	Bedard, G., et al. (2016)	Patients with advanced cancer	276	+	+	0	0	+	0	+
EORTC QLQ-C15-PAL	Groenvold, M., et al. (2006)	Patients with advanced cancer	41	+	0	0	0	0	0	0
	Aaronson N. K., et al. (1993)	Newly diagnosed cancer patients	346	+	+	?	0	0	?	?
	Bedard, G., et al. (2014)	Palliative advanced cancer patients	369	+	?	0	0	+	0	?
EORTC QLQ-C30	Giesinger, J. M., et al. (2016)	Pre-treatment cancer patients	3,282	+	0	0	0	0	?	?

	Kaasa, S., et al. (1995)	Patients treated with palliative radiotherapy	247	+	+	?	0	0	?	0
	McLachlan, S. A., et al. (1998)	Patients with metastatic breast cancer	150	+	?	0	0	0	0	?
	Osoba, D., et al. (1994)	Patients with a variety of cancers	535	+	+	?	0	0	?	?
	Petersen, M. A., et al. (2006)*	Palliative cancer patients	267	?	0	0	0	0	0	0
EORTC QLQ-C30, ESAS, POS, MOOL, MSAS	Stromgren, A. S., et al. (2002)	Patients with advanced cancer	171	?	0	0	0	0	0	0
EORTC QLQ-OH17	Hjermstad, M. J., et al. (2012)	Cancer patients	311	+	0	?	0	0	0	?
EORTC QLQ-SWB36	Vivat, B., et al. (2013)	Palliative cancer patients	113	0	0	0	0	0	0	0
EORTC-QLQ-30, FACT, QLI	Sharp, L. K., et al. (1999)	Metastatic prostate cancer	110	?	+	?	0	0	0	?
EQ-5D	Krabbe, P. F. M., et al. (2004)	Patients who underwent surgical management for colorectal liver metastases	75	?	?	0	0	0	?	?
	Bedard, G., et al. (2013)	Patients seen for consultation at radiotherapy	421	0	0	0	0	+	?	+
	Cheng, V. T., et al. (2000)	Cancer patients	233	+	?	?	?	0	0	0
	Nekolaichuk CL et al. (1999)	Advanced cancer patients	32	?	0	0	?	?	0	0
ESAS	Phillip J, et al. (1998)	Patients with incurable cancer	80	?	?	0	0	0	0	0
ESAS-r	Watanabe, S. M., et al. (2012)	Patients who had been referred to the palliative care programs	160	+	0	0	?	0	0	0

ESAS-WB	Bush, S. H., et al. (2010)	Patients with advanced cancer	213	+	-	0	0	0	?	0
	Ribeudo J. M., et al (2000)	Cancer patients and HIV-infected individuals	213	-	0	?	0	0	+	0
FAACT	Salsman, J. M., et al. (2014)	Patients diagnosed with unresectable stage III or IV NSCLC	383	?	+	?	0	?	?	?
FACIT-G, and EORTC QLQ-C30, MIDOS	Stiel, S., et al. (2011)	Patients receiving palliative care treatments	144	?	?	0	0	0	0	?
	Lyons, K. D., et al. (2009)	Persons with advanced cancer	256	+	?	?	0	0	0	?
	Zeng, L., et al. (2013)	Advanced cancer patients	60	+	0	0	0	0	0	0
FACIT-Pal	Thavarajah, N., et al. (2014)	Patients with brain metastases	40	+	?	?	+	0	?	?
FACT-Br	Geo, W., et al. (2012)	Cancer outpatients	714	?	0	?	0	0	0	0
GHQ-12	Le Fevre, P. et al. (1999)	Hospice patients	79	?	?	0	0	0	?	?
HADS and GHQ-12	Hopwood, P., et al. (1991)	Patients with advanced breast cancer	204	?	?	0	0	0	0	?
HADS and RSCL	McMillan, S. C. & Mahon, M. (1994)	Patients with cancer and their primary care givers	68	-	-	?	?	0	0	0
	McMillan, S. C. & Weitzner, M. (1998)	Hospice home care patients with cancer	255	+	-	+	0	0	0	0
HQLI	Locke, D. E. C., et al. (2007)	Newly diagnosed high-grade glioma patients	205	+	?	?	0	0	0	?
LASAs	Cleesens, P., et al. (2011)	Hospitalized palliative cancer patients, family members, and nurses	37	?	+	?	0	0	0	?

	Heam, J. & Higginson, I. J (1999)	Advanced cancer patients	450	+		+		?		?	0	?	?
	Siebert, R. J., et al. (2010)	Palliative care patients	231	+		0		0		0	0	0	0
	Romero, M. M., et al. (2015)	Patients diagnosed with primary brain tumours	10	?		-		0		0	0	0	0
PROMIS-Cancer scales	Yost, K. J., et al. (2011)	Advanced-stage cancer	101	?		0		0		0	-	0	?
	Hadorn, D. C., et al. (1995)	Patients with newly diagnosed advanced-stage cancer	394	?		+		0		0	0	?	?
QLHQ	Shahidi, J., et al. (2010)	Palliative cancer patients	110	0		0		0		0	0	0	0
OOLTI-P	Steinhauser, K. E., et al. (2002)	Patients with stage IV cancer, CHF, COPD, and dialysis-dependent ESRD patients	200	+		0		-		0	0	0	?
	Lo, C., et al.	Patients with stage IV cancer, congestive heart failure, END stage renal disease, and chronic obstructive pulmonary disease	248	+		+		-		-	0	0	?
QUAL-E	Steinhauser, K. E., et al. (2004)	Advanced cancer	468	+		+		+		0	0	0	0
QUAL-EC	Steel, K., et al. (2003)	Patients	149	?		0		0		?	0	0	0
RAL-PC	de Haes J. C. J. M., et al. (1990)	Cancer patients	611	+		0		+		0	0	0	0
RSCL	de Jager Meezenbroek, E. et al. (2012)	A student, a healthy population, a healthy interested, a curative	1,635	+		+		+		?	0	0	0

Discussion

Our systematic literature review identified 39 self-administered instruments measuring HRQoL mainly in patients with advanced cancer. None of the included studies reported sufficient information on psychometric properties of these measurement instruments according to the COSMIN criteria. Surprisingly, even basic psychometric properties such as construct validity and reliability were often inadequately tested. It appears that selecting an appropriate measurement instrument for testing construct validity and formulating specific hypotheses can be challenging. Furthermore, our findings show that adequate testing of responsiveness was not a priority in previous studies. PROMs are often used in clinical practice to monitor symptoms over time, it is therefore of great importance that a measurement instrument is responsive to changes. Despite incomplete information in the included studies, results of this review indicate that the EORTC QLQ-C15-PAL is an adequate instrument to measure HR in patients with advanced cancer. The EORTC QLQ-BM22, a module for patients with bone metastases, also appears to be suitable in this patient population. The EORTC QLQ-BM22 is a module and should be administered together with the EORTC QLQ-C30. Consequently, the measurement instrument is more extensive compared to the EORTC QLQ-C15-PAL. The length of a measurement instrument should be taken into account because there is little time for administration in clinical practice and a lower burden can foster compliance [99].

Due to medical advances, cancer is increasingly perceived as a chronic illness. Patients stretch the palliative phase by a longer survival and there is an increasing awareness to detect the palliative phase at an earlier stage when patients are relatively fit. The EORTC QLQ-C15-PAL may not be appropriate to administer in the beginning of the palliative phase due to its focus on symptoms at the end of life. When the EORTC QLQ-C15-PAL

is administered in relatively healthy patients, a patients' actual HRQoL may be lower than what the EORTC QLQ-C15-PAL scores indicate and the EORTC QLQ-C30 will provide a more accurate reflection of a patients' HRQoL. The EORTC QLQ-C30 is the most commonly used disease-specific measure world-wide [100] and has been used in more than 3000 studies [101]. The routine use of the EORTC QLQ-C30 in clinical practice appears to improve physician–patient communication and HRQoL [102], but the implementation has its challenges (e.g. timing, frequency, interpretations of scores by health care professionals, and the absence of thresholds for clinical importance) [103]. Surprisingly, the present review showed that the psychometric quality of this measurement instrument has been examined many times but not adequately in patients with advanced cancer. Therefore, a thorough validation of the internal consistency, reliability, responsiveness, and interpretability of the EORTC QLQ-C30 in advanced cancer patients is advocated.

Another consideration regarding the reviewed HRQoL measurement instruments is that many of the instruments did not measure all aspects of HRQoL. Moreover, measurement instruments that only addressed one domain of HRQoL were excluded from our study. The spiritual domain is especially important at the end of life, but this domain was not often included in existing measurement instruments [28]. For instance, the EORTC QLQ-C15-PAL also did not include certain topics that appear to be relevant for patients in the end of life: Quality of care, Preparation for death, Spirituality or Transcendence [78, 90, 104–107]. The EORTC QLQ-C15-PAL was derived from the EORTC QLQ-C30 and the authors confirmed that existential or spiritual issues were mentioned by health care professionals and some patients as important additional topics to the measurement instrument. Therefore, the authors suggested that the EORTC QLQ-C15-PAL is supplemented by single items, modules, or

questionnaires regarding spirituality when deemed necessary. This suggestion is especially valuable for clinical practice where the spirituality domain is not easily assessed in a regular doctor's appointment and many oncologists have not received specific training in palliative care.

Practical implications

For clinical practice it is important to monitor whether the latent construct that is being measured is represented by the selected instrument at the time of measurement and take the objective of measurement instrument into account when selecting an instrument. For instance, when interested in change over time one could argue that the EORTC QLQ-C15-PAL is less sensitive compared to the EORTC QLQ-C30 because it uses fewer items. However, sensitivity to change may also be improved by eliminating items that poorly represent the construct they were designed to measure [108]. In other words, improving measurement precision will enlarge sensitivity. Therefore, the EORTC QLQ-C15-PAL may actually be more sensitive to change over time when measuring HRQoL at the end of life in specific. However, because the EORTC QLQ-C15-PAL does not include items on spirituality the latent construct of HRQoL at the end of life is not fully measured. This reduces the sensitivity of the measurement instrument because the range where change can be detected over time is small [108]. Up to now, little is known about the measurement invariance of the QLQ-C15-PAL or EORTC QLQ-C30 in advanced cancer patients. Further validation to improve available information regarding minimal important differences and clinical relevance of differences in scores can aid interpretability in clinical practice [30]. PROMs have the potential to personalize care by identifying patients' needs but an accurate image of the patients' needs can only be achieved when administering the right measurement instrument at the right time for the right purposes.

This study has certain strength and limitations. It is important that the validation of instruments is performed in a consistent manner and evaluated as such. Using the COSMIN criteria in this review promoted a consistent evaluation. A limitation of this review is that there is no guarantee that our study selection procedure was sufficiently extensive. Even though references of included studies were checked, it is possible that certain validation studies were missed. Finally, this review only included measurement instruments that were not cancer site specific, meaning that the target population of the instrument was not focussed at patients with specific primary cancer sites. It is possible that for certain cancer sites, the EORTC QLQ-C15-PAL may not be the most adequate measure.

In conclusion, this review identified many self-administered instruments that measure HRQoL in patients with advanced cancer in clinical practice. Many of the existing measurement instruments have not yet been evaluated in an adequate manner, making it difficult to compare instruments. Considering the available information, the EORTC QLQ-C15-PAL and the EORTC QLQ-BM22 appeared to have best psychometric properties. However, there is no 'one size fits all', meaning that when selecting a measurement instrument in clinical practice it is important to take certain aspects into account such as the burden of administration and the objective of measurement (e.g. change over time). It is important that health care professionals possess up-to-date knowledge on the quality of HRQoL measurement instruments to make an adequate selection in clinical practice. For instance, health care professionals should be aware that it is important to supplement existing measurement instruments with relevant items on spirituality or preparation of dying, depending on the patients' position within the palliative phase to accurately measure HRQoL. Validation of self-

administered HRQoL measurement instruments is an important ongoing development because information on psychometric properties will enhance comparisons between instruments. This review contributes to improved clarity regarding the availability and quality of HRQoL measurement instruments for patients with advanced cancer and supports health care professionals in an adequate selection of suitable PROMs in advanced cancer patients in clinical practice. Being able to accurately and routinely measure HRQoL in patients with advanced cancer will stimulate the personalized health care approach leading to improved cancer care, clinical outcomes, and HRQoL.

References

1. WHO.(2002). Definition palliative care. <http://www.hoint/cancer/palliative/definition/en/>. Accessed November 23 2016.
2. Temel, J. S., Greer, J. A., Muzikansky, A., et al. (2010). Early palliative care for patients with metastatic non-small-cell lung cancer. *New England Journal of Medicine*, 363(8), 733–742.
3. Coons, S. J., Rao, S., Keininger, D. L., & Hays, R. D. (2000). A comparative review of generic quality-of-life instruments. *Pharmacoeconomics*, 17(1), 13–35.
4. Kaasa, S., & Loge, J. H. (2003). Quality of life in palliative care: Principles and practice. *Palliative Medicine*, 17(1), 11–20.
5. Conroy, T., Bleiberg, H., & Glimelius, B. (2003). Quality of life in patients with advanced colorectal cancer: What has been learnt? *European Journal of Cancer*, 39(3), 287–294.
6. Saeteren, B., Lindström, U., & Nåden, D. (2011). Latching onto life: Living in the area of tension between the possibility of life and the necessity of death. *Journal of Clinical Nursing*, 20(5–6), 811–818.
7. Detmar, S. B., Aaronson, N. K., Wever, L. D., et al. (2000). How are you feeling? Who wants to know? Patients' and oncologists' preferences for discussing health-related quality-of-life issues. *Journal of Clinical Oncology*, 18(18), 3295–3301.
8. Mystakidou, K., Tsilika, E., Parpa, E., et al. (2008). Demographic and clinical predictors of spirituality in advanced cancer patients: A randomized control study. *Journal of Clinical Nursing*, 17(13), 1779–1785.
9. Edwards, A., Pang, N., Shiu, V., et al. (2010). The understanding of spirituality and the potential role of spiritual care in end-of-life and palliative care: A meta-study of qualitative research. *Palliative Medicine*, 24(8), 753–770.
10. Winkelman, W. D., Lauderdale, K., Balboni, M. J., et al. (2011). The relationship of spiritual concerns to the quality of life of advanced

cancer patients: Preliminary findings. *Journal of Palliative Medicine*, 14(9), 1022–1028.

11. Kimmel, P. L., Emont, S. L., Newmann, J. M., et al. (2003). ESRD patient quality of life: Symptoms, spiritual beliefs, psychosocial factors, and ethnicity. *American Journal of Kidney Diseases*, 42(4), 713–721.
12. Steinhauser, K. E., Christakis, N. A., Clipp, E. C., et al. (2000). Factors considered important at the end of life by patients, family, physicians, and other care providers. *JAMA*, 284(19), 2476–2482.
13. Etkind, S. N., Daveson, B. A., Kwok, W., et al. (2015). Capture, transfer, and feedback of patient-centered outcomes data in palliative care populations: Does it make a difference? A systematic review. *Journal of Pain and Symptom Management*, 49(3), 611–624.
14. Basch, E., Deal, A. M., Kris, M. G., et al. (2016). Symptom monitoring with patient-reported outcomes during routine cancer treatment: A randomized controlled trial. *Journal of Clinical Oncology*, 34(6), 557–565.
15. Fayers, P., & Machin, D. (2008). Quality of life: The assessment, analysis and interpretation of patient-reported outcomes. *Biometrics*, 64(3), 996.
16. Kotronoulas, G., Kearney, N., Maguire, R., et al. (2014). What is the value of the routine use of patient-reported outcome measures toward improvement of patient outcomes, processes of care, and health service outcomes in cancer care? A systematic review of controlled trials. *Journal of Clinical Oncology*, 32(14), 1480–1501.
17. Takeuchi, E. E., Keding, A., Awad, N., et al. (2011). Impact of patient-reported outcomes in oncology: A longitudinal analysis of patient-physician communication. *Journal of Clinical Oncology*, 29(21), 2910–2917.
18. Marshall, S., Haywood, K., & Fitzpatrick, R. (2006). Impact of patient-reported outcome measures on routine practice: A structured review. *Journal of Evaluation in Clinical Practice*, 12(5), 559–568.
19. Howell, D., Molloy, S., Wilkinson, K., et al. (2015). Patient reported outcomes in routine cancer clinical practice: A scoping review of use,

- impact on health outcomes, and implementation factors. *Annals of Oncology*, 26(9), 1846–1858.
20. Bruley, D. K. (1999). Beyond reliability and validity: Analysis of selected quality-of-life instruments for use in palliative care. *Journal of Palliative Medicine*, 2(3), 299–309.
 21. Hearn, J., & Higginson, I. J. (1997). Outcome measures in palliative care for advanced cancer patients: A review. *Journal of Public Health Medicine*, 19(2), 193–199.
 22. Jordhoy, M. S., Inger Ringdal, G., Helbostad, J. L., et al. (2007). Assessing physical functioning: A systematic review of quality of life measures developed for use in palliative care. *Palliative Medicine*, 21(8), 673–682.
 23. Kaasa, S., & Loge, J. H. (2002). Quality-of-life assessment in palliative care. *Lancet Oncology*, 3(3), 175–182.
 24. Kirkova, J., Davis, M. P., Walsh, D., et al. (2006). Cancer symptom assessment instruments: A systematic review. *Journal of Clinical Oncology*, 24(9), 1459–1473.
 25. Massaro, T., & McMillan, S. C. (2000). Instruments for assessing quality of life in palliative care settings. *International Journal of Palliative Nursing*, 6(9), 429–433.
 26. McMillan, S. C. (1996). Quality-of-Life Assessment in Palliative Care. *Cancer Control*, 3(3), 223–229.
 27. Mularski, R. A., Dy, S. M., Shugarman, L. R., et al. (2007). A systematic review of measures of end-of-life care and its outcomes. *Health Services Research*, 42(5), 1848–1870.
 28. Albers, G., Echteld, M. A., de Vet, H. C., et al. (2010). Evaluation of quality-of-life measures for use in palliative care: A systematic review. *Palliative Medicine*, 24(1), 17–37.
 29. Mokkink, L. B., Terwee, C. B., Patrick, D. L., et al. (2010). The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: An international Delphi study. *Quality of Life Research*, 19(4), 539–549.

30. Hensch, I., Axelsson, B., & Bergman, B. (2010). The Assessment of Quality of life at the End of Life (AQEL) questionnaire: A brief but comprehensive instrument for use in patients with cancer in palliative care. *Quality of Life Research*, 19(5), 739–750.
31. Thavarajah, N., Ray, S., Bedard, G., et al. (2015). Psychometric validation of the Brain Symptom and Impact Questionnaire (BASIQ) version 1.0 to assess quality of life in patients with brain metastases. *CNS Oncology*, 4(1), 11–23.
32. Chang, V. T., Hwang, S. S., Kasimis, B., & Thaler, H. T. (2004). Shorter symptom assessment instruments: The Condensed Memorial Symptom Assessment Scale (CMSAS). *Cancer Investigation*, 22(4), 526–536.
33. Chow, E., Hird, A., Velikova, G., et al. (2009). The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire for patients with bone metastases: The EORTC QLQ-BM22. *European Journal of Cancer*, 45(7), 1146–1152.
34. Chow, E., Nguyen, J., Zhang, L., et al. (2012). International field testing of the reliability and validity of the EORTC QLQ-BM22 module to assess health-related quality of life in patients with bone metastases. *Cancer*, 118(5), 1457–1465.
35. Zeng, L., Chow, E., Bedard, G., et al. (2012). Quality of life after palliative radiation therapy for patients with painful bone metastases: Results of an international study validating the EORTC QLQ-BM22. *International Journal of Radiation Oncology Biology Physics*, 84(3), 337–342.
36. Zeng, L., Chow, E., Zhang, L., et al. (2012). An international prospective study establishing minimal clinically important differences in the EORTC QLQ-BM22 and QLQ-C30 in cancer patients with bone metastases. *Supportive Care in Cancer: Official Journal of the Multinational Association of Support Care Cancer*, 20(12), 3307–3313.
37. Wong, E., Zhang, L., Kerba, M., et al. (2015). Minimal clinically important differences in the EORTC QLQ-BN20 in patients with brain metastases. *Support Care Cancer*, 23(9), 2731–2737.

38. Bedard, G., Zeng, L., Zhang, L., et al. (2016). Minimal important differences in the EORTC QLQ-C15-PAL to determine meaningful change in palliative advanced cancer patients. *Asia Pacific Journal of Clinical Oncology*, 12(1), 38–46.
39. Groenvold, M., Petersen, M. A., Aaronson, N. K., et al. (2006). The development of the EORTC QLQ-C15-PAL: A shortened questionnaire for cancer patients in palliative care. *European Journal of Cancer*, 42(1), 55–64.
40. Bedard, G., Zeng, L., Zhang, L., et al. (2014). Minimal important differences in the EORTC QLQ-C30 in patients with advanced cancer. *Asia Pacific Journal of Clinical Oncology*, 10(2), 109–117.
41. Giesinger, J. M., Kieffer, J. M., Fayers, P. M., et al. (2016). Replication and validation of higher order models demonstrated that a summary score for the EORTC QLQ-C30 is robust. *Journal of Clinical Epidemiology*, 69, 79–88.
42. Aaronson, N. K., Ahmedzai, S., Bergman, B., et al. (1993). The European Organization for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. *Journal of the National Cancer Institute*, 85(5), 365–376.
43. Kaasa, S., Bjordal, K., Aaronson, N., et al. (1995). The EORTC core quality of life questionnaire (QLQ-C30): Validity and reliability when analysed with patients treated with palliative radiotherapy. *European Journal of Cancer*, 31A(13–14), 2260–2263.
44. McLachlan, S. A., Devins, G. M., & Goodwin, P. J. (1998). Validation of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (QLQ-C30) as a measure of psychosocial function in breast cancer patients. *European Journal of Cancer*, 34(4), 510–517.
45. Osoba, D., Zee, B., Pater, J., et al. (1994). Psychometric properties and responsiveness of the EORTC quality of Life Questionnaire (QLQ-C30) in patients with breast, ovarian and lung cancer. *Quality of Life Research*, 3(5), 353–364.

46. Petersen, M. A., Groenvold, M., Aaronson, N., et al. (2006). Item response theory was used to shorten EORTC QLQ-C30 scales for use in palliative care. *Journal of Clinical Epidemiology*, 59(1), 36–44.
47. Stromgren, A. S., Groenvold, M., Pedersen, L., et al. (2002). Symptomatology of cancer patients in palliative care: Content validation of self-assessment questionnaires against medical records. *European Journal of Cancer*, 38(6), 788–794.
48. Sharp, L. K., Knight, S. J., Nadler, R., et al. (1999). Quality of life in low-income patients with metastatic prostate cancer: Divergent and convergent validity of three instruments. *Quality of Life Research*, 8(5), 461–470.
49. Stiel, S., Psych, D., Kues, K., et al. (2011). Assessment of quality of life in patients receiving palliative care: Comparison of measurement tools and single item on subjective well-being. *Journal of Palliative Medicine*, 14(5), 599–606.
50. Hjermstad, M. J., Bergenmar, M., Fisher, S. E., et al. (2012). The EORTC QLQ-OH17: A supplementary module to the EORTC QLQ-C30 for assessment of oral health and quality of life in cancer patients. *European Journal of Cancer*, 48(14), 2203–2211.
51. Vivat, B., Young, T., Efficace, F., et al. (2013). Cross-cultural development of the EORTC QLQ-SWB36: A stand-alone measure of spiritual wellbeing for palliative care patients with cancer. *Palliative Medicine*, 27(5), 457–469.
52. Bedard, G., Zeng, L., Zhang, L., et al. (2013). Minimal clinically important differences in the Edmonton symptom assessment system in patients with advanced cancer. *Journal of Pain and Symptom Management*, 46(2), 192–200.
53. Chang, V. T., Hwang, S. S., & Feuerman, M. (2000). Validation of the edmonton symptom assessment scale. *Cancer*, 88(9), 2164–2171.
54. Bush, S. H., Parsons, H. A., Palmer, J. L., et al. (2010). Multiple-item instruments in the assessment of quality of life in patients with advanced cancer. *Journal of Pain and Symptom Management*, 39(3), 564–571.

55. Nekolaichuk, C. L., Maguire, T. O., Suarez-Almazor, M., et al. (1999). Assessing the reliability of patient, nurse, and family caregiver symptom ratings in hospitalized advanced cancer patients. *Journal of Clinical Oncology*, 17(11), 3621–3630.
56. Philip, J., Smith, W. B., Craft, P., & Lickiss, N. (1998). Concurrent validity of the modified Edmonton symptom assessment system with the rotterdam symptom checklist and the brief pain inventory. *Support Care Cancer*, 6(6), 539–541.
57. Watanabe, S. M., Nekolaichuk, C. L., & Beaumont, C. (2012). The Edmonton Symptom Assessment System, a proposed tool for distress screening in cancer patients: Development and refinement. *Psychooncology*, 21(9), 977–985.
58. Claessens, P., Menten, J., Schotsmans, P., & Broeckaert, B. (2011). Development and validation of a modified version of the Edmonton Symptom Assessment Scale in a Flemish palliative care population. *American Journal of Hospice and Palliative Medicine*, 28(7), 475–482.
59. Krabbe, P. F., Peerenboom, L., Langenhoff, B. S., & Ruers, T. J. (2004). Responsiveness of the generic EQ-5D summary measure compared to the disease-specific EORTC QLQ C-30. *Quality of Life Research*, 13(7), 1247–1253.
60. Ribaud, J. M., Cella, D., Hahn, E. A., et al. (2000). Re-validation and shortening of the Functional Assessment of Anorexia/Cachexia Therapy (FAACT) questionnaire. *Quality of Life Research*, 9(10), 1137–1146.
61. Salsman, J. M., Beaumont, J. L., Wortman, K., et al. (2015). Brief versions of the FACIT-fatigue and FAACT subscales for patients with non-small cell lung cancer cachexia. *Support Care Cancer*, 23(5), 1355–1364.
62. Thavarajah, N., Bedard, G., Zhang, L., et al. (2014). Psychometric validation of the functional assessment of cancer therapy–brain (FACT-Br) for assessing quality of life in patients with brain metastases. *Support Care Cancer*, 22(4), 1017–1028.
63. Lyons, K. D., Bakitas, M., Hegel, M. T., et al. (2009). Reliability and validity of the Functional Assessment of Chronic Illness Therapy-

Palliative care (FACIT-Pal) scale. *Journal of Pain and Symptom Management*, 37(1), 23–32.

64. Zeng, L., Bedard, G., Cella, D., et al. (2013). Preliminary results of the generation of a shortened quality-of-life assessment for patients with advanced cancer: The FACIT-Pal-14. *Journal of Palliative Medicine*, 16(5), 509–515.
65. Gao, W., Stark, D., Bennett, M. I., et al. (2012). Using the 12-item General Health Questionnaire to screen psychological distress from survivorship to end-of-life care: Dimensionality and item quality. *Psychooncology*, 21(9), 954–961.
66. Le Fevre, P., Devereux, J., Smith, S., et al. (1999). Screening for psychiatric illness in the palliative care inpatient setting: A comparison between the Hospital Anxiety and Depression Scale and the General Health Questionnaire-12. *Palliative Medicine*, 13(5), 399–407.
67. McMillan, S. C., & Mahon, M. (1994). Measuring quality of life in hospice patients using a newly developed Hospice Quality of Life Index. *Quality of Life Research*, 3(6), 437–447.
68. McMillan, S. C., & Weitzner, M. (1998). Quality of life in cancer patients: Use of a revised Hospice Index. *Cancer Practice*, 6(5), 282–288.
69. Hopwood, P., Howell, A., & Maguire, P. (1991). Screening for psychiatric morbidity in patients with advanced breast cancer: Validation of two self-report questionnaires. *British Journal of Cancer*, 64(2), 353–356.
70. Locke, D. E., Decker, P. A., Sloan, J. A., et al. (2007). Validation of single-item linear analog scale assessment of quality of life in neuro-oncology patients. *Journal of Pain and Symptom Management*, 34(6), 628–638.
71. Pratheepawarit, N., Salek, M. S., & Finlay, I. G. (1999). The applicability of quality-of-life assessment in palliative care: Comparing two quality-of-life measures. *Palliative Medicine*, 13(4), 325–334.

72. Lua, P. L., Salek, S., Finlay, I., & Lloyd-Richards, C. (2005). The feasibility, reliability and validity of the McGill Quality of Life Questionnaire-Cardiff Short Form (MQOL-CSF) in palliative care population. *Quality of Life Research*, 14(7), 1669–1681.
73. Cohen, S. R., & Mount, B. M. (2000). Living with cancer: “Good” days and “bad” days—what produces them? Can the McGill quality of life questionnaire distinguish between them? *Cancer*, 89(8), 1854–1865.
74. Cohen, S. R., Mount, B. M., Tomas, J. J., & Mount, L. F. (1996). Existential well-being is an important determinant of quality of life. Evidence from the McGill Quality of Life Questionnaire. *Cancer*, 77(3), 576–586.
75. Cohen, S. R., Mount, B. M., Strobel, M. G., & Bui, F. (1995). The McGill Quality of Life Questionnaire: A measure of quality of life appropriate for people with advanced disease. A preliminary study of validity and acceptability. *Palliative Medicine*, 9(3), 207–219.
76. Cohen, S. R., Mount, B. M., Bruera, E., et al. (1997). Validity of the McGill Quality of Life Questionnaire in the palliative care setting: A multi-centre Canadian study demonstrating the importance of the existential domain. *Palliative Medicine*, 11(1), 3–20.
77. Webber, K., & Davies, A. N. (2011). Validity of the memorial symptom assessment scale-short form psychological subscales in advanced cancer patients. *Journal of Pain and Symptom Management*, 42(5), 761–767.
78. Byock, I. R., & Merriman, M. P. (1998). Measuring quality of life for patients with terminal illness: The Missoula-VITAS quality of life index. *Palliative Medicine*, 12(4), 231–244.
79. Schwartz, C. E., Merriman, M. P., Reed, G., & Byock, I. (2005). Evaluation of the Missoula-VITAS Quality of Life Index—revised: Research tool or clinical tool? *Journal of Palliative Medicine*, 8(1), 121–135.
80. Romero, M. M., Flood, L. S., Gasiewicz, N. K., et al. (2015). Validation of the National Institutes of Health Patient-Reported Outcomes Measurement Information System Survey as a Quality-of-Life

Instrument for Patients with Malignant Brain Tumors and Their Caregivers. *Nursing Clinics of North America*, 50(4), 679–690.

81. Yost, K. J., Eton, D. T., Garcia, S. F., & Cella, D. (2011). Minimally important differences were estimated for six Patient-Reported Outcomes Measurement Information System-Cancer scales in advanced-stage cancer patients. *Journal of Clinical Epidemiology*, 64(5), 507–516.
82. Antunes, B., Murtagh, F., Bausewein, C., et al. (2015). Screening for depression in advanced disease: Psychometric properties, sensitivity, and specificity of two items of the Palliative Care Outcome Scale (POS). *Journal of Pain and Symptom Management*, 49(2), 277–288.
83. Hearn, J., & Higginson, I. J. (1999). Development and validation of a core outcome measure for palliative care: The palliative care outcome scale. Palliative Care Core Audit Project Advisory Group. *Quality in Health Care*, 8(4), 219–227.
84. Siegert, R. J., Gao, W., Walkey, F. H., & Higginson, I. J. (2010). Psychological well-being and quality of care: A factor-analytic examination of the palliative care outcome scale. *Journal of Pain and Symptom Management*, 40(1), 67–74.
85. Muriel, A. C., Moore, C. W., Baer, L., et al. (2012). Measuring psychosocial distress and parenting concerns among adults with cancer: The Parenting Concerns Questionnaire. *Cancer*, 118(22), 5671–5678.
86. Chochinov, H. M., Hassard, T., McClement, S., et al. (2008). The patient dignity inventory: A novel way of measuring dignity-related distress in palliative care. *Journal of Pain and Symptom Management*, 36(6), 559–571.
87. Albers, G., Pasman, H. R., Rurup, M. L., et al. (2008). Analysis of the construct of dignity and content validity of the patient dignity inventory. *Cancer*, 112(11), 2509–2517.
88. Mack, J. W., Nilsson, M., Balboni, T., et al. (2008). Peace, equanimity, and acceptance in the cancer experience (PEACE): Validation of a scale to assess acceptance and struggle with terminal illness. *Cancer*, 112(11), 2509–2517.

89. Hadorn, D. C., Sorensen, J., & Holte, J. (1995). Large-scale health outcomes evaluation: How should quality of life be measured? Part II—Questionnaire validation in a cohort of patients with advanced cancer. *Journal of Clinical Epidemiology*, 48(5), 619–629.
90. Steinhauser, K. E., Bosworth, H. B., Clipp, E. C., et al. (2002). Initial assessment of a new instrument to measure quality of life at the end of life. *Journal of Palliative Medicine*, 5(6), 829–841.
91. Steinhauser, K. E., Clipp, E. C., Bosworth, H. B., et al. (2004). Measuring quality of life at the end of life: Validation of the QUAL-E. *Palliat Support Care*, 2(1), 3–14.
92. Lo, C., Burman, D., Swami, N., et al. (2011). Validation of the QUAL-EC for assessing quality of life in patients with advanced cancer. *European Journal of Cancer*, 47(4), 554–560.
93. Shahidi, J., Bernier, N., & Cohen, S. R. (2010). Quality of life in terminally ill cancer patients: Contributors and content validity of instruments. *Journal of Palliative Medicine*, 26(2), 88–93.
94. Steel, K., Ljunggren, G., Topinkova, E., et al. (2003). The RAIPC: An assessment instrument for palliative care in all settings. *American Journal of Hospice and Palliative Medicine*, 20(3), 211–219.
95. de Haes, J. C., van Knippenberg, F. C., & Neijt, J. P. (1990). Measuring psychological and physical distress in cancer patients: Structure and application of the Rotterdam Symptom Checklist. *British Journal of Cancer*, 62(6), 1034–1038.
96. Janssen, S. J., Teunis, T., van Dijk, E., et al. (2017). Validation of the Spine Oncology Study Group-Outcomes Questionnaire to assess quality of life in patients with metastatic spine disease. *Spine Journal*, 17(6), 768–776.
97. de Jager Meezenbroek, E., Garssen, B., Van den Berg, M., et al. (2012). Measuring spirituality as a universal human experience: Development of the Spiritual Attitude and Involvement List (SAIL). *Journal of Psychosocial Oncology*, 30(2), 141–167.
98. Sharma, R. K., Astrow, A. B., Texeira, K., & Sulmasy, D. P. (2012). The Spiritual Needs Assessment for Patients (SNAP): Development and

validation of a comprehensive instrument to assess unmet spiritual needs. *Journal of Pain and Symptom Management*, 44(1), 44–51.

99. Steinmann, D., Schafer, C., van Oorschot, B., et al. (2009). Effects of radiotherapy for brain metastases on quality of life (QoL). Prospective pilot study of the DEGRO QoL working party. *Strahlentherapie und Onkologie*, 185(3), 190–197.
100. Garratt, A., Schmidt, L., Mackintosh, A., & Fitzpatrick, R. (2002). Quality of life measurement: Bibliographic study of patient assessed health outcome measures. *BMJ*, 324(7351), 1417.
101. EORTC.(2017). Questionnaires. <http://group.s.eortc.be/qol/eortc-qlq-c30>. Accessed March 12 2017.
102. Velikova, G., Booth, L., Smith, A. B., et al. (2004). Measuring quality of life in routine oncology practice improves communication and patient well-being: A randomized controlled trial. *Journal of Clinical Oncology*, 22(4), 714–724.
103. Wintner, L. M., Sztankay, M., Aaronson, N., et al. (2016). The use of EORTC measures in daily clinical practice-A synopsis of a newly developed manual. *European Journal of Cancer*, 68, 73–81.
104. Aspinall, F., Hughes, R., Dunkley, M., & Addington-Hall, J. (2006). What is important to measure in the last months and weeks of life?: A modified nominal group study. *International Journal of Nursing Studies*, 43(4), 393–403.
105. Teno, J. M., Byock, I., & Field, M. J. (1999). Research agenda for developing measures to examine quality of care and quality of life of patients diagnosed with life-limiting illness. *Journal of Pain and Symptom Management*, 17(2), 75–82.
106. Stewart, A. L., Teno, J., Patrick, D. L., & Lynn, J. (1999). The concept of quality of life of dying persons in the context of health care. *Journal of Pain and Symptom Management*, 17(2), 93–108.
107. Fok, C. C., & Henry, D. (2015). Increasing the sensitivity of measures to change. *Prevention Science*, 16(7), 978–986.
108. Cocks, K., King, M. T., Velikova, G., et al. (2011). Evidence based guidelines for determination of sample size and interpretation of the European Organisation for the Research and Treatment of Cancer

Quality of Life Questionnaire Core 30. *Journal of Clinical Oncology*, 29(1), 89–96.

Supplement 1. Keyword search string

Topic	Keywords
Palliative	("Palliative Care/psychology"[MAJOR] OR Palliative care [MH] OR Palliative Medicine [MH] OR palliative [ALL] OR palliat* [AL] OR Terminal care [MH] or terminal [ALL] OR Terminally ill [MH] OR "end of life" [TW] OR Hospice Care [MH] OR "advanced cancer" [TW] OR "life-sustaining" [TW] OR "proximity to death" [TW] OR "neoplasm metastasis"[MeSH Terms] OR "metastasis"[All Fields] OR "metastases"[All Fields] OR "metastatic"[All Fields] OR "metastasized"[All Fields] OR "end stage cancer" [TW] OR "advanced stage cancer"[TW])
Measurement instruments	(Validation Studies [PTYP] OR "validation studies as topic"[MH] OR validation studies [TW] OR Psychometrics [MH] OR Surveys and Questionnaires [MH] OR Sensitivity and Specificity[MH] OR Reproducibility of Results [MH] OR validity [TW] OR responsiveness [TW] OR reliability [TW] OR measurement error [TW] OR "reproducibility of results" [TW] OR psychometrics [TW] OR clinimetric [TW]) OR ((Validation Studies [PTYP]) AND ("Brief Hospice Inventory"[TW] OR Cambridge Palliative Audit Schedule[TW] OR "Demoralization Scale"[TW] OR "Edmonton Functional Assessment Tool"[TW] OR Emanuel and Emanuel Medical Directive [TW] OR "EORTC-QLQ" [TW] OR "ESAS" [TW] OR "FACIT-PAL" [TW] OR "HQLI" [TW] OR "Life Closure Scale" [TW] OR "Life Evaluation Questionnaire" [TW] OR McMaster Quality of Life Scale [TW] OR "McGill Quality of Life Questionnaire" [TW] OR McCanse Readiness for Death Instrument [TW] OR "Memorial Symptom Assessment Scale" [TI] OR "Condensed Memorial Symptom Assessment Scale" [TW] OR "MSAS-GDI" [TW] OR "MVQOLI" [TW] OR "NA-ACP" [TW] OR "Patient Dignity Inventory" [TW] OR Problems and Needs in Palliative Care questionnaire [TW] OR "Palliative care Outcome Scale" [TW] OR "QODD" [TW] OR "QUAL-E" [TW] OR Spiritual Needs Inventory [TW]))
Quality of life	(Quality of life [MH] OR quality of life OR QOL[TW])
Publication type	NOT ("addresses"[Publication Type] OR "biography"[Publication Type] OR "case reports"[Publication Type] OR "clinical trial"[Publication Type] OR "clinical trial, phase i"[Publication Type] OR "clinical trial, phase ii"[Publication Type] OR "clinical trial, phase iii"[Publication Type] OR "clinical trial, phase iv"[Publication Type] OR "comment"[Publication Type] OR "comparative study"[Publication Type] OR "congresses"[Publication Type] OR "consensus development conference"[Publication Type] OR "controlled clinical trial"[Publication Type] OR "editorial"[Publication Type] OR "electronic supplementary materials"[Publication Type] OR "guideline"[Publication Type] OR "historical articles"[Publication Type] OR "introductory journal article"[Publication Type] OR "lectures"[Publication Type] OR "letter"[Publication Type] OR "meta analysis"[Publication Type] OR "practice guideline"[Publication Type] OR "publication components"[Publication Type] OR "randomized controlled trial"[Publication Type] OR "retracted publication"[Publication Type] OR "retraction of publication"[Publication Type])

Supplement 2. Quality Criteria for Measurement Properties

Property	Quality criteria	
Content validity		A clear description is provided of the measurement aim, the target population, the concepts that are being measured and the item selection AND target population AND (investigators OR experts) were involved in item selection AND a full copy of the instrument should be available
	+	
	?	A clear description of above mentioned aspects is lacking OR only target population involved OR doubtful design or method OR a full copy of the instrument is lacking;
	-	No target population involvement;
Construct validity	0	No information found on target population involvement.
	+	Specific hypotheses were formulated AND at least 75% of the results are in accordance with these hypotheses
	?	Doubtful design or method (e.g. no hypotheses)
	-	Less than 75% of hypotheses were confirmed, despite adequate design and methods
	0	No information found on construct validity
Internal consistency	+	Factor analyses performed on adequate sample (7* number of items AND >100) (to assess unidimensionality) AND Cronbach's alpha calculated per dimension AND Cronbach's alpha between 0.7 – 0.95
	?	No factor analysis OR doubtful design (1)
	-	Cronbach's alpha <0.7 or >0.95, despite adequate design and method (2)
	0	No information found on internal consistency
Reliability	+	ICC or weighted Kappa >0.7 AND time interval at least one week (3)
	?	Doubtful design or method (e.g. spearman or no two measurements; administrations should be independent, time interval not mentioned, time interval not appropriate, patients were not stable in the interim period, test conditions for both measurements were not comparable (administration, environment, instructions))
	-	ICC or weighted Kappa <0.7, despite adequate design and method
	0	No information found on reliability
Absolute measurement error	+	SEM or MIC < SDC OR MIC outside the LOA OR convincing arguments that the measurements error is acceptable
	?	Doubtful design or method (e.g. not two independent measurements, patient not stable in interim period, no appropriate time interval (recall bias), test conditions similar) (OR SEM or MIC not defined AND no convincing argument that the measurement error is acceptable)
	-	SEM >= MIC or SDC ≥ MIC or MIC equals or inside LOA OR RR ≤ 1.96 OR AUC<0.7, despite adequate design and methods
	0	No information on absolute measurement error

Responsiveness		Specific hypotheses were formulated AND at least 75% of the results are in accordance with these hypotheses AND at least two measurements are available AND the time interval is described OR SDC<MIC or MIC outside the LOA or RR >0.96 OR AUC>=0.7
	+	
	?	Doubtful design or method (e.g., no hypotheses)
	-	Less than 75% of hypotheses were confirmed, despite adequate design and methods OR SDC>=MIC or MIC equals or inside LOA OR RR<=1.96 OR AUC<0.7, despite adequate design and method
Interpretability	0	No information on responsiveness
	+	Subgroups of patients AND MIC defined AND no floor/ceiling effects were present
	?	Doubtful design or method OR no subgroups OR no MIC defined OR floor/ceiling effects were present
	0	No information found on interpretability

Abbreviations: ICC = intraclass correlation SEM = standard error of measurement; MIC = minimal important change; SDC = smallest detectable change; LOA = limits of agreement; AUC = area under the curve; RR = responsiveness ratio.

^a + = positive rating; ? = indeterminate rating; - = negative rating; 0 = no information available.

^b Doubtful design or method = lacking of a clear description of the design or methods of the study, sample size smaller than 50 subjects (should be at least 50 in every (subgroup) analysis), or no clear description of handling of (%) missing items or any important methodological weakness in the design or execution of the study (e.g., only included complete patients (selection bias); comparison of long and short version when responses of short were obtained with the longer version).

(1) 75% of Cronbach's alphas between 0.70 and 0.90 AND no Cronbach's alpha <0.50

(2) <75% of Cronbach's alphas between 0.70 and 0.90 OR Cronbach's alpha <0.50

(3) time interval at least one week OR less than one week when the instrument contains 30 or more items OR less than one week when convincing arguments were given that the time interval was appropriate (to avoid recall bias).

PART 2

Assessing quality of life and care experiences

CHAPTER 5

Prospective cohort study of patients with advanced cancer and their relatives on the experienced quality of care and life (eQuiPe study): a study protocol

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Abstract

Background: Palliative care is becoming increasingly important because the number of patients with an incurable disease is growing and their survival is improving. Previous research tells us that early palliative care has the potential to improve quality of life (QoL) in patients with advanced cancer and their relatives. According to limited research on palliative care in the Netherlands, patients with advanced cancer and their relatives find current palliative care suboptimal. The aim of the eQuiPe study is to understand the experienced quality of care (QoC) and QoL of patients with advanced cancer and their relatives to further improve palliative care.

Methods: A prospective longitudinal observational cohort study is conducted among patients with advanced cancer and their relatives. Patients and relatives receive a questionnaire every 3 months regarding experienced QoC and QoL during the palliative trajectory. Bereaved relatives receive a final questionnaire 3 to 6 months after the patients' death. Data from questionnaires are linked with detailed clinical data from the Netherlands Cancer Registry (NCR). By means of descriptive statistics we will examine the experienced QoC and QoL in our study population. Differences between subgroups and changes over time will be assessed while adjusting for confounding factors.

Discussion: This study will be the first to prospectively and longitudinally explore experienced QoC and QoL in patients with advanced cancer and their relatives simultaneously. This study will provide us with population-based information in patients with advanced cancer and their relatives including changes over time. Results from the study will inform us on how to further improve palliative care.

Trial registration: Trial NL6408 (NTR6584). Registered in Netherlands Trial Register on June 30, 2017.

Background

Death comes to us all. In 2017, almost 47.000 people died of cancer in the Netherlands, which was with 31% the most common cause of death, followed by cardiovascular disease (25%) and mental disorders or diseases of the nervous system (14%) [1]. The number of people who die of cancer is relatively stable over time [2], despite increasing incidence of cancer and new treatment modalities in cancer, such as immunotherapies and targeted therapies. Fortunately, early detection and advances in cancer treatments have greatly improved survival. Consequently, the time patients live after their diagnosis of advanced cancer is prolonged and the number of patients diagnosed with advanced cancer has increased.

The disease trajectory of advanced cancer for patients is often depicted as a chronic illness, eventually followed by a steep decline and an inevitable death [3]. For relatives of patients with advanced cancer, the disease trajectory also includes a bereavement period after the death of a loved one. At some point in the advanced cancer trajectory, palliative care becomes important. Palliative care is an approach that provides prevention and relief of suffering by means of early identification and assessment and treatment of pain and other physical, psychosocial and spiritual problems [4]. Ideally, palliative care is timely and gradually integrated in oncological care so patients and relatives benefit most from palliative care services [3]. It is important that palliative care is timely integrated in standard oncological care because quality of life (QoL) is improved when patients with advanced cancer receive early palliative care [5–8].

Despite rapid developments [9], the integration and quality of palliative care in oncological care in the Netherlands could be further improved. Recent research shows that patients with advanced cancer are only

reasonably satisfied with hospital care [10, 11]. This is worrisome, as the study by Engel et al. suggests that the experienced quality of care (QoC) and QoL may be positively associated. The effect evaluation of the Dutch National Quality Improvement Program Palliative Care showed that most patients and relatives are satisfied with palliative care, but improvements regarding psychosocial and spiritual support and post-bereavement care for relatives are needed [12]. Other research among relatives of patients who died in a University hospital showed that bereaved relatives reported a broad range of experiences, which suggest a widespread variance of the QoC [13]. For instance, Witkamp et al. showed that only 64% of bereaved relatives reported that they had been told that the patient's death was imminent and 53% stated that the patients' symptoms and problems in the last 24 h had been sufficiently alleviated. The same study found that according to bereaved relatives, only 42% of the patients had been sufficiently involved in medical decision making [13]. Unfortunately, solid and conclusive information on the experienced QoC and QoL in patients with advanced cancer and their relatives is scarce. Moreover, longitudinal research during the advanced cancer trajectory in patients and relatives is lacking.

A prospective longitudinal observational cohort study on experienced QoC and QoL in patients with advanced cancer and their relatives in the Netherlands is needed. This study will provide more insight into the care experiences, needs and QoL of patients with advanced cancer and their relatives that can guide us in improving daily oncological care and the integration of palliative care.

Methods

Aim

The aim of this study is to gain insight into the care experiences and QoL

of patients with advanced cancer and their relatives. The following research questions will be addressed:

- What is the experienced QoC according to patients with advanced cancer and their relatives?
- What is the experienced QoL in patients with advanced cancer and their relatives?
- Which factors are associated with the experienced QoC and QoL in patients with advanced cancer and their relatives?

Study design

The study is a prospective longitudinal observational cohort study on experienced QoC and QoL in patients with advanced cancer and their relatives (eQuiPe study). Patients and their relatives are invited to complete questionnaires on experienced QoC and QoL every 3 months until death. Three to 6 months after a patient is deceased, the bereaved relative will receive a short final questionnaire. The survey data will be directly linked to the detailed clinical data routinely collected on patient characteristics, tumour characteristics, and treatment from the Netherlands Cancer Registry (NCR).

Setting

The eQuiPe study is a nationwide study that is conducted in multiple hospitals (n = 40) in the Netherlands. Per hospital, the departments of medical oncology, pulmonology, and/or urology are participating in the study to identify eligible patients between November 2017 and January 2020.

Study population

All patients with a diagnosis of a solid metastasized tumor (stage IV) are eligible for inclusion. Additional inclusion criteria are required for patients diagnosed with breast cancer and with prostate cancer to reduce variation

and overrepresentation of patients with advanced cancer with a relatively good prognosis. Patients diagnosed with breast cancer are eligible when their metastases are located in multiple organ systems. Patients suffering from prostate cancer are eligible when their cancer is metastasized and castrate-resistant. These criteria are based on information regarding the mean survival time of these groups (NCR). Relatives of included patients, as chosen by the patient, will also be invited to participate in the study. Patients or relatives can participate in the study irrespective of the participation of the other. Patients are also allowed to invite more than one relative to participate in the study. Table 1 provides an overview of the inclusion and exclusion criteria.

Table 1. Inclusion- and exclusion criteria

Inclusion criteria	
Patients are eligible for inclusion if they are;	<ul style="list-style-type: none"> • diagnosed with (progression of) a solid tumour (stage IV) with metastases • additional criteria are in place for the following diagnosis: <ul style="list-style-type: none"> - breast cancer (stage IV with metastases in multiple organ systems) - prostate cancer (stage IV and Castrate-Resistant) • older than 18 years • able to complete a Dutch self-report questionnaire • able to understand the objective of the study and have signed the informed consent
Relatives of patients are eligible for inclusion if they are;	<ul style="list-style-type: none"> • indicated by the patient as relative • older than 18 years • able to complete a Dutch self-report questionnaire • able to understand the objective of the study and have signed the informed consent
Exclusion criteria	
Patients and their relatives are excluded for participation in the study if;	<ul style="list-style-type: none"> • they suffer from dementia • they have a history of severe psychiatric illness

Recruitment

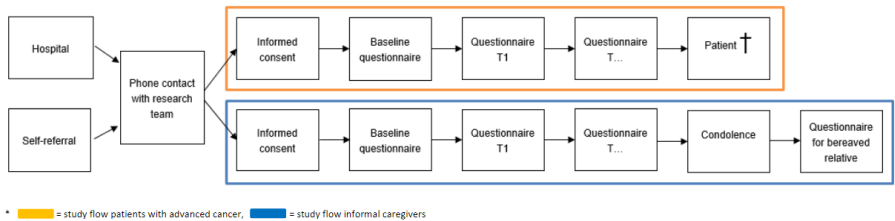
Health care professionals of participating hospitals will identify patients who meet the inclusion and exclusion criteria. Health care professionals will hand out a patient information leaflet and ask eligible patients if they may be approached by the research team. The patient information leaflet will include comprehensive and understandable information regarding the study. Health care professionals will hand over the patients' name and phone number to the research team after receiving consent from the patient, which is noted in the patient file or noted on a research sheet. These contact details will be given by phone, secured email or an online secured shared document, whichever route is preferred by the hospital. There is a possibility of self-referral for patients with advanced cancer and their relatives. Advertisement is spread via a Dutch online platform for patients and relatives who are confronted with cancer (www.kanker.nl). Patients and relatives can leave a contact request for the researcher. The recruitment procedure is similar for patients referred by their health care professional.

Study procedures

Inclusion

A flowchart of the study procedures are presented in Fig. 1. Within a few days after receiving the patient's contact information a researcher will phone the patient to explain the study and discuss participation. The patient is asked whether the researcher may approach one of his/her relatives. The relative is informed about the study via a similar procedure. When the patient and/or relative are willing to participate in the study, they are given the option to choose for the informed consent and questionnaires on paper or a web-based version via the Patient Reported Outcomes Following Initial treatment and Long-term Evaluation of Survivorship (PROFILES) registry [14].

Figure 1. Flowchart of study process



Data collection

For the web-based version: after giving consent, participants will receive a letter that contains a link to a secure website (www.profielstudie.nl) where the patient can complete the web survey with their own login codes. The login codes are not directly linked to the patient. Patients who complete the online questionnaire can stop and save their data at each desired moment so they can continue the questionnaire at another time. If the participant prefers a paper version of the survey, they receive a paper version with a stamped self-addressed envelope to return the questionnaire to the researcher. If patients do not complete their questionnaire within 2 weeks, a reminder via email or letter will be sent, including the questionnaire. If the patient does not complete their questionnaire within 2 weeks after the reminder, they will be contacted by phone. A questionnaire regarding QoC and QoL will be sent in the same manner every 3 months, till participants indicate that they no longer want to participate in the study, or until death. After the death of a patient, the participating relative will receive our condolences by a personal postcard. Three to 6 months after the death of the patient, the participating bereaved relative will receive a final request to complete the last questionnaire regarding his or her experiences with care in the last

phase of life of their loved one, QoL, the patient's quality of death, and post-bereavement needs and support.

Questionnaires

A qualitative study was conducted (METC16.2050) to gather input from patients with advanced cancer and their relatives in the development of our questionnaire [15] (Van Roij et al: Shared perspectives of patients with advanced cancer and their informal caregivers on essential aspects of health care: a qualitative study, submitted). Participants of the focus groups and interviews shared their experiences regarding QoC and QoL, which helped us identify relevant themes for this cohort study. Therefore, the questionnaires involve many topics related to QoC and QoL that were raised by patients with advanced cancer and relatives themselves. Additionally, a systematic literature review was conducted to identify suitable and valid measurement instruments to use in our study [16]. Furthermore, the approved Dutch Quality framework regarding palliative care [17] has also been taken into account while selecting relevant measurement instruments for the eQuiPe study to maximize the comparability of our results. Subsequently, socio-demographic variables such as marital status, ethnicity, educational level, and religion were self-administered and added to the questionnaires. Table 2 provides an overview of all measurement instruments included in the study.

The questionnaires were tested on completion time, appropriateness, and burden in a pilot study (n = 31) among patients with advanced cancer and relatives. The pilot consisted of the 'think-aloud' method with six participants (two patients with advanced cancer, two relatives, and two bereaved relatives) and 15 participants gave postal feedback. Results of the pilot study indicated that the mean completion time for the most extensive questionnaire (baseline measurement for patients) was 38 min and completing the questionnaire was not experienced as a great burden,

confrontational, incomprehensible, or inappropriate. Suggestions made by the participants of the pilot study were taken into account to further improve the questionnaire. Results from the pilot suggested that the questionnaire length is suitable for our study population. For patients who also participate in national tumor-specific cohort studies (PLCRC, POCOP, PACAP) [41], the questionnaires will be aligned and adjusted in order to decrease the response burden for participants.

Table 2. Overview measurement instruments and times points at which the questionnaires are administered during the study

Measurement	Measurement instrument	Baseline*	Follow-up (every three months)	After patients' death
Patients				
Quality of care	QLQ-IN-PATSAT32 [18], items CQ-index [19], items based on Dutch Quality framework Palliative Care [17]	X	X	
Health care consumption	Self-administered items	X	X	
Shared decision making	CPS [20], DEPS [21], Self-administered items	X	X	
Health care needs	PNPC-sv patient form [22]	X	X	
Quality of life	EORTC QLQ-C30 [23]	X	X	
Spiritual wellbeing	FACIT-sp [24]	X	X	
Social support	FACT-G scale [25]	X	X	
Use of social network	Self-administered item	X	-	
Sexual health	single items EORTC	X	X	
Body image	BIS [26]	X	X	

Relationship satisfaction ¹	Relationship ladder of the DAS [27]	X	X	
Illness perception	BIP [28]	X	X	
Individual coping	Brief COPE Inventory [29]	X	X	
Resilience	Connor-Davidson Resilience Scale [30]	X	X	
Dyadic coping ¹	DCI [31]	X	-	
Self-management	HeiQ [32]	X	-	
Depression	HADS depression scale [33]	X	-	
Relatives				
Quality of care	INPATSAT32 [18], CQ-index [19], items based on Dutch Quality framework Palliative Care [17]	X	X	-
Health care consumption	Self-administered items	X	X	
Health care needs	PNPC-sv caregiver form [22]	X	X	-
Evaluation of services	VOICES-SF [34], items based on Dutch Quality framework Palliative Care [17]	-	-	X
Quality of life	EORTC QLQ-C30 items [23]	X	X	X
Sexual health	single items EORTC	X	X	-
Social support	FACT-G scale [25]	X	X	X
Personal self-care	Personal Self-Care subscale of the SCPS [35]	X	X	X
Caregiver burden	ZARIT-12 [36], SRB [37]	X	X	-
Relationship satisfaction ¹	Relationship ladder from the DAS [27]	X	X	-
Individual coping	brief COPE Inventory [29]	X	X	-

Resilience	Connor-Davidson Resilience Scale [30]	X	X	-
Pre-death grief	Pre-death grief [38]	X	X	-
Dyadic coping ¹	DCI [31]	X	-	-
Circumstances of death	Self-administered items	-	-	X
Openness of communication about illness and death	CCID [39]	-	-	X
Impact of death	IES [40]	-	-	X

¹only provided to those patients and relatives with a partner.

Abbreviations: BIP = Brief Illness Perception, BIS = Body Image Scale, BMI = Body mass index, CCID=Caregiver's Communication with the Patient about Illness and Death, CPS=Control Preferences Scale, CQ-index = Consumer Quality Index, DAS = Dyadic Adjustment Scale, DCI = Dyadic Coping Inventory, DEPS=Decision-making Participation Self-efficacy scale, EORTC QLQ-C30 = European organization for research and treatment of cancer quality of life questionnaire Core 30 items, FACIT-sp = Functional Assessment of Chronic Illness Therapy Spiritual Well-Being, FACT-G= Functional Assessment of Cancer Therapy General, HADS=Hospital Anxiety and Depression Scale, HeiQ=Health Education Impact Questionnaire, IES = Impact of Event Scale, INPATSAT32 = In-Patient Satisfaction with care measure 32 items, PNPC-sv=Problems and Needs in Palliative Care short form, SCPS=Self Care Practices Scale, SRB= Self-Rated Burden scale, VOICES-SF = Views Of Informal Carers' Evaluation of Services Short Form, ZARIT-12=Zarit Burden.

PROFILES and NCR

PROFILES will be used for the logistics of the questionnaires. 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 people confronted with cancer. PROFILES follows the quality guidelines that are formulated in the 'Data Seal of Approval' document (www.datasealofapproval.org), developed by Data Archiving and Networked Services. The PROFILES registry is an ongoing data collection

of patient reported outcomes within the sampling frame of the NCR and can be linked with clinical data of all individuals newly diagnosed with cancer in the Netherlands. For the eQuiPe study, sociodemographic and clinical data will be obtained from the NCR. Socio-demographic variables include date of birth, sex, and socio-economic status. Clinical data include cancer type, stage, and date of diagnosis.

Study parameters

Main outcome

The main outcome of this study is the experienced QoC and QoL in patients with advanced cancer and their relatives. This includes all domains of QoL such as physical, psychological, social, and spiritual wellbeing.

Secondary outcomes

Secondary outcomes in this study are health care needs, shared decision making, and health care consumption of patients and relatives. Furthermore, social support, resilience, body image, sexual wellbeing, illness perception, individual coping, self-management, depression and use of social networks are measured (Table 2). Relatives will also receive questions on caregiver burden and personal self-care. For patients and relatives with a partner, also relationship satisfaction and dyadic coping will be assessed. In bereaved relatives, health care services in the last days of the patients' life and aftercare will be evaluated. Furthermore, circumstances and impact of the patient's death and the communication between relative and patient about illness and death are assessed.

Statistical analysis

We aim for a large study population of approximately 1500 patients with advanced cancer and 1000 relatives. Including a large group of patients and relatives is necessary to assess the QoC and QoL of these participants

at different time points in the palliative care trajectory and its course. A study sample of this size enables us to perform subgroup analyses, for example per age group, primary tumor site, cancer treatment, diagnosis, sex, and geographical region. Also, high dropout and lower response rates due to disease-related characteristics of our study population have to be taken into account. Due to the nature of this observational study, no sample size calculations have been performed but the number of patients are based on annual incidence of advanced cancer in the Netherlands as recorded in the NCR.

All statistical analysis will be performed using statistical packages STATA version 16. For all analyses a two-sided significance level of $p < 0.05$ will be used. Descriptive statistics (frequencies, median, mean) will be used to analyze the experienced QoC, QoL, healthcare use, advance care planning, symptom burden of patients and relatives. Further, univariate analyses will be used to analyze the crude differences between subgroups regarding QoC or QoL using parametric tests, provided that the assumptions of these tests are met. If not, non-parametric tests will be used. When testing differences between subgroups, we will adjust for confounders which are theoretically relevant and statistically associated with the outcome variable of interest. Additionally, multi-level analyses will be used to analyze the primary and secondary outcomes over time.

Dissemination

The funding party (Roparun) and accredited METC of this study will receive a final report of the study with recommendations. Furthermore, results of this study will be published in multiple peer-reviewed publications in scientific journals. The study aims to provide an (inter-)nationally accessible source of data. These data will be available for (internal) auditing and policy making, as all data of the PROFILES registry. PROFILES will perform first analyses on the data to check the quality and

validity. After this process, the data will be freely available for research questions from other noncommercial groups in the Netherlands and abroad, subject to study question, privacy, and confidentiality restrictions, and registration [14].

Discussion

The eQuiPe study aims to gain more insight into the experienced QoC and QoL in patients with advanced cancer and their relatives. Results from the study will raise awareness regarding the poor prognosis of advanced cancer and palliative care needs of patients and their relatives. Furthermore, the eQuiPe study is a unique national project in which many health care professionals unite to gain a deeper understanding of experienced palliative care. Results from this study will inform us on how to further improve palliative care in the Netherlands for patients with advanced cancer and their relatives.

This prospective longitudinal observational cohort study has several strengths. First, we will include about 1500 patients with solid metastasized tumor of any type and approximately 1000 relatives. Due to this large study population it is possible to assess the experienced QoC and QoL of patients and relatives at different time points in the palliative care trajectory. Moreover, this large study sample also enables us to perform subgroup analyses, for example per age group, primary tumor site, cancer treatment, diagnosis, sex, and geographical region. Second, both advanced cancer patients and their relatives are included. Our explorative qualitative study on QoL in patients with advanced cancer and their relatives, as preparation for this current study, showed that advanced cancer has a substantial impact on social engagement, social identity, and social networks for both patients and relatives [15]. Therefore, in order to improve palliative care it is of essence to focus on relatives to really

comprehend their experiences. The inclusion of patients and relatives simultaneously also gives rise to the opportunity to assess them as a dyad, thus taking the interaction between patients and relatives into account. Third, the eQuiPe study is a longitudinal study. In contrast to the majority of the conducted studies on palliative care, patients and relatives will now be followed over time, from inclusion until death and thereafter for the relatives. This will provide insight in changes in their experiences over time which are currently only limitedly known to us. Fourth, our approach of including patients and relatives is highly personal. All patients and relatives will be contacted by phone by the research team to discuss participation. Participants will also be contacted by phone when they have not completed one of the questionnaires. At last, this is a national study. Already 40 of the 80 hospitals in the Netherlands are collaborating with the eQuiPe study, covering a range of academic, teaching and general hospitals and the study has a good geographic spread. Therefore, the conclusions that will follow from the results of the eQuiPe study are likely to be representative for the Netherlands and generalizable for different regions and care settings.

We also expect to encounter some challenges and potential limitations in the eQuiPe study. Firstly, selection bias cannot be ruled out because patients with a higher QoL may be more likely to participate in the study compared to patients with a lower QoL [42]. Health care professionals may contribute to this bias by only asking patients with a higher QoL to participate in our study but also patients that are self-referred may be more inclined to participate when having a higher QoL. For this reason, we emphasize during the initiation visit that professionals can ask all patients with metastasized disease who fulfill the inclusion criteria. Furthermore, attrition may occur because the condition of the patient might worsen over time such that further participation becomes

impossible. As a result, information on the last months of life may be limited. Besides that, the life expectancy of patients varies depending on primary tumor type, which means that some patients will live for 3 months while others may live much longer. In an attempt to reduce this variation and overrepresentation of patients with advanced cancer with a relatively good prognosis, additional inclusion criteria are required for patients with breast cancer and with prostate cancer. A possible alternative for the starting point we considered was the surprise question: "Would I be surprised if this patient died in the next 12 months?". However, according to the review of Downar et al [43], the surprise question seems to be a poor to modestly predictive tool for patients with a near death. Therefore, we opted for an objective measure, namely having metastatic cancer. Another possible limitation is the length of the questionnaires. Due to the length, the workload for participants can become high, which can lead to a higher drop-out, especially in patients experiencing more symptoms from their disease. However, a meta-analysis showed no clear indication that response rates are attributable to the length of questionnaires [44]. A possible solution could be to use computer adaptive testing, but when using computer adaptive testing, it is of essence that all participants use the same mode (i.e., a computer) to answer the questionnaires, otherwise scores are not comparable. We wanted participants to have the option to complete questionnaires on paper as this remains a commonly preferred mode of participation [45]. At last, the clinical data are collected by the NCR, but these are mostly based on initial diagnosis and treatment. Therefore, some clinical data, for example information about treatment in the complete palliative care trajectory, will be collected via the questionnaires. However, some patients may not be fully aware of the specifics of the treatment they receive, hence, information regarding these clinical data may be incomplete.

References

1. CBS. 2017. sterfgevallen. Last checked April 24th 2019.
2. CBS. 2014. <https://www.cbs.nl/nl-nl/nieuws/2014/50/de-meestemensensterven-aan-kanker-en-hart-en-vaatziekten>. Last checked April 24th 2019.
3. Murray SA, Kendall M, Boyd K, Sheikh A. Illness trajectories and palliative care. *BMJ*. 2005;330(7498):1007–11.
4. WHO. Definition palliative care. 2002. <http://www.hooint/cancer/palliative/definition/en/>. Accessed 23 Nov 2016.
5. Temel JS, Greer JA, Muzikansky A, Gallagher ER, Admane S, Jackson VA, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med*. 2010;363(8):733–42.
6. Haun MW, Estel S, Rucker G, Friederich HC, Villalobos M, Thomas M, et al. Early palliative care for adults with advanced cancer. *Cochrane Database Syst Rev*. 2017;6:CD011129.
7. Hui D, Kim YJ, Park JC, Zhang Y, Strasser F, Cherny N, et al. Integration of oncology and palliative care: a systematic review. *Oncologist*. 2015;20(1):77–83.
8. Kaasa S, Loge JH, Aapro M, Albrecht T, Anderson R, Bruera E, et al. Integration of oncology and palliative care: a lancet oncology commission. *Lancet Oncol*. 2018;19(11):e588–653.
9. Woitha K, Garralda E, Martin-Moreno JM, Clark D, Centeno C. Ranking of palliative care development in the countries of the European Union. *J Pain Symptom Manag*. 2016;52(3):370–7.
10. Engel M, Brinkman-Stoppelenburg A, Nieboer D, van der Heide A. Satisfaction with care of hospitalised patients with advanced cancer in the Netherlands. *Eur J Cancer Care (Engl)*. 2018;27(5):e12874.
11. Dutch federation of Cancer Patients Organisations (NFK). Als je niet meer beter wordt wat heb je dan nodig? 2018. <https://nfk.nl/resultaten/als-je-nietmeer-beter-wordt-wat-heb-je-dan-nodig>. Accessed 15 May 2019.

12. Raijmakers NJFA. Kwaliteit van palliatieve zorg door de ogen van patiënten en nabestaanden. Tijdschrift over Kwaliteit en Veiligheid in Zorg. 2015;25(3):8–11.
13. Witkamp FE, van Zuylen L, Borsboom G, van der Rijt CC, van der Heide A. Dying in the hospital: what happens and what matters, according to bereaved relatives. J Pain Symptom Manag. 2015;49(2):203–13.
14. van de Poll-Franse LV, Horevoorts N, van Eenbergen M, Denollet J, Roukema JA, Aaronson NK, et al. The patient reported outcomes following initial treatment and long term evaluation of survivorship registry: scope, rationale and design of an infrastructure for the study of physical and psychosocial outcomes in cancer survivorship cohorts. Eur J Cancer. 2011;47(14):2188–94.
15. van Roij J, Brom L, Youssef-El Soud M, van de Poll-Franse L, Raijmakers NJH. Social consequences of advanced cancer in patients and their informal caregivers: a qualitative study. Support Care Cancer. 2019;27(4):1187–95.
16. van Roij J, Fransen H, van de Poll-Franse L, Zijlstra M, Raijmakers N. Measuring health-related quality of life in patients with advanced cancer: a systematic review of self-administered measurement instruments. Qual Life Res. 2018;27(8):1937–55.
17. Palliactief TNCCOI. Kwaliteitskader palliatieve zorg Nederland. 2017.
18. Bredart A, Bottomley A, Blazeby JM, Conroy T, Coens C, D'Haese S, et al. An international prospective study of the EORTC cancer in-patient satisfaction with care measure (EORTC IN-PATSAT32). Eur J Cancer. 2005;41(14):2120–31.
19. Sixma HHM, Boer D, Delnoij D. Handboek CQI Metingen: richtlijnen en voorschriften voor metingen met een CQI meetinstrument 2008; 2008.
20. Degner LF, Sloan JA, Venkatesh P. The control preferences scale. Can J Nurs Res. 1997;29(3):21–43.

21. Arora NK, Weaver KE, Clayman ML, Oakley-Girvan I, Potosky AL. Physicians' decision-making style and psychosocial outcomes among cancer survivors. *Patient Educ Couns*. 2009;77(3):404–12.
22. Osse BH, Vernooij MJ, Schade E, Grol RP. Towards a new clinical tool for needs assessment in the palliative care of cancer patients: the PNPIC instrument. *J Pain Symptom Manag*. 2004;28(4):329–41.
23. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*. 1993;85(5):365–76.
24. Peterman AH, Fitchett G, Brady MJ, Hernandez L, Cella D. Measuring spiritual well-being in people with cancer: the functional assessment of chronic illness therapy--spiritual well-being scale (FACIT-Sp). *Ann Behav Med*. 2002; 24(1):49–58.
25. Cella DF, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, et al. The functional assessment of cancer therapy scale: development and validation of the general measure. *J Clin Oncol*. 1993;11(3):570–9.
26. Hopwood P, Fletcher I, Lee A, Al Ghazal S. A body image scale for use with cancer patients. *Eur J Cancer*. 2001;37(2):189–97.
27. Spanier GB. Measuring dyadic adjustment: new scales for assessing the quality of marriage and similar dyads. *J Marriage Fam*. 1976;38:15–28.
28. Weinman JPK, Moss-Morris R, Horne R. The Illness Perception Questionnaire: a new method for assessing the cognitive representation of illness. *Psychol Health*. 1996;11:431–45.
29. Carver CS. You want to measure coping but your protocol's too long: consider the brief COPE. *Int J Behav Med*. 1997;4(1):92–100.
30. Vaishnavi S, Connor K, Davidson JR. An abbreviated version of the Connor-Davidson Resilience Scale (CD-RISC), the CD-RISC2: psychometric properties and applications in psychopharmacological trials. *Psychiatry Res*. 2007; 152(2–3):293–7.
31. Bodenmann G. *Dyadisches Coping Inventar: Testmanual [Dyadic coping inventory: testmanual]*. Bern: Huber; 2008.

32. Osborne RH, Elsworth GR, Whitfield K. The health education impact questionnaire (heiQ): an outcomes and evaluation measure for patient education and self-management interventions for people with chronic conditions. *Patient Educ Couns*. 2007;66(2):192–201.
33. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67(6):361–70.
34. Hunt KJ, Richardson A, Darlington AE, Addington-Hall JM. Developing the methods and questionnaire (VOICES-SF) for a national retrospective mortality follow-back survey of palliative and end-of-life care in England. *BMJ Support Palliat Care*. 2019;9(1):e5.
35. Lee JJ, Bride B, Miller SE. Development and initial validation of the self-care practices scale (SCPS). In: Poster session presented at the meeting of the Society for Social Work and Research, Washington, DC; 2016.
36. Bedard M, Molloy DW, Squire L, Dubois S, Lever JA, O'Donnell M. The Zarit burden interview: a new short version and screening version. *Gerontologist*. 2001;41(5):652–7.
37. van Exel NJ, Scholte op Reimer WJ, Brouwer WB, van den Berg B, Koopmanschap MA, van den Bos GA. Instruments for assessing the burden of informal caregiving for stroke patients in clinical practice: a comparison of CSI, CRA, SCQ and self-rated burden. *Clin Rehabil*. 2004; 18(2):203–14.
38. van Doorn C, Kasl SV, Beery LC, Jacobs SC, Prigerson HG. The influence of marital quality and attachment styles on traumatic grief and depressive symptoms. *J Nerv Ment Dis*. 1998;186(9):566–73.
39. Mesters I, van den Borne H, McCormick L, Pruyn J, de Boer M, Imbos T. Openness to discuss cancer in the nuclear family: scale, development, and validation. *Psychosom Med*. 1997;59(3):269–79.
40. Horowitz M, Wilner N, Alvarez W. Impact of event scale: a measure of subjective stress. *Psychosom Med*. 1979;41(3):209–18.
41. Coebergh van den Braak RRJ, van Rijssen LB, van Kleef JJ, Vink GR, Berbee M, van Berge Henegouwen MI, et al. Nationwide comprehensive gastrointestinal cancer cohorts: the 3P initiative. *Acta Oncol*. 2018;57(2):195–202.

42. de Rooij BH, Ezendam NPM, Mols F, Vissers PAJ, Thong MSY, Vlooswijk CCP, et al. Cancer survivors not participating in observational patient-reported outcome studies have a lower survival compared to participants: the population-based PROFILES registry. *Qual Life Res.* 2018;27(12):3313–24.
43. Downar J, Goldman R, Pinto R, Englesakis M, Adhikari NK. The “surprise question” for predicting death in seriously ill patients: a systematic review and meta-analysis. *CMAJ.* 2017;189(13):E484–E93.
44. Rolstad S, Adler J, Ryden A. Response burden and questionnaire length: is shorter better? A review and meta-analysis. *Value Health.* 2011;14(8):1101–8.
45. Horevoorts NJ, Vissers PA, Mols F, Thong MS, van de Poll-Franse LV. Response rates for patient-reported outcomes using web-based versus paper questionnaires: comparison of two invitational methods in older colorectal cancer patients. *J Med Internet Res.* 2015;17(5):e111.

CHAPTER 6

Quality of life and quality of care as experienced by patients with advanced cancer and their relatives: a multicenter observational cohort study (eQuiPe)

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Abstract

Aim: This study aims to assess the quality of life and quality of care as experienced by patients with advanced cancer and their relatives while taking their interdependency into account.

Methods: A prospective multicentre observational study (eQuiPe study) was conducted. Quality of life scores (EORTC QLQ-C30) was compared to a matched normative population and logistic regression analyses were conducted to assess the relation between high emotional functioning (EF, measured with the EORTC QLQ-C30) and experienced quality of care (IN-PATSAT32, CQ-index PC).

Results: In total, 1103 (65%) patients and 831 (71%) relatives completed the baseline questionnaire, including 699 unique patient-relative couples. Patients experienced lower EF than the normative population (78 versus 87, $p < .001$). Compared to patients, relatives reported clinically relevantly lower EF (69 versus 78, $p < .001$). Being more satisfied with care in general ($p < .05$) and clarity about the key health-care provider ($p < .05$) was positively associated with high EF in patients. For relatives, experienced continuity of care ($p < .01$) and information for the patient ($p < .05$) were positively associated with high EF. The EF of patients ($p < .001$) and relatives ($p < .001$) were positively associated with each other and continuity of care as perceived by relatives was positively associated with high EF in patients ($p < .01$).

Conclusions: Patients with advanced cancer reported low levels of EF but their relatives reported even lower levels of EF. Experienced integrated organisation and satisfaction with care were positively related to EF. The interdependent relation between patients' and relatives' EF and their care experiences suggests that a family-centred approach can optimise palliative cancer care.

Introduction

More than one-fifth of all patients with cancer in the Netherlands are diagnosed with primary metastases [1] and up to 65% of patients with cancer will develop metastases during their disease trajectory [2]. Advanced cancer often impacts quality of life (QoL), including emotional functioning (EF, e.g. feeling tense, worried, irritable or down) of patients and their relatives by causing emotional distress [3] due to prognostic uncertainty [4], preparatory grief [5] or death anxiety [6]. Relatives can experience additional emotional distress due to the increasing caregiving burden throughout the cancer trajectory [7,8]. Previous research showed that emotional distress experienced by patients with advanced cancer and their relatives is also interdependent: emotional distress of the patient affects the EF of the relative and vice versa [9,10].

General satisfaction with care is associated with higher EF in patients with advanced cancer [11,12] and their relatives [13]. Moreover, satisfaction with care in patients and relatives is likely to be interdependent. However, how the quality of care and EF of patients has an impact on relatives' EF and vice versa has not yet been assessed. A recent meta-analysis on the effects of family-centred care interventions showed that interventions that involved family members lead to a better QoL in patients with chronic illness [14]. Therefore, taking a family approach in care may also have beneficial effects on patients with advanced cancer.

For the organisation of high-quality integrated palliative oncological care as defined in international guidelines [15,16], it is essential to identify elements of care associated with the QoL of patients with advanced cancer and their relatives. Especially, the relation between the experiences of the patient and the outcome of the relatives and vice versa has not been assessed. Therefore, we aim to (1) assess the QoL of patients

with advanced cancer and their relatives, (2) the association of the QoL with quality of care, and (3) the interdependency between patients and relatives by assessing how EF and care in patients is related to the EF of relatives and vice versa.

Methods

Study design

A prospective, longitudinal, multicentre, observational study on the experienced QoL and care of patients with advanced cancer and their relatives was conducted in the Netherlands [17]. Patients and their relatives were invited by their treating physician from one of the 40 participating hospitals or self-enrolled between November 2017 and January 2020. After written informed consent, patients and relatives completed a paper or online questionnaire every three months till the patient's death via the Patient Reported Outcomes Following Initial treatment and Long-term Evaluation of Survivorship (PROFILES) registry [18]. Primary outcomes of the eQuiPe study were QoL and experienced quality of care. Clinical data were obtained from the Netherlands Cancer Registry (NCR). The study was assessed by the Medical Research Ethics Committee of the Antoni van Leeuwenhoek hospital (METC17.1491). For this study baseline data of patients and relatives was used.

Study population and setting

All adult patients with metastatic cancer were eligible. For patients with breast or prostate cancer additional criteria were defined: patients with breast cancer with metastases in multiple organ systems and patients with prostate cancer with castrate-resistant cancer.

Measures

QoL

QoL was measured by the European Organization for Research and

Treatment of Cancer quality of life questionnaire (EORTC QLQ-C30) [19]. For relatives, only the subscales emotional and social functioning and the global QoL were used. Scores were transformed to a 0-100 scale where a higher score indicates better health and a higher symptom burden. The thresholds of clinical importance by Giesinger et al. [20] were used to compare patients and relatives with high (>71) or low (≤ 71) EF). The QLQ-C30 is the most commonly used questionnaire worldwide to measure QoL in patients with cancer and has good psychometric properties [21]. The QLQ-C30 has been previously used in studies to measure QoL in relatives of patients with cancer [22], although not validated in this group.

Satisfaction with care

General satisfaction and satisfaction with the interpersonal skills of health-care providers was measured by the validated satisfaction with in-patient cancer care (IN-PATSAT32) [23]. Respondents rated the empathic skills of healthcare providers by a self-developed item. All items used a 5-point Likert scale ranging from 'poor' to 'excellent' and were linearly transformed to a 0-100 score where higher scores indicate higher satisfaction.

Organisation of patient's care

Continuity of care and information as experienced by patients and relatives was measured by the Consumer Quality Index Palliative Care (CQ-index PC) [24]. The items were rated on a 4-point scale ranging from never to always. Responses were linearly transformed to 0-100, where higher scores indicated higher continuity of care or information. Patients rated the availability of health-care providers by three self-administered items based on the Netherlands Quality Framework for Palliative Care [25]: 'Is it clear to you who your key health-care provider is?', 'Have you discussed who to call first when you need help?' and 'Is this person or

team/department available day and night?'. We compared confirming patients (yes) to the other patients (no/do not know).

Relatives' involvement in patient's care

Relatives' involvement in decision making was assessed by three items: (1)'Were you involved in decisions of care providers about the care for your relative with advanced cancer?', (2)'Were you able to let the physician know if you had any concerns or questions about what he/she recommended to your relative?' and (3)'Have you discussed with the physician what is important to you about the care for your relative?'. The first two used a 4-point Likert scale and scores were linearly transformed to a 0-100 scale. For the last item, we compared confirming patients (yes) to the other patients (no/don't know).

Support for relatives

Three self-developed items assessed experienced support for relatives by healthcare providers: (1)'To what extent have you been informed by a health-care provider about relevant support options for yourself?', (2)'To what extent have you been able to openly discuss your concerns, fears, hopes, and expectations with a healthcare provider?' and (3)'Did health-care providers pay attention to your dual role as a caregiver and a relative?'. The items were rated according to the 4-point Likert scale of the EORTC QLQ C30 ranging from 'not at all' to 'very much' and linearly transformed to a 0-100 scale.

Socio-demographic and clinical characteristics

Education, marital status, relation to the patient (partner, daughter/son or other family or friend) and ethnicity were self-reported. Comorbidity at the time of survey was measured by the Self-administered Comorbidity Questionnaire (SCQ) [26]. Furthermore, gender, age, primary tumor type and the date of primary cancer diagnosis were obtained from the NCR.

Normative population

QoL data of a normative population from 2017 were obtained from CentERpanel, an online household panel that is a representative of the Dutch population [18]. Individuals from the normative population ($n = 721$) were matched (1:1) based on gender and age categories to compare their QoL scores with patients.

Statistical analysis

Descriptive statistical analyses on all variables were conducted. EORTC QLQ-C30 scores were calculated for the study population and the normative population and compared using paired t-tests. Respondents were dichotomised into two groups based on the clinically important threshold of 71 for EF [20]. First, associations between EF and care elements were explored by multivariable logistic regression analysis for patients and relatives separately. The following confounding factors were controlled for: gender, age, education, relation to the patient and patients' symptom burden. We included all symptoms that are used in the EORTC QLQ-C15-PAL questionnaire to measure QoL in patients with advanced cancer. Second, a multivariable logistic regression model was built to analyse the interdependent relation of patients and relatives on each other's EF. In this analysis, we included unique patient/relative couples. When multiple relatives of a single patient were included in the eQuiPe study (this was the case for $n = 39$ patients), we sequentially selected the partner, offspring or other family/friend to include one relative for each patient and avoid multiple dependent observations within a patient-relative node. All patient-related and relative-related variables associated with EF ($p < .10$) in the separate multivariable logistic regressions were included in this analysis. The Odds ratios (OR) were calculated for every 10-point difference on continuous outcome measures, which range between 0 and 100. A $p\text{-value} < .05$ was

considered statistically significant. As Little's test showed the data were not missing completely at random, multiple imputations were applied to handle missing data (missing data ranged between .8% and 5.9% for patients and 4.8%-12.4% for relatives). All statistical procedures were conducted in STATA 16.0.

Results

In total, 1695 patients and 1171 relatives were contacted (Fig. 1). Of them, 255 (15%) patients did not want to participate and 337 (20%) patients dropped out after giving consent. Finally, 1103 (65%) patients and 831 (71%) relatives consented to participate and completed the baseline questionnaire of the eQuiPe study. Among them were 699 unique patient-relative couples.

Socio-demographic and clinical characteristics

Fifty-one percent of the patients and 39% of the relatives were male and had a mean age of 65 and 60 years, respectively (Table 1). Most patients had lung cancer (29%), colorectal cancer (19%), breast cancer (15%) or prostate cancer (12%). The majority of the relatives were the partner of the patient (74%).

QoL

Patients experienced statistically significant and clinically relevant lower levels of functioning in all QoL domains and more symptoms than the normative population ($p < .001$) (Fig. 2). Relatives experienced significantly lower EF compared to patients, respectively 69(SD 22) versus 78(SD 21), $p < .001$). Thirty-two percent of all patients and 47% of all relatives had an EF 71, indicating clinically important emotional problems.

Figure 1. Flowchart study process

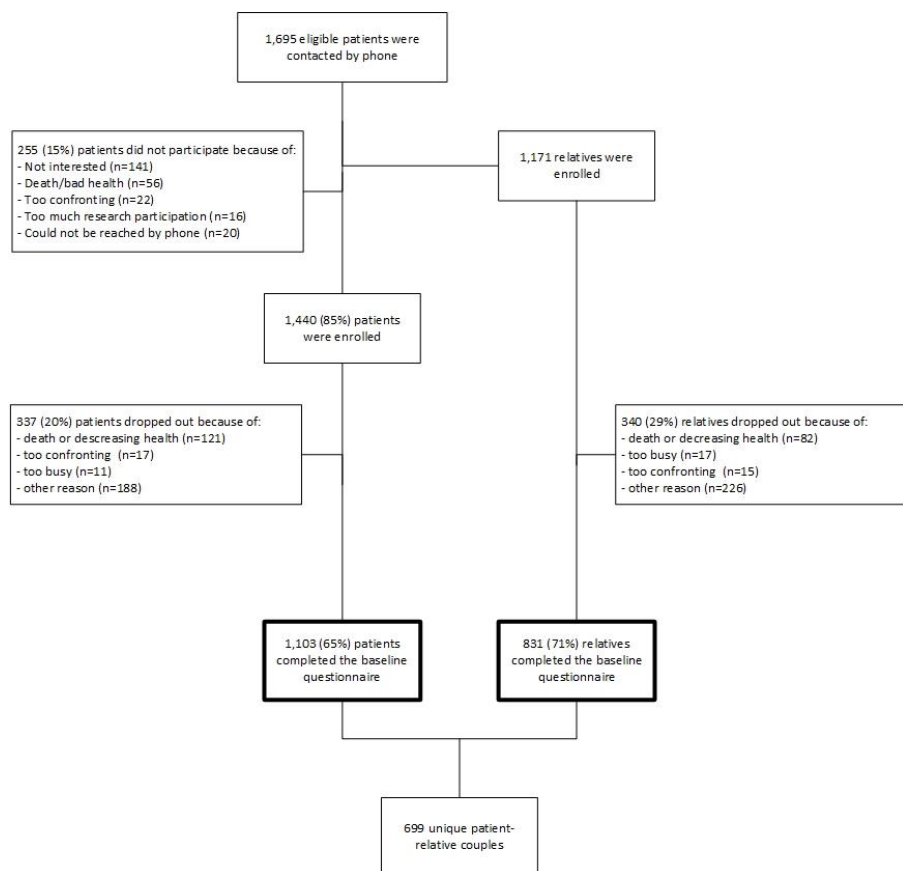
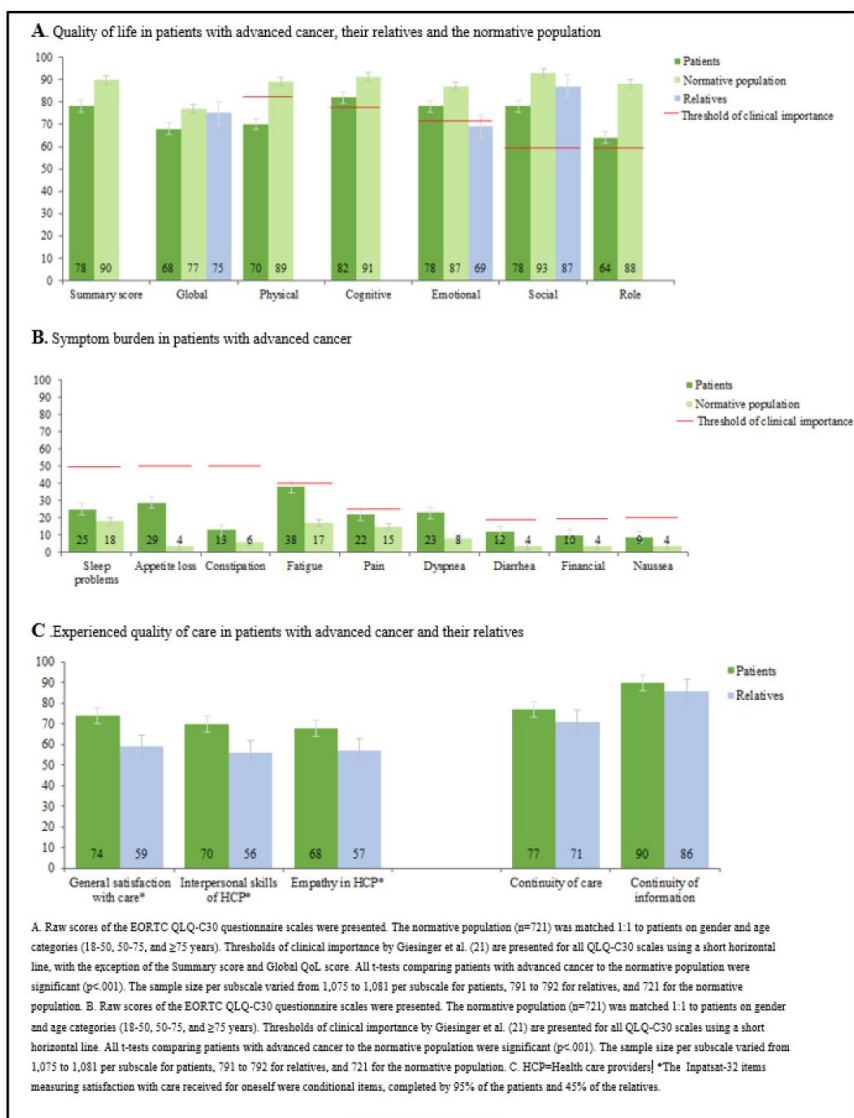


Table 1. Socio-demographic and clinical characteristics of study population.

	Patients (n=1,103)	Relatives (n=831)
	n (%)	n (%)
Gender		
Male	562 (51)	324 (39)
Female	541 (49)	507 (61)
Age		
Mean (SD), range	65 (10), 29-93	60 (13), 18-87
18-50	74 (7)	174 (21)
50-75	834 (76)	557 (67)
≥75	191 (17)	71 (9)
Education ^a		
Low	328 (30)	208 (25)
Medium	450 (41)	373 (45)
High	314 (28)	243 (29)
Ethnicity		
Dutch	1,001 (91)	812 (98)
Other	35 (3)	15 (2)
missing	67 (6)	4 (0)
Primary tumor		
Lung	322 (29)	-
Colorectal	205 (19)	-
Breast	168 (15)	-
Prostate	128 (12)	-
Other	265 (24)	-
Time since primary tumor diagnosis		
<1 year	356 (33)	-
1-5 years	521 (48)	-
>5 years	210 (19)	-
Treatment in the past three months		
Yes	809 (74)	-
No	286 (26)	-
Number of comorbidities ^b		
0	453 (41)	-
1	376 (34)	-
>1	274 (25)	-
Relation to patient		
Partner	-	612 (74)
Daughter/son	-	140 (17)
Other (other family, friend)	-	72 (9)

Missing data: did not exceed 5% unless stated otherwise. ^aEducation levels are categorized according to International Standard Classification of Education guidelines. ^bComorbidities refer to physical conditions from the Self-administered Comorbidities Questionnaire (35).

Figure 2. Quality of life (A), symptoms (B) and experienced quality of care (C) in patients with advanced cancer and their relatives



Quality of care as experienced by patients and relatives

Patients were generally satisfied with care (Fig. 2). Relatives ($n = 345$) were less satisfied with care compared to patients, respectively, 74.4 and 58.7 ($p < .001$).

Quality of care elements associated with high EF of patients and their relatives

Being more satisfied with care in general ($OR = 1.13$ (95%CI:1.00-1.27), $p < .05$) was positively associated with high EF in patients (Table 2). Feeling clarity about who their key health-care provider ($OR = 3.16$ (95%CI:1.14-8.75), $p < .05$) was also positively associated with high EF in patients. Patients who experienced less fatigue ($OR = .76$ (95%CI:.71-.83), $p < .001$), sleep problems ($OR = .87$ (95%CI:.83-.92), $p < .001$), pain ($OR = .92$ (95%CI:.80-.96), $p < .01$) and nausea or vomiting symptoms ($OR = .88$ (95% CI:.80-.96), $p < .01$) have higher odds to have high EF. Also, higher education ($p < .01$) was positively associated with high EF in patients.

Experienced continuity of care ($OR = 1.10$ (95% CI:1.03-1.18), $p < .01$) and continuity of information about care for the patient ($OR = 1.08$ (95% CI:1.01-1.15), $p < .05$) were positively associated with high EF in relatives (Table 2). Relatives who had discussed what is important in the care for the patient with health-care providers had lower odds of a high EF ($OR = .71$ (95%CI:.52-.97), $p < .05$). Older age ($OR = 1.04$ (95%CI:1.02-1.05), $p < .001$) was positively associated with high EF in relatives. Also, relatives who are a child or other family/friend of the patient had higher EF than partners of patients, $p < .001$.

Table 2. Logistic regression analysis of factors associated with high emotional functioning^a of patients with advanced cancer and relatives.

	Patients (n=1,103)	Relatives (n=831)
	OR(CI95%)	OR(CI95%)
Age	1.01 (.99 to 1.02)	1.04 (1.02 to 1.05)***
Gender		
Male	1	1
Female	.77 (.56 to 1.04)	.89 (.66-1.19)
Education		
Low	1	1
Medium	1.63 (1.14 to 2.33)**	1.00 (.70 to 1.43)
High	1.93 (1.29 to 2.89)**	1.21 (.81 to 1.80)
Relation to patient		
Partner	-	1
Daughter/son		3.11 (1.78 to 5.42)***
Other (other family, friend)		3.30 (1.85 to 5.88)***
Patient's symptoms		
Fatigue	.76 (.71 to .83)***	-
Pain	.92 (.80 to .96)**	-
Dyspnea	.98 (.93 to 1.04)	-
Sleep problems	.87 (.83 to .92)***	-
Nausea/vomiting	.88 (.80 to .96)**	-
Appetite loss	1.00 (.94 to 1.07)	-
Constipation	1.00 (.94 to 1.07)	-
Experienced satisfaction with care ^b		
General satisfaction with care	1.13 (1.00 to 1.27)*	-
Interpersonal skills scale	.90 (.77 to 1.06)	-
Empathy	1.08 (.96 to 1.23)	-
Experienced organisation of patient's care		
Continuity of care	1.00 (.93 to 1.08)	1.10 (1.03 to 1.18)**
Continuity of information	1.02 (.94 to 1.10)	1.08 (1.01 to 1.15)*
Clear who is key health-care provider (No)	1	
Yes	3.16 (1.14 to 8.75)*	-
Discussed who to call first (No)	1	
Yes	1.12 (.66 to 1.89)	-
Health-care provider available day and night (No)	1	
Yes	1.19 (.85 to 1.67)	-
Relatives' involvement in patient's care		
Discussed what is important in care for the patient (No)		1
Yes	-	.71 (.52 to .97)*
Involved in decision-making	-	1.01 (.95 to 1.07)
Let the physician know your concerns about the recommendations	-	1.02 (.97 to 1.08)
Experienced support for relatives		
Informed about support options	-	1.03 (.95 to 1.13)
Attention for dual role (being a caregiver and relative)	-	.98 (.89 to 1.09)
Openly discuss your concerns	-	1.01 (.94 to 1.09)

Abbreviations: OR=Odds Ratio, CI=Confidence Interval.

Notes: Multiple imputation was applied to handle missing data. The Odds ratios (OR) were calculated for every 10-point difference on continuous outcome measures. ^a Emotional functioning ≤71=low and >71=high, according to threshold of clinical importance (32). ^b The Inpatsat-32 items measured satisfaction with care received for oneself. *p<.05, **p<.01, ***p<.001

Interdependency between patients and their relatives

Multivariable logistic regression analyses in 699 unique couples showed that high EF in patients was positively associated with the EF of relatives and vice versa ($p < .001$, Table 3). Also, in addition to the significant associations found in the previous analysis, continuity of care as experienced by relatives was positively associated with high EF in patients (OR = 1.13 (95%CI:1.04-1.23), $p < .01$) and relatives (OR = 1.07 (95%CI:1.00-1.15), $p < .05$).

Table 3. Logistic regression analysis of the reciprocal relation (dyadic approach) of patients with advanced cancer and their relatives on high emotional functioning^a (n=699).

	Patients (n=699)	Relatives (n=699)
	OR(CI95%)	OR(CI95%)
Age	.99 (.97 to 1.01)	1.03 (1.01 to 1.05)***
Gender		
Male	1	1
Female	.67 (.45 to 1.01)	.89 (.64 to 1.24)
Education		
Low	1	1
Medium	1.64 (1.02 to 2.62)*	.97 (.66 to 1.43)
High	2.56 (1.48 to 4.41)**	.98 (.63 to 1.52)
Relation to patient		
Partner	-	1
Daughter/son		2.64 (1.39 to 5.00)**
Other (other family, friend)		3.29 (1.68 to 6.45)**
Emotional functioning patient	-	1.28 (1.16 to 1.41)***
Emotional functioning relative	1.18 (1.07 to 1.29)***	-
Patient's symptoms		
Fatigue	.70 (.64 to .77)***	.98 (.90 to 1.07)
Pain	.93 (.86 to 1.01)	1.03 (.96 to 1.10)
Sleep problems	.82 (.77 to .88)***	1.02 (.96 to 1.08)
Nausea/vomiting	.87 (.78 to .98)*	.97 (.88 to 1.07)
Experienced satisfaction with care ^b		
General satisfaction with care (reported by patients)	1.11 (1.01 to 1.22)*	1.02 (.94 to 1.10)
Experienced organisation of patient's care		
Clear who is key health-care provider (No) (reported by patients)	1	1
Yes	6.48 (1.62 to 25.83)**	.63 (.18 to 2.18)
Continuity of care (reported by relatives)	1.13 (1.04 to 1.23)**	1.07 (1.00 to 1.15)*
Continuity of information (reported by relatives)	1.01 (.92 to 1.11)	1.08 (1.01 to 1.17)*

Relatives' involvement in patient's care		
Discussed what is important in care for the patient (No)		
(reported by relatives)		
Yes	1 1.23 (.81 to 1.88)	1 .71 (.50 to .99)*

Abbreviations: OR=Odds Ratio, CI=Confidence Interval.

Notes: Multiple imputation was applied to handle missing data. The Odds ratios (OR) were calculated for every 10-point difference on continuous outcome measures.

^a Emotional functioning ≤ 71 =low and >71 =high, according to threshold of clinical importance (32)

^b The Inpatsat-32 items measured satisfaction with care received for oneself.

* $p<.05$, ** $p<.01$, *** $p<.001$

Discussion

This study including >1000 patients with advanced cancer and their relatives showed that patients scored significantly lower on all QoL domains than a gender and age-matched normative population. Remarkably, EF of relatives and their satisfaction with health-care were lower than that of patients. EF of patients and relatives was positively associated with general satisfaction with care, clarity regarding the key health-care provider, continuity of care and continuity of information regarding care for the patient. Not surprisingly, patient's symptom burden was negatively associated with their EF. Also, higher education in patients and older age of relatives and being a child or other family/friend of the patient (compared to the partner) was positively associated with their own EF. Moreover, the EF of patients and relatives was related to the EF of the other person and continuity of care according to relatives was associated with high EF in patients.

EF is an important aspect of QoL in palliative care. One-third of the patients and almost half of all relatives had an EF score 71 indicating clinically important problems. Previous studies also found lower or similar QoL scores among relatives than patients with advanced cancer [27-29], but higher scores for relatives have also been found [30]. Why relatives often are not only tenser, worried, irritable or down than patients could be because relatives support the patient but also have to balance

established roles and responsibilities and have their own emotional response to the diagnosis and prognosis of advanced cancer.

General satisfaction with care and satisfaction with interpersonal skills of health-care providers of patients with advanced cancer was quite high in our study and is comparable with previous studies in oncology [23,31,32]. Relatives were much less satisfied with health-care they received for themselves compared to patients. Furthermore, our study shows that the assessment of care by the relatives is related to both the EF of the relative and of the patient, underscoring the importance of involving relatives into palliative care. For instance, by asking relatives about daily life in the home setting or by involving relatives more actively in treatment decision making processes. Remarkably, relatives who did not discuss what they found important in care for the patient with health-care providers had more often high EF scores. This finding may reflect that relatives who did not discuss their concerns may have had fewer concerns to discuss. However, due to the cross sectional nature of our study, further investigation in subsequent studies is warranted. More research is necessary to assess the causality of the observed association between EF and health-care-related factors because higher EF may also lead to higher satisfaction with health-care.

Our study showed interdependent relations between organisation (i.e. continuity of care, continuity of information, and clarity about the key health-care provider) of and satisfaction with care and EF within patient-relative couples. Although effect sizes were weak to moderate [33], results indicate that care for patients with advanced cancer may be optimised by including the relatives' perspective and applying a family-centred approach. In a family-centred approach the patient-physician dyad is not the focus of care but the patient-relatives-physician triad is. This is in line with a recent qualitative interview study showing that healthcare providers

view relatives as important stakeholders in the care of the patient [34]. Relatives have in-depth knowledge about the patient's values and beliefs before the cancer diagnosis, and their observations at home provide valuable insights into how the patient is coping with the disease burden. Moreover, their involvement can be useful in decision making and may also support the continuity of care during the transitions between care settings at the end of life [34]. Besides the direct added value of relatives' involvement in the quality of care for the patient, there also seems to be a reciprocal relation regarding the relatives' own healthcare use. A recent study showed that cancer survivors' spouses are more likely to receive supportive care if the patient also received supportive care [35]. This suggests that when health-care providers pay attention to the relatives' experiences they are likely to (indirectly) optimise care for the patient and improve the outcomes for patients and the relative.

Strengths and limitations

Our prospective multicentre study includes >1000 patients with advanced cancer and their relatives. The response rate for both groups was high, respectively, 65% and 71%. Also some limitations need to be addressed. First, generalisability of our results may be limited because compared to patients who died of cancer in the general population in 2018 [36], patients in our study were more often male, younger and more likely to have been diagnosed with prostate or breast cancer. Also, patients with worse health status might be less often included in our study (selection bias), leading to a potential overestimation of QoL and underestimation of symptoms. However, our study population's QoL scores were similar to a previous population-based analysis of patients with cancer 12 months prior to their death [37]. Lastly, not all measures of the quality of care used were validated, especially those in relatives.

Conclusions

Our findings suggest that patients may become less tense, worried, irritable or down when providing high quality care since their EF is associated with general satisfaction with care, clarity about the key health-care provider, continuity of care and continuity of information about care for the patient. Moreover, the interdependent relation between the experiences of patients and relatives provides an opportunity to improve EF of both by using a family-centred approach in palliative oncological care that considers both perspectives.

References

- 1 IKNL. Uitgezaaide kanker in beeld. 2020.
- 2 Riihimaki M, Thomsen H, Sundquist K, Sundquist J, Hemminki K. Clinical landscape of cancer metastases. *Cancer Med* 2018;7(11):5534-42.
- 3 Mitchell AJ, Chan M, Bhatti H, Halton M, Grassi L, Johansen C, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *Lancet Oncol* 2011; 12(2):160-74.
- 4 Medicine) Ilo. Dying in America: improving quality and honoring individual preferences near the end of life. Washington, DC: The National Academies Press; 2015.
- 5 Periyakoil VS, Kraemer HC, Noda A, Moos R, Hallenbeck J, Webster M, et al. The development and initial validation of the terminally ill grief or depression scale (TIGDS). *Int J Method Psychiatr Res* 2005;14(4):202-12.
- 6 Neel C, Lo C, Rydall A, Hales S, Rodin G. Determinants of death anxiety in patients with advanced cancer. *BMJ Support Palliat Care* 2015;5(4):373-80.
- 7 Stenberg U, Ruland CM, Miaskowski C. Review of the literature on the effects of caring for a patient with cancer. *Psycho Oncol* 2010;19(10):1013-25.
- 8 Kim Y, Carver CS, Shaffer KM, Gansler T, Cannady RS. Cancer caregiving predicts physical impairments: roles of earlier caregiving stress and being a spousal caregiver. *Cancer* 2015;121(2): 302-10.
- 9 Jacobs JM, Shaffer KM, Nipp RD, Fishbein JN, MacDonald J, El-Jawahri A, et al. Distress is interdependent in patients and caregivers with newly diagnosed incurable cancers. *Ann Behav Med* 2017;51(4):519-31.
- 10 Streck BP, Wardell DW, LoBiondo-Wood G, Beauchamp JES. Interdependence of physical and psychological morbidity among

patients with cancer and family caregivers: review of the literature. *Psycho Oncol* 2020;29(6):974-89.

- 11 Aboshaiqah A, Al-Saedi TS, Abu-Al-Ruyhaylah MM, Aloufi AA, Alharbi MO, Alharbi SS, et al. Quality of life and satisfaction with care among palliative cancer patients in Saudi Arabia. *Palliat Support Care* 2016;14(6):621-7.
- 12 Scarpa M, Saadeh LM, Fasolo A, Alfieri R, Cagol M, Cavallin F, et al. Health-related quality of life in patients with oesophageal cancer: analysis at different steps of the treatment pathway. *J Gastrointest Surg* 2013;17(3):421-33.
- 13 Morishita M, Kamibeppu K. Quality of life and satisfaction with care among family caregivers of patients with recurrent or metastasized digestive cancer requiring palliative care. *Support Care Cancer* 2014;22(10):2687-96.
- 14 Hartmann M, Bazner E, Wild B, Eisler I, Herzog W. Effects of interventions involving the family in the treatment of adult patients with chronic physical diseases: a meta-analysis. *Psychother Psychosom* 2010;79(3):136-48.
- 15 Ferrell BR, Temel JS, Temin S, Alesi ER, Balboni TA, Basch EM, et al. Integration of palliative care into standard oncology care: American society of clinical oncology clinical practice guideline update. *J Clin Oncol* 2017;35(1):96-112.
- 16 Jordan K, Aapro M, Kaasa S, Ripamonti CI, Scotte F, Strasser F, et al. European Society for Medical Oncology (ESMO) position paper on supportive and palliative care. *Ann Oncol* 2018; 29(1):36-43.
- 17 van Roij J, Zijlstra M, Ham L, Brom L, Fransen H, Vreugdenhil A, et al. Prospective cohort study of patients with advanced cancer and their relatives on the experienced quality of care and life (eQuiPe study): a study protocol. *BMC Palliat Care* 2020;19(1):139.
- 18 van de Poll-Franse LV, Horevoorts N, van Eenbergen M, Denollet J, Roukema JA, Aaronson NK, et al. The Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship registry: scope, rationale and design of an infrastructure for the study of physical and psychosocial outcomes in cancer survivorship cohorts. *Eur J Cancer* 2011;47(14): 2188-94.

- 19 Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993;85(5):365-76.
- 20 Giesinger JM, Loth FLC, Aaronson NK, Arraras JL, Caocci G, Efficace F, et al. Thresholds for clinical importance were established to improve interpretation of the EORTC QLQ-C30 in clinical practice and research. *J Clin Epidemiol* 2020;118:1-8.
- 21 Kaasa S, Bjordal K, Aaronson N, Moum T, Wist E, Hagen S, et al. The EORTC core quality of life questionnaire (QLQ-C30): validity and reliability when analysed with patients treated with palliative radiotherapy. *Eur J Cancer* 1995;31A(13e14):2260-3.
- 22 Kohler N, Perner A, Anders D, Brahler E, Papsdorf K, Gotze H. Family caregivers of palliative cancer patients: health-related quality of life and care-related burden. *Psychother Psychosom Med Psychol* 2012;62(5):157-62.
- 23 Bredart A, Bottomley A, Blazeby JM, Conroy T, Coens C, D'Haese S, et al. An international prospective study of the EORTC cancer in-patient satisfaction with care measure (EORTC IN-PATSAT32). *Eur J Cancer* 2005;41(14):2120-31.
- 24 Sixma HHM, Boer Dd, Delnoij D. Handboek CQI Metingen: richtlijnen en voorschriften voor metingen met een CQI meetinstrument 2008. 2008.
- 25 Palliatief TNCCOI. Kwaliteitskader palliatieve zorg Nederland. 2017.
- 26 Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The SelfAdministered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis Rheum* 2003;49(2):156-63.
- 27 Duimering A, Turner J, Chu K, Huang F, Severin D, Ghosh S, et al. Informal caregiver quality of life in a palliative oncology population. *Support Care Cancer* 2020;28(4):1695-702.
- 28 Dionne-Odom JN, Azuero A, Lyons KD, Hull JG, Tosteson T, Li Z, et al. Benefits of early versus delayed palliative care to informal family

- caregivers of patients with advanced cancer: outcomes from the ENABLE III randomized controlled trial. *J Clin Oncol* 2015;33(13):1446-52.
- 29 Engel M, Brinkman-Stoppelenburg A, Nieboer D, van der Heide A. Satisfaction with care of hospitalised patients with advanced cancer in The Netherlands. *Eur J Cancer Care (Engl)*. 2018;27(5):e12874.
 - 30 Lin Y, Hu C, Xu Y, Zhao J, Li Q. The mutual impact and moderating factors of quality of life between advanced cancer patients and their family caregivers. *Support Care Cancer* 2020; 28(11):5251-62.
 - 31 Bredart A, Kop JL, Griesser AC, Fiszer C, Zaman K, PanesRuedin B, et al. Assessment of needs, health-related quality of life, and satisfaction with care in breast cancer patients to better target supportive care. *Ann Oncol* 2013;24(8):2151-8.
 - 32 Ning X, Krishnan A, Li X, Liu Z, Li J, Dai X, et al. Perceived quality of care and its associated factors among Chinese patients with advanced cancer: findings from the APPROACH study in Beijing. *Support Care Cancer* 2020;29(3):1395-401.
 - 33 Chinn S. A simple method for converting an odds ratio to effect size for use in meta-analysis. *Stat Med* 2000;19(22):3127e31.
 - 34 Bergerod IJ, Braut GS, Wiig S. Resilience from a stakeholder perspective: the role of next of kin in cancer care. *J Patient Saf* 2020;16(3):e205-10.
 - 35 Litzelman K, Choi H, Maher ME, Harnish A. Role of cancer survivor health and health service use in spouses' use of mental health-related care. *Cancer* 2020;127(7):1146-53.
 - 36 Statline C. Overledenen; belangrijke doodsoorzaken (korte lijst), leeftijd, geslacht. https://opendatacbn.nl/#/CBS/nl/dataset/7052_95/table Last. [Accessed 15 December 2020].
 - 37 Raijmakers NJH, Zijlstra M, van Roij J, Husson O, Oerlemans S, van de Poll-Franse LV. Health-related quality of life among cancer patients in their last year of life: results from the PROFILES registry. *Support Care Cancer* 2018;26(10): 3397-404.

CHAPTER 7

Self-care, resilience, and caregiver burden in relatives of patients with advanced cancer: results from the eQuiPe study

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Abstract

Purpose: Relatives are often involved in caregiving for patients with advanced cancer and carry a heavy burden. Self-care and resilience might be beneficial to enhance their wellbeing and burden-bearing capacity. This study assessed the engagement in self-care and resilience in relatives of patients with advanced cancer and its association with their caregiver burden.

Methods: This study analyzed baseline data of the eQuiPe study, a prospective longitudinal, multicenter, observational study on quality of care and life of patients with advanced cancer and their relatives in which self-care (Self-care Practices Scale), resilience (Connor-Davidson Resilience Scale), and caregiver burden (Zarit Burden Interview (ZBI)) of relatives were included. Their scores were compared with a gender- and age-matched normative population. Multivariable logistic regression analysis was performed to assess the association between self-care and resilience with caregiver burden.

Results: Most of the 746 relatives were the patient's partner (78%) and 54% reported to be an informal caregiver of the patient. The median hours of caregiving a week for all relatives was 15 and 11% experienced high caregiver burden (ZBI >20). Relatives who reported a high caregiver burden engaged less often in self-care (OR = .87) and were less resilient (OR = .76) compared to relatives with low/medium caregiver burden. Relatives with high caregiver burden were younger (OR = .96), highly educated (OR = 2.08), often reported to be an informal caregiver of the patient (OR = 2.24), and were less well informed about the importance of self-care (OR = .39).

Conclusion: A significant number of relatives of patients with advanced cancer experienced high caregiver burden. As more self-care and

resilience were associated with lower experienced caregiver burden, creating awareness of the beneficial potential of self-care is important. Future studies should illuminate the causal relation.

Background

The responsibility of caring for patients with a life-threatening illness such as advanced cancer is increasingly placed on their relatives [1]. As the number of patients living with advanced cancer is rising and their prognosis is improving [2], the number of relatives and other informal caregivers who are providing care and support to these patients is also likely to increase. Relatives of patients with advanced cancer often experience that caring for their loved one is fulfilling but may also carry a high caregiving burden. Informal caregivers of patients with advanced cancer typically provide 18 to 33 h a week care for their loved one [3, 4]. Furthermore, a systematic literature review on caregiver burden of informal caregivers of elderly patients with cancer showed that up to 35% of these caregivers experienced a high burden [5]. Moreover, informal caregivers of patients with advanced cancer often experience a low quality of life [3, 4, 6–10]. More specifically, for these informal caregivers, high rates of depression and anxiety are found [3, 4] as well as feelings of social isolation [9, 11] and loss of self-identity [10].

Caregiver burden has been defined as a “multidimensional biopsychosocial reaction resulting from an imbalance of care demands relative to caregivers’ personal time, social roles, physical and emotional states, financial resources, and formal care resources given the other multiple roles they fulfill” [12]. This definition suggests that the balance between burden and burden-bearing capacity in informal caregivers is crucial for their wellbeing and may prevent them from developing health issues themselves [13]. Moreover, higher caregiver burden in informal caregivers is associated with poorer physical and mental health of patients with advanced cancer [14]. When caregiving becomes a structural demand or its intensity increases, it is essential to restore the imbalance to prevent negative consequences in informal caregivers and patients.

This imbalance can be restored by either decreasing the burden, for example, by respite care or by enhancement of the burden-bearing capacity of caregivers.

Resilience might contribute to burden-bearing capacity of informal caregivers, as it appears to be a predictor of adequate adaptation to negative life events [15]. Quantitative studies have shown that resilience in informal caregivers of patients with advanced cancer is related to less depression, better health, and positive social support and might be a protective factor for caregiver burden [16–18]. Another promising approach to enhance the burden-bearing capacity of informal caregivers seems promoting self-care. Self-care has been defined as a “process of purposeful engagement in practices that promote overall health and wellbeing of the self” [19]. Research on self-care in informal caregivers of patients with cancer is scarce. To our knowledge, only one study from Dionne-Odom et al. showed that low engagement in self-care practices was associated with more anxiety, depression, and lower mental quality of life in informal caregivers of patients with advanced cancer [4].

Overall, self-care and resilience may have potential to enhance the burden-bearing capacity of relatives of patients with advanced cancer and decrease their experienced caregiver burden. However, these concepts have received little attention yet. Therefore, this study aimed to assess the association between self-care engagement and resilience with perceived caregiver burden in relatives of patients with advanced cancer.

Methods

Study design

A prospective, longitudinal, multicentre, observational study on the experienced quality of care and quality of life of patients with advanced cancer and their relatives was conducted in the Netherlands (eQuiPe

study). Patients were invited by their treating physician in the 40 participating hospitals or were self-enrolled between November 2017 and January 2020. Patients were contacted by phone by the research team to discuss participation and all patients were asked if a relative was interested in participating in the study. After giving written informed consent, patients and relatives completed a questionnaire every 3 months till the patient's death. Questionnaires were completed on paper or online via the Patient Reported Outcomes Following Initial treatment and Long-term Evaluation of Survivorship (PROFILES) registry [20]. Clinical data of the patient was obtained by linking the information to the Netherlands Cancer Registry (NCR). The study was exempted from medical ethical review according to the Dutch Medical Research Involving Human Subjects Act (WMO), declared by the Medical Research Ethics Committee of the Antoni van Leeuwenhoek hospital (METC17.1491). The study is registered as NTR6584 in the Netherlands Trial Register. Details of the study protocol are reported elsewhere [21].

Study population

Relatives of patients with advanced cancer (metastatic solid cancer stage IV) were eligible to participate. To limit inclusion of patients with a relatively long prognosis, additional inclusion criteria for breast and prostate cancer were respectively metastases in multiple organ systems and castration-resistant disease. Both patients and relatives had to be 18 years or older and be able to complete a Dutch questionnaire. In total, 1695 patients and 1171 relatives gave written informed consent. Of these relatives, 340 (29%) dropped out before baseline assessment due to various reasons (decreasing health or death of the patient (7%), too busy (1%), too confronting (1%), or unknown reason (19%)), resulting in 831 relatives (71%) who responded to the baseline questionnaire. For this study, we used baseline data of relatives in the eQuiPe study and

randomly selected one relative per patient [39] patients had multiple relatives in the study to avoid dependent measures. This resulted in 746 relatives of unique patients with advanced cancer.

Measures

Caregiver burden

Caregiver burden was measured by the 12-item Zarit Burden Interview (ZBI) [22] using a five-point Likert scale between “never” and “nearly always.” Total sum score ranges between 0 and 48, where higher scores indicate a greater caregiver burden. Cut-off scores of the ZBI are as follows: 0–10: low caregiver burden, 11–20: medium caregiver burden, and >20: high caregiver burden. The ZBI has good psychometric properties and has been validated in informal caregivers of advanced cancer patients [22–24].

Self-care

Self-care was measured by the Personal Self-care subscale of the Self-care Practices Scale (SCPS) [25, 26]. The Personal Self-care subscale consists of nine items using a 5-point Likert scale ranging from “never” to “very often.” Respondents were asked to indicate how often they engage in self-care activities. The sum score ranged between 0 and 36, where higher scores indicate more self-care. Mean scores were calculated when all items of the Personal Self-Care scale were completed. The SCPS was originally developed for healthcare professionals; the psychometric properties of the self-care scale are good [25].

Resilience

Resilience, the extent to which people are able to “bounce back” after negative life events and their adaptability, was measured with a short version of the validated Connor-Davidson Resilience Scale (CD-RISC 2) [27]. This short version included two items, using a 5-point Likert scale

ranging from “not at all true” to “almost always true.” Mean scores were calculated when both items of the Resilience Scale were completed. A higher sum score (range 0–8) indicates more resilience [28]. The CD-RISC has been adequately validated in the general population and patients with psychiatric or medical conditions [29] but had not previously been used in caregivers of patients with advanced cancer.

Socio-demographics and clinical characteristics

Socio-demographic characteristics including gender, age, marital status, having children, educational level, and the nature of the relationship to the patient were all self-reported. To assess if relatives considered themselves as an informal caregiver, three self-developed questions were used: “Are you an informal caregivers of your relative with cancer?” (yes/no), “How many hours a week do you provide care?” (open-ended question), and “To what extent did a health care professional explain to you that it is also important to take care of yourself and not only of your relative?” The latter used a 5-point Likert scale ranging from “bad” to “perfect.” Clinical characteristics of the patients that were linked to the relative included primary tumor type, time since primary diagnosis (at time of patients’ baseline questionnaire completion), and comorbidities assessed with the Self-administered Comorbidity Questionnaire (SCQ) [30].

Normative population

Data of a normative population from 2018 were obtained from CentERpanel, an online household panel that is representative of the Dutch population [20]. Individuals from the normative population ($n = 620$) were matched (1:1) based on gender and age categories of relatives of patients with advanced cancer to compare their self-care and resilience scores.

Statistical analysis

Descriptive statistics were performed to examine the sociodemographic characteristics, self-care, and resilience of relatives who experienced low, medium, or high caregiver burden. Because relatives often do not recognize their caregiving role or activities, we used the full sample of relatives regardless of their self-reported status (being an informal caregiver yes/no) in our analysis. Resilience and self-care scores of relatives with low, medium, or high caregiver burden were compared to a gender- and age-matched normative population by means of ANOVA analysis with Tukey post hoc tests. A chi-square test was conducted to compare subgroups based on the amount of experienced caregiver burden (low, medium, high) on being informed by health care professionals about the importance of self-care. Cronbach alpha showed that the reliability of the Personal Self-care scale (0.73 for relatives and 0.73 for normative population), resilience (0.73 for relatives and 0.69 for normative population), and caregivers' burden (0.88 for relatives) was adequate. A logistic multivariable regression analysis was performed to examine the association between self-care and resilience levels (independent continuous variables) with caregiver burden (dependent categorical variable: high versus low/medium caregiver burden). Multiple imputation was applied prior to the logistic regression analysis to handle missing data which ranged between 0 and 10% per variable and were not missing completely at random. Multiple imputation did not affect the results of the analysis (when compared to the regression results based on the original data). The following covariates were included: age, educational level, the nature of the relation to the patient (e.g., being partner, a daughter/son, or other family or friend), considering oneself to be an informal caregiver of the patient, and being informed about the importance of self-care because univariate analyses showed that relatives with high caregiver burden differed significantly compared to relatives

with low and medium caregiver burden (all $p < 0.05$). While gender was not significant ($p = 0.31$), gender was included based on previous studies showing relevant gender differences in informal caregivers of patients with advanced cancer [31–33]. A p -value of < 0.05 was considered statistically significant. All analyses were performed in STATA version 16.

Results

Socio-demographic characteristics and caregiver burden of relatives

Sixty percent of relatives were female with a mean age of 61 years (range 18–87) (Table 1). Most relatives were the patient’s partner (78%) and the median hours of caregiving a week was 15. The mean score of all relatives on caregiver burden was 10 (SD 7.3), indicating low caregiver burden. For those relatives reporting to be informal caregivers (54%), the mean score of caregiver burden was 11 (SD 7.5) and 14% of them experienced a high caregiver burden.

Table 1. Socio-demographic characteristics of relatives of patients with advanced cancer (n=746)

	All relatives (n=746)	Relatives with low caregiver burden (n=420) ^a	Relatives with medium caregiver burden (n=230) ^a	Relatives with high caregiver burden (n=81) ^a	p-value
	n (%)	n (%)	n (%)	n (%)	
Gender					
Male	297 (40)	156 (37)	105 (46)	28 (35)	.07
Female	449 (60)	264 (63)	125 (54)	53 (65)	
Age					
mean (SD), range	61 (13), 18-87	63 (12), 24-86	50 (13), 18-87	56 (14), 23-83	<.001*
18-54 years	178 (24)	81 (20)	60 (27)	34 (43)	
55-63 years	168 (23)	86 (21)	60 (27)	20 (25)	
64-69 years	181 (24)	115 (28)	49 (22)	13 (16)	
≥70 years	193 (26)	122 (30)	54 (24)	12 (15)	

Educational level					
Low	199 (27)	129 (31)	52 (23)	15 (19)	.01*
Medium	328 (44)	184 (44)	105 (46)	34 (42)	
High	212 (28)	101 (24)	73 (32)	32 (40)	
Relationship to patient					
Partner	583 (78)	325 (78)	186 (82)	60 (74)	.01*
Daughter/Son	99 (13)	50 (12)	28 (12)	19 (23)	
Other family member or friend	58 (8)	41 (10)	14 (6)	2 (2)	
Marital status					
With partner	717 (96)	402 (96)	221 (96)	79 (98)	.79
No partner	28 (4)	17 (4)	9 (4)	2 (2)	
Having children					
Yes	609 (82)	348 (84)	176 (77)	71 (88)	.03*
No	132 (18)	68 (16)	54 (23)	10 (12)	
Being an informal caregiver of patient					
Yes	405 (54)	205 (49)	140 (61)	55 (68)	.001*
No	336 (45)	211 (51)	90 (39)	26 (32)	
Hours of caregiving per week ^b	n=373	n=189	n=131	n=49	.96
median (25%, 75%)	15 (7, 28)	15 (5, 27)	15 (8, 29)	18 (9, 30)	
missing	32 (8)	16 (8)	9 (6)	6 (1)	
Primary tumor of patient					
Lung	203 (27)	121 (28)	59 (26)	23 (28)	.07
Colorectal	121 (16)	83 (19)	29 (13)	9 (11)	
Breast	94 (13)	54 (12)	24 (10)	16 (20)	
Prostate	82 (11)	52 (12)	23 (10)	7 (9)	
Other	174 (24)	93 (22)	68 (30)	13 (16)	
Missing	71 (10)	31 (7)	26 (11)	13 (16)	
Time since primary diagnosis of patient					
<1 year	225 (30)	133 (32)	73 (32)	15 (19)	.12
<1 year	326 (44)	177 (42)	99 (43)	40 (49)	
1-5 years	124 (17)	80 (19)	31 (13)	13 (16)	
>5 years	71 (10)	30 (7)	27 (12)	13 (16)	
Missing					
#Physical comorbidities patient					
None	350 (47)	189 (45)	113 (49)	42 (52)	.58
1	234 (31)	139 (33)	70 (30)	20 (25)	
>1	162 (22)	92 (22)	47 (20)	19 (23)	

Abbreviations: SD=standard deviation.

Notes: Education levels are categorized according to International Standard Classification of

Education guidelines. Missings did not exceed 5% unless stated otherwise.

a Subpopulations based on caregiver burden do not add up to 100% (n=746) due to missingness on the ZARIT Burden Interview (n=15). Cut-off scores of the ZBI are as follows: 0–10: low caregiver burden, 11–20: medium caregiver burden, and >20: high caregiver burden. A Chi square test was conducted to compare subgroups based on the amount of experienced caregiver burden (low, medium, high).

b Hours of caregiving is a conditional item and only reported by relatives who reported to be a caregiver of the patient (n=405). * A p-value <.05 is considered significant.

Socio-demographic characteristics of relatives according to level of caregiver burden

Eleven percent of all relatives experienced a high caregiver burden, 31% experienced a medium caregiver burden, and 57% a low caregiver burden. Relatives with high caregiver burden were higher educated compared to relatives with low or medium caregiver burden ($p < 0.01$). They also were more often a child of the patient compared to being a partner or other family ($p = 0.01$). Moreover, relatives with a high caregiver burden more often reported to be an informal caregiver of the patient (68%), compared to relatives with a medium (61%) or low (49%) caregiver burden ($p = 0.001$). The average number of caregiving hours per week of these relatives did not differ between those with a low, medium, or high caregiving burden ($p = 0.96$).

Self-care and resilience

Relatives with high caregiver burden were less resilient than the normative population ($p < 0.001$) while relatives with low caregiver burden were more resilient ($p < 0.05$) than the normative population (Table 2). All relatives, irrespective of their level of caregiver burden, were less likely to engage in self-care activities compared to the normative population ($p < 0.001$). Twenty-one percent of the relatives with low caregiver burden, 27% of the relatives with medium caregiver burden, and 44% of the relatives with high caregiver burden felt they had been poorly informed about the importance of self-care ($p < 0.001$).

Table 2. Self-care and resilience in relatives of patients with advanced cancer by level of caregiver burden (n=746) and the normative population (n=620)

	Relatives with <u>low</u> caregiver burden (n=420) ^a	Relatives with <u>medium</u> caregiver burden (n=230) ^a	Relatives with <u>high</u> caregiver burden (n=81) ^a	Normative population (n=620)
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Resilience (total score 0-8)	6.3 (1.6)*	5.9 (1.5)	5.3 (1.5)*	6.0 (1.4)
Self-care (total score 0-36)	21.0 (4.6)*	19.1 (4.4)*	17.3 (4.5)*	22.0 (4.5)
Items Self-Care measure (total score 0-4)				
I participate in physical activities	2.3 (1.1)*	2.3 (1.1)*	2.0 (1.0)*	2.6 (1.1)
I laugh	2.9 (.7)	2.5 (.7)*	2.2 (.8)*	3.0 (.7)
I am involved in spiritual activities	.7 (1.1)*	.8 (1.1)	.8 (1.1)	1.0 (1.1)
I get enough sleep for my body	2.8 (.8)	2.4 (.9)*	2.1 (.9)*	2.9 (.8)
I spend time with people I care about	3.2 (.6)	2.9 (.7)*	2.7 (.8)*	3.1 (.7)
I participate in activities that I enjoy	2.7 (.8)	2.4 (.9)*	2.1 (.9)*	2.8 (.8)
I accept help from others	2.2 (.8)	2.0 (.8)*	2.1 (.8)	2.3 (.8)
I experience physical intimacy	2.2 (1.1)	2.0 (1.0)	1.7 (.9)*	2.1 (1.1)
I do things to fulfill my emotional needs	2.0 (1.1)*	1.9 (.9)*	1.7 (.9)*	2.3 (.9)
	n (%)	n (%)	n (%)	p-value ^b
Informed about the importance of self-care				
Bad	90 (21)	61 (27)	36 (44)	<.001
Reasonable	74 (18)	65 (28)	22 (27)	
(very) good /perfect	200 (48)	89 (39)	21 (26)	
Missing	56 (13)	15 (7)	2 (2)	

Abbreviations: SD=standard deviation.

a Anova-tests with Tukey post-hoc tests were conducted to compare subgroups based on the amount of experienced caregiver burden (low, medium, high) with the normative population.

b A Chi square test was conducted to compare subgroups based on the amount of experienced caregiver burden (low, medium, high) on being informed by health care professionals about the importance of self-care.

* A p-value <.05 is considered significant.

Associations between self-care, resilience, and caregiver burden

Relatives with high caregiver burden engaged less often in self-care activities (OR = 0.87, 95%CI 0.82–0.92) and were less resilient (OR = 0.76, 95%CI 0.65–0.89) compared to relatives with low or medium caregiver burden (Table 3). Also, relatives who experience a high caregiver burden were less often well informed about the importance of self-care by health care professionals (OR = 0.39, 95%CI 0.21–0.73). Being younger (OR = 0.96, 95%CI 0.94–0.99), highly educated (OR = 2.08, 95%CI 1.00–4.32), and being an informal caregiver of the patient (OR = 2.24, 95%CI 1.28–3.93) were positively associated with high caregiver burden.

Table 3. Odds ratios of the multivariable logistic regression model estimating the associations of self-care and resilience with high caregiver burden in relatives of patients with advanced cancer (n=746)

	Odds ratio (95%CI)	p-value
Gender		
Male	1	
Female	1.58 (.92-2.71)	.08
Age	.96 (.94-.99)	.004*
Education		
Low	1	
Medium	1.52 (.77-3.00)	.23
High	2.08 (1.00-4.32)	.05
Relation to patient		
Partner	1	
Daughter/son	1.07 (.46-2.51)	.87
Other family or friend	.40 (.09-1.82)	.24
Informal caregiver		
No	1	
Yes	2.24 (1.28-3.93)	.01*
Informed about self-care		
Bad	1	
Reasonable	.63 (.34-1.19)	.16
(very) good/perfect	.39 (.21-.73)	.003*
Resilience	.76 (.65-.89)	.001*
Self-care	.87 (.82-.92)	<.001*

Abbreviations: CI=Confidence Interval.

Notes: -2LL = -210.93, Adjusted R² = .11.

* A p-value <.05 is considered significant.

Discussion

This study shows that a significant part of relatives of patients with advanced cancer experience a high caregiver burden. Relatives who experience a high caregiver burden engage less often in self-care activities and are less resilient than the general population and compared to relatives who experience a lower caregiver burden. Moreover, relatives with high caregiver burden are also younger, higher educated, more often define themselves as being an informal caregiver of the patient, and are less often well informed about the importance of self-care compared to relatives with a lower caregiver burden.

Some findings deserve attention. Overall, 11% of the informal caregivers of patients with advanced cancer experience a high caregiver burden. This percentage is similar to findings of other studies among informal caregivers of patients with advanced cancer in the UK and Thailand [34–37]. However, a systematic literature review regarding the prevalence of caregiver burden in relatives of elderly cancer patients showed that high burden ranged from 1% to greater than 35% [5].

We also found that relatives of patients with advanced cancer engage less often in self-care activities compared to the general population. It is clearly challenging to engage in self-care activities when time and energy are limited due to caregiving activities. Especially relatives with high caregiver burden engage little in self-care activities which may result in a lower wellbeing and in an imbalance in burden and burden-bearing capacity in informal caregivers. Stenberg et al. found that informal caregivers of patients with cancer often restrict their leisure time and social time to meet the patients' needs [38] Some informal caregivers also tend to give priority to the patients' needs over their own [39]. Clearly, when the patient's needs increase over time due to disease progression,

relatives will even have less time available for self-care activities. This is worrisome as selfcare activities are important for the wellbeing of relatives and for their ability to continue caregiving activities. Less self-care in caregivers has been found to be associated with poorer performance in caregiving activities, such as being less prepared for caregiving tasks and responsibilities [4]. Hence, self-care in relatives is important for the wellbeing of the relative and may also be beneficial for the patient.

Self-care for relatives who care for a patient with advanced cancer is important and this can be emphasized by healthcare professionals, especially in palliative care where quality of life of both patients and relatives is an important focus of care [40]. Unfortunately, our study showed that a significant part of the relatives reported to be poorly informed about the importance of self-care. To our knowledge, no other studies regarding the information about selfcare for relatives in the advanced cancer setting are present.

Clearly, the quality of life of relatives of patients with advanced cancer is affected and decreases further as the disease progresses [6, 41]. Early palliative care [42, 43] including caregivers support such as respite care might be potential interventions to improve the quality of life of relatives. Unfortunately, the support for these relatives seems no common practice, as unmet health care needs are still prevalent in this population [44]. A barrier for receiving adequate support as mentioned by informal caregivers was the focus of care on the patient, rather than on the relatives [45]. According to a previous qualitative study among informal caregivers of patients with cancer [46], health care professionals can support informal caregivers by establishing a personal relation. Being seen and heard by health care professionals may enhance resilience in informal caregivers [46]. Other factors that may foster resilience that were mentioned are as follows: the availability of palliative care; adequate information and

communication on illness, prognosis, and death, and facilitating a good relationship between the informal caregiver and the patient [46]. These factors may also be associated with caregiver mastery, the caregivers' sense of control over their situation [47]. Caregiver mastery, but also how patients and relatives cope with their situation, may influence the wellbeing and burden as experienced by relatives [7, 48].

Last, we found no association between caregiver burden and type of relationship (e.g., partner, child, or other family or friend). This was unexpected as a recent review on the risk factors of caregiver burden showed that living in the same household was a risk factor, together with being female, low educational level, higher number of hours spent caregiving, and lack of choice in being a caregiver [49]. Another study showed that especially adult daughters of patients with cancer experience high levels of caregiver burden [50]. A possible explanation for these differences might be that we included relatives of patients with advanced cancer, while Adelman et al. [49] included informal caregivers of patients with various illnesses with a more chronic (longer term) character, including stroke. For these relatives, the caregiver burden will persist longer and is more unpredictable due to the possible cognitive or behavioral changes in patients, compared to the often shorter and more predictable illness trajectory of advanced cancer [51].

We also found that younger age is associated with higher caregiver burden; this is in line with a previous study among family caregivers of elderly patients with cancer [5]. Younger caregiver may experience more burden because their caregiving interferes with their personal and social activities [52]. The social activities and network of both the patient and the relative are often more extensive when younger, which might be beneficial (more support and resources) but also burdensome (more to juggle).

Limitations

This study has some limitations. First, it is unclear to what extent relatives were engaged in self-care activities and were resilient before the cancer diagnosis of the patient. It is possible that our study population differed from the normative population prior to the cancer diagnosis of the patient as we only matched on age and gender. Second, relatives might have interpreted the self-constructed questions regarding being an informal caregiver and the hours spent on caregiving differently, as we did not define informal caregiver and caregiving activities in the questionnaire. Some relatives may not consider themselves to be an informal caregiver while other relatives, who engaged in similar caregiving activities, did consider themselves to be an informal caregiver of the patient. Moreover, it is likely that the time spent on caring for the patient and also the caregiver burden is higher in relatives of patients who experience more symptoms or with disease progression [53]. Unfortunately, we did not assess whether the burden was higher for relatives of patient with more symptom burden or disease progression. Fourth, the Personal Self-Care Measure was initially developed and validated for social workers [25] and not validated in relatives of patients with advanced cancer. To our knowledge, no measurement instruments assessing self-care in relatives of patients with advanced cancer exist. Last, this cross-sectional analysis only provides insight into associations, not in causal relations. Therefore, it is unclear if relatives with high caregiver burden experience less time to engage in self-care activities or if a lack of selfcare activities leads to high caregiver burden.

Practical implications and future research

It is important for health care professionals to be aware that younger and highly educated relatives of patients with advanced cancer are more at risk to high caregiver burden. Moreover, it is important to assess whether

these relatives are resilient and engage in self-care activities because it can potentially protect them from high caregiver burden. Also, as harmful effects of self-care are unlikely, it is an appropriate step to inform relatives about the importance of their wellbeing and the role of self-care. More research is needed to find ways to increase caregiver wellbeing and their burden-bearing capacities, such as caregiver support, self-care, and resilience, and to clarify directional effects by means of longitudinal research. Also, the relation between the two concepts (self-care and resilience) needs to be further explored as more resilient relatives may also be more prone to engage in self-care activities and vice versa. To adequately assess these concepts, the validation of appropriate measures for relatives is needed.

Conclusions

A significant number of relatives of patients with advanced cancer experience high caregiver burden. More self-care and resilience are associated with lower caregiver burden, but relatives' engagement in self-care activities is still limited. Creating awareness of the potential of self-care could be beneficial for relatives, although more insight into the causal relation is needed. Future studies should focus on the potential of self-care to promote caregivers' wellbeing and to enhance burden-bearing capacity of relatives of patients with advanced cancer.

References

1. Pasacreata JV, McCorkle R (2000) Cancer care: impact of interventions on caregiver outcomes. *Annu Rev Nurs Res* 18:127–148
2. Siegel RL, Miller KD, Jemal A (2015) Cancer statistics, 2015. *CA Cancer J Clin* 65(1):5–29
3. Trevino KM, Prigerson HG, Maciejewski PK (2018) Advanced cancer caregiving as a risk for major depressive episodes and generalized anxiety disorder. *Psychooncology* 27(1):243–249
4. Dionne-Odom JN, Demark-Wahnefried W, Taylor RA, Rocque GB, Azuero A, Acemgil A et al (2017) The self-care practices of family caregivers of persons with poor prognosis cancer: differences by varying levels of caregiver well-being and preparedness. *Support Care Cancer* 25(8):2437–2444
5. Ge L, Mordiffi SZ (2017) Factors associated with higher caregiver burden among family caregivers of elderly cancer patients: a systematic review. *Cancer Nurs* 40(6):471–478
6. Wadhwa D, Burman D, Swami N, Rodin G, Lo C, Zimmermann C (2013) Quality of life and mental health in caregivers of outpatients with advanced cancer. *Psychooncology* 22(2):403–410
7. Nipp RD, El-Jawahri A, Fishbein JN, Gallagher ER, Stagl JM, Park ER et al (2016) Factors associated with depression and anxiety symptoms in family caregivers of patients with incurable cancer. *Ann Oncol* 27(8):1607–1612
8. Ito E, Tadaka E (2017) Quality of life among the family caregivers of patients with terminal cancer at home in Japan. *Jpn J Nurs Sci* 14(4):341–352
9. Goldstein NE, Concato J, Fried TR, Kasl SV, Johnson-Hurzeler R, Bradley EH (2004) Factors associated with caregiver burden among caregivers of terminally ill patients with cancer. *J Palliat Care* 20(1):38–43

10. Ugalde A, Krishnasamy M, Schofield P (2012) Role recognition and changes to self-identity in family caregivers of people with advanced cancer: a qualitative study. *Support Care Cancer* 20(6):1175–1181
11. van Roij J, Brom L, Youssef-El Soud M, van de Poll-Franse L, Raijmakers NJH (2019) Social consequences of advanced cancer in patients and their informal caregivers: a qualitative study. *Support Care Cancer* 27(4):1187–1195
12. Given CW, Given B, Azzouz F, Kozachik S, Stommel M (2001) Predictors of pain and fatigue in the year following diagnosis among elderly cancer patients. *J Pain Symptom Manage* 21(6):456–466
13. Pool G, Heuvel F, Ranchor AV, Sanderman R (2004) *Handboek psychologische interventies bij chronisch somatische aandoeningen*. Assen: Koninklijke Van Gorcum BV
14. Semere W, Althouse AD, Rosland AM, White D, Arnold R, Chu E, et al (2021) Poor patient health is associated with higher caregiver burden for older adults with advanced cancer. *J Geriatr Oncol*
15. (APA) APA. The road to resilience. Available from: <http://www.apaorg/helpcenter/road-resilience.aspx>. Cited 2019 nov 13th
16. Hwang IC, Kim YS, Lee YJ, Choi YS, Hwang SW, Kim HM et al (2018) Factors associated with caregivers' resilience in a terminal cancer care setting. *Am J Hosp Palliat Care* 35(4):677–683
17. Karabekiroglu A, Demir EY, Aker S, Kocamanoglu B, Karabulut GS (2018) Predictors of depression and anxiety among caregivers of hospitalised advanced cancer patients. *Singapore Med J* 59(11):572–577
18. Palacio C, Krikorian A, Limonero JT (2018) The influence of psychological factors on the burden of caregivers of patients with advanced cancer: resiliency and caregiver burden. *Palliat Support Care* 16(3):269–277
19. Lee JJ, Miller SE (2013) A self-care framework for social workers: building a strong foundation for practice. *Fam Soc* 94(2):96–103
20. van de Poll-Franse LV, Horevoorts N, van Eenbergen M, Denollet J, Roukema JA, Aaronson NK et al (2011) The Patient Reported

Outcomes Following Initial treatment and Long term Evaluation of Survivorship registry: scope, rationale and design of an infrastructure for the study of physical and psychosocial outcomes in cancer survivorship cohorts. *Eur J Cancer* 47(14):2188–2194

21. van Roij J, Zijlstra M, Ham L, Brom L, Fransen H, Vreugdenhil A et al (2020) Prospective cohort study of patients with advanced cancer and their relatives on the experienced quality of care and life (eQuiPe study): a study protocol. *BMC Palliat Care* 19(1):139
22. Bedard M, Molloy DW, Squire L, Dubois S, Lever JA, O'Donnell M (2001) The Zarit Burden Interview: a new short version and screening version. *Gerontologist* 41(5):652–657
23. Chattat R, Cortesi V, Izzicupo F, Del Re ML, Sgarbi C, Fabbo A et al (2011) The Italian version of the Zarit Burden interview: a validation study. *Int Psychogeriatr* 23(5):797–805
24. Higginson IJ, Gao W, Jackson D, Murray J, Harding R (2010) Short-form Zarit Caregiver Burden Interviews were valid in advanced conditions. *J Clin Epidemiol* 63(5):535–542
25. Lee JJ, Bride B, & Miller SE (2016) Development and initial validation of the self-care practices scale (SCPS). Poster session presented at the meeting of the Society for Social Work and Research, Washington, DC
26. Dorociak KE, Rupert PA, Bryant FB, Zahniser E (2017) Development of the Professional Self-Care Scale. *J Couns Psychol* 64(3):325–334
27. Connor KM, Davidson JR (2003) Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC). *Depress Anxiety* 18(2):76–82
28. Vaishnavi S, Connor K, Davidson JR (2007) An abbreviated version of the Connor-Davidson Resilience Scale (CD-RISC), the CD-RISC2: psychometric properties and applications in psychopharmacological trials. *Psychiatry Res* 152(2–3):293–297
29. Davidson C. Resilience Scale: <http://www.connordavidson-resiliencescale.com/about.php>. last accessed 24th Jun 2020
30. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN (2003) The Self-Administered Comorbidity Questionnaire: a new method to assess

comorbidity for clinical and health services research. *Arthritis Rheum* 49(2):156–163

31. Romito F, Goldzweig G, Cormio C, Hagedoorn M, Andersen BL (2013) Informal caregiving for cancer patients. *Cancer* 119(Suppl 11):2160–2169
32. Langenberg S, van Herpen CML, van Opstal CCM, Wymenga ANM, van der Graaf WTA, Prins JB (2019) Caregivers' burden and fatigue during and after patients' treatment with concomitant chemoradiotherapy for locally advanced head and neck cancer: a prospective, observational pilot study. *Support Care Cancer* 27(11):4145–4154
33. Papastavrou E, Charalambous A, Tsangari H (2009) Exploring the other side of cancer care: the informal caregiver. *Eur J Oncol Nurs* 13(2):128–136
34. Harding R, Gao W, Jackson D, Pearson C, Murray J, Higginson IJ (2015) Comparative analysis of informal caregiver burden in advanced cancer, dementia, and acquired brain injury. *J Pain Symptom Manage* 50(4):445–452
35. Chindaprasit J, Limpawattana P, Pakkaratho P, Wirasorn K, Sookprasert A, Kongbunkiat K et al (2014) Burdens among caregivers of older adults with advanced cancer and risk factors. *Asian Pac J Cancer Prev* 15(4):1643–1648
36. Higginson IJ, Gao W (2008) Caregiver assessment of patients with advanced cancer: concordance with patients, effect of burden and positivity. *Health Qual Life Outcomes* 6:42
37. Naoki Y, Matsuda Y, Maeda I, Kamino H, Kozaki Y, Tokoro A et al (2018) Association between family satisfaction and caregiver burden in cancer patients receiving outreach palliative care at home. *Palliat Support Care* 16(3):260–268
38. Stenberg U, Ruland CM, Miaskowski C (2010) Review of the literature on the effects of caring for a patient with cancer. *Psychooncology* 19(10):1013–1025

39. Williams LA (2007) Whatever it takes: informal caregiving dynamics in blood and marrow transplantation. *Oncol Nurs Forum* 34(2):379–387
40. WHO (2002) Definition palliative care. <http://www.hoint/cancer/palliative/definition/en/> Accessed Nov 23 2016
41. Duimering A, Turner J, Chu K, Huang F, Severin D, Ghosh S et al (2020) Informal caregiver quality of life in a palliative oncology population. *Support Care Cancer* 28(4):1695–1702
42. McDonald J, Swami N, Hannon B, Lo C, Pope A, Oza A et al (2017) Impact of early palliative care on caregivers of patients with advanced cancer: cluster randomised trial. *Ann Oncol* 28(1):163–168
43. Dionne-Odom JN, Azuero A, Lyons KD, Hull JG, Tosteson T, Li Z et al (2015) Benefits of early versus delayed palliative care to informal family caregivers of patients with advanced cancer: outcomes from the ENABLE III Randomized Controlled Trial. *J Clin Oncol* 33(13):1446–1452
44. Wang T, Molassiotis A, Chung BPM, Tan JY (2018) Unmet care needs of advanced cancer patients and their informal caregivers: a systematic review. *BMC Palliat Care* 17(1):96
45. Nissim R, Hales S, Zimmermann C, Deckert A, Edwards B, Rodin G (2017) Supporting family caregivers of advanced cancer patients: a focus group study. *Family Relations* 66(5)
46. Roen I, Stifoss-Hanssen H, Grande G, Brenne AT, Kaasa S, Sand K et al (2018) Resilience for family carers of advanced cancer patients-how can health care providers contribute? A qualitative interview study with carers. *Palliat Med* 32(8):1410–1418
47. Christensen KA, Stephens MA, Townsend AL (1998) Mastery in women's multiple roles and well-being: adult daughters providing care to impaired parents. *Health Psychol* 17(2):163–171
48. Nijboer C, Tempelaar R, Triemstra M, van den Bos GA, Sanderman R (2001) The role of social and psychologic resources in caregiving of cancer patients. *Cancer* 91(5):1029–1039
49. Adelman RD, Tmanova LL, Delgado D, Dion S, Lachs MS (2014) Caregiver burden: a clinical review. *JAMA* 311(10):1052–1060

- Kim Y, Baker F, Spillers RL (2007) Cancer caregivers' quality of life: effects of gender, relationship, and appraisal. *J Pain Symptom Manage* 34(3):294–304
51. Murray SA, Kendall M, Boyd K, Sheikh A (2005) Illness trajectories and palliative care. *BMJ* 330(7498):1007–1011
 52. Williamson GM, Shaffer DR, Schulz R (1998) Activity restriction and prior relationship history as contributors to mental health outcomes among middle-aged and older spousal caregivers. *Health Psychol* 17(2):152–162
 53. Wood R, Taylor-Stokes G, Smith F, Chaib C (2019) The humanistic burden of advanced non-small cell lung cancer (NSCLC) in Europe: a real-world survey linking patient clinical factors to patient and caregiver burden. *Qual Life Res* 28(7):1849–1861

PART 3

A dyadic perspective among couples

CHAPTER 8

Dyadic coping and its association with emotional functioning in couples confronted with advanced cancer: Results of the multicenter observational eQuiPe study

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Submitted

Abstract

Objective: How patients and their partners cope with advanced cancer as a couple, may impact their emotional functioning (EF). The aim of this study was to assess dyadic coping (DC) of couples confronted with advanced cancer and its association with EF.

Methods: Actor-partner interdependence models were used to analyse baseline data of 566 couples facing advanced cancer participating in an observational study on quality of care and life. Measures included the Dyadic Coping Inventory and the EORTC QLQ-C30.

Results: Negative DC (mean 86-88) was most often used and common DC (both mean 66) was least often used. We found small to moderate interdependence ($r=.27-.56$) between patients' and partners' DC perceptions. Compared to partners, patients were more satisfied with their DC ($p<.001$). Partners' satisfaction with DC was positively associated with their own ($B=.40$, $p<.001$) and patients' ($B=.23$, $p=.04$) EF. Partners' supportive DC was negatively associated with patients ($B=-.31$, $p=.03$) and partners' EF ($B=-.34$, $p=.003$). We found positive actor (patients $B=.37$ $B=.13$, $p=.04$) and partners (both $B=.17$, $p<.05$) associations for negative DC in patients and partners.

Conclusions: This study demonstrates an association between DC and the EF of patients with advanced cancer and their partners. These findings highlight the importance of DC (especially from the partners' perspective) for EF in advanced cancer but also differences in the experience of these patients and their partners. Future research is needed to understand the mechanisms of such relations and the common and unique support options that may facilitate adjustment in patients with advanced cancer and their partners.

Background

A diagnosis of advanced cancer is a shared interpersonal experience that impacts both patients and their partners (1-3). The emotional impact of advanced cancer on patients and their partners is intertwined (4, 5) and evidence suggests that death anxiety, dysfunctional attitudes and their quality of life are linked (6). This suggest that how couples cope with an advanced cancer diagnosis is also likely to affect their emotional functioning (feeling tense, worried, irritable or down).

When confronted with a stressful life event such as an advanced cancer diagnosis, couples tend to communicate their stress to each other and to cope together with it, which is called dyadic coping (7). Dyadic coping includes the coping efforts of both partners of a dyad and its reciprocal nature (i.e., the coping of one person may affect the other person and vice versa). Just like individual coping, dyadic coping efforts can be categorized into different coping styles, including negative dyadic coping (i.e., hostile, ambivalent or superficial responses) or common dyadic coping (i.e., working together to handle stress) (7). When both partners cope adequately together, they are able to communicate their stress to each other and provide and receive support in a manner that is constructive to their situation and relationship. However, coping styles are not mutually exclusive and one coping style does not necessarily prevail.

Some studies on the effect of coping on quality of life of couples confronted with advanced cancer have been conducted, showing that acceptance coping (i.e., letting go of any resistance towards the stressor) in patients with advanced cancer is associated with less depression in their partners, while seeking emotional support by patients is associated with more depressive symptoms in their partners (8). Another study found that the use of avoidance (i.e., denial or minimization of the stressor), emotion-

focused coping (i.e., regulation of the emotional response to stress), and problem-focused coping (i.e., targeting the cause of stress) in partners are associated with poorer physical functioning and higher symptom burden in patients with advanced cancer (9). Two studies showed that more common dyadic coping is related to less severe depressive symptoms but to more cancer-related distress in patients with metastatic breast cancer. In their partners, more common dyadic coping was related to less cancer-related distress but to more severe depressive symptoms (10-12). However, to the best of our knowledge, only one study also included the dyadic effects of dyadic coping efforts among couples coping with advanced cancer (13). This study showed that supportive dyadic coping of the partner was positively associated with better mental functioning of patients. Also, satisfaction with dyadic coping according to partners was negatively associated with physical functioning of patients (13).

It is of great importance to gain a better understanding on dyadic coping and dyadic effects in couples coping with advanced cancer together, as their dyadic coping may impact each other's emotional functioning. Therefore, the aim of this study is to describe dyadic coping in couples coping with advanced cancer, including their interdependence. We also aim to assess the association between dyadic coping and emotional functioning in patients and partners. We hypothesize that there is moderate to high interdependence between patients and their partners regarding their dyadic coping perceptions. Because dyadic coping in couples coping with cancer is positively associated with emotional functioning (15), we also hypothesize that dyadic coping of both patients and their partners would be positively associated with the emotional functioning of the other party.

Methods

Study design

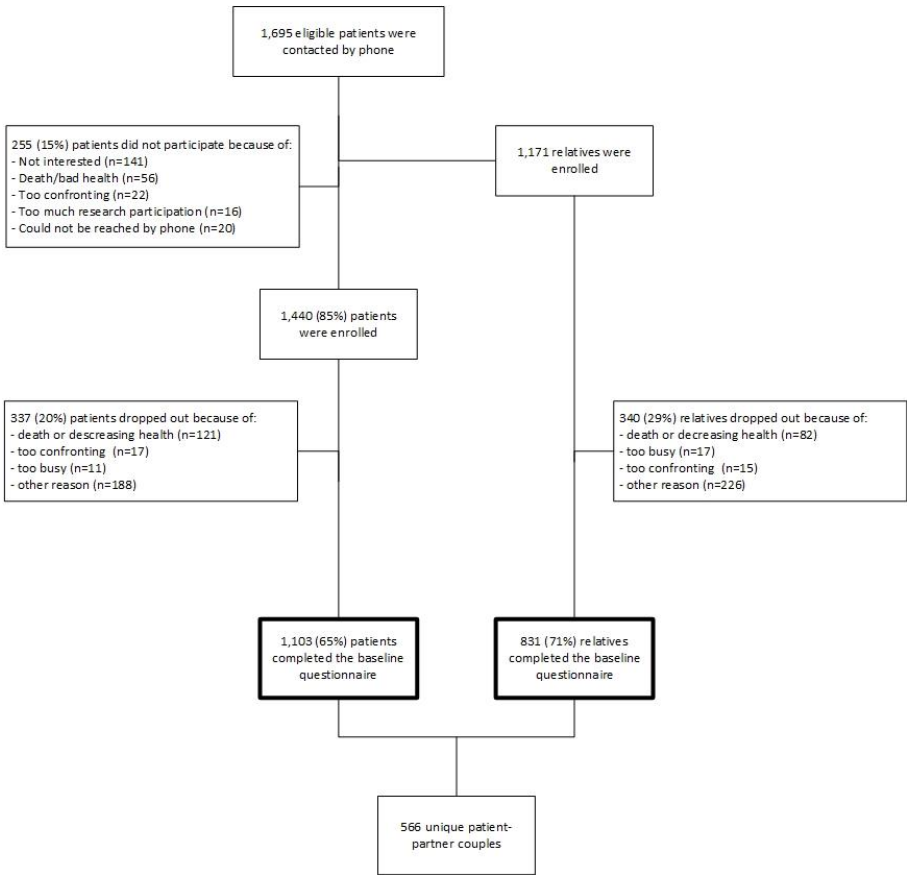
We used baseline data of patients and their partners who participated in a prospective, longitudinal, multicentre, observational study on the experienced quality of care and quality of life of patients with advanced cancer and their relatives that was conducted in the Netherlands. Patients and their relatives were invited to participate by their treating physician from one of the 40 participating hospitals or were self-enrolled between November 2017 and January 2020. Patients were contacted by phone by the research team to discuss participation and were asked if a relative was interested in participating in the study. After giving written informed consent, patients and relatives completed questionnaires every three months until the patient's death. Questionnaires were completed on paper or online via the Patient Reported Outcomes Following Initial treatment and Long-term Evaluation of Survivorship (PROFILES) registry (14). Clinical data of the patient were obtained by linking the information to the Netherlands Cancer Registry (NCR). The study was exempted from medical ethical review according to the Dutch Medical Research Involving Human Subjects Act (WMO), reviewed declared by the Medical Research Ethics Committee of the Antoni van Leeuwenhoek hospital (METC17.1491). The study is registered as NTR6584 in the Netherlands Trial Register. Details of the study protocol are reported elsewhere (15).

Study population

Patients with advanced cancer (metastatic solid cancer stage IV) and their relatives were eligible. Additional criteria for patients with breast or prostate cancer were present, respectively metastases in multiple organ systems and castration-resistant disease. Participants had to be 18 years or older and able to complete a Dutch questionnaire. In total, 1,695 patients were eligible and invited to participate (Figure 1). Of these

patients, 255 (15%) did not want to participate. Via participating patients we were able to enrol 1,171 relatives in the study. Another 337 (20%) patients and 340 (29%) relatives dropped out, resulting in 1,103 patients and 831 relatives who completed the baseline questionnaire. For this study, baseline data of unique patient-partner couples (n=566) were used.

Figure 1. Flow chart of study process



Measurements

Emotional functioning

Emotional functioning was assessed with the European Organization for Research and Treatment of Cancer Quality of life-C30 Questionnaire (EORTC QLQ-C30) (16). The emotional functioning subscale consists of four items measuring feeling tense, worried, irritable or down using a four-point Likert scale from 1 "Not at all" to 4 "Very much". A higher score indicates better emotional functioning. While the EORTC QLQ-C30 is developed to measure quality of life of patients with cancer, it has also previously been used to assess quality of life in partners of patients with cancer (17).

Dyadic coping

Dyadic coping was assessed with the Dyadic Coping Inventory (DCI) (7). This 37-item questionnaire assesses dyadic coping as perceived by (i) each partner about their own coping ("what I do when I am stressed and what I do when my partner is stressed"), (ii) each partner's perception of the other's coping ("what my partner does when he or she is stressed, and what my partner does when I am stressed"), and (iii) each partner's view of how they cope as a couple ("what we do when we are stressed as a couple"). The DCI includes four coping scales: common coping (working together to handle stress), delegated coping (taking over responsibilities), negative coping (hostile, ambivalent or superficial responses), and supportive coping (problem- and/or emotion-focused support). The DCI also has an evaluation of dyadic coping scale (satisfied with your coping as a couple) and a stress communication scale (letting your partner know how you feel). Item scores range from 1 "very rarely" to 5 "very often" and were transformed to a 0-100 scale. The total DCI score is a sum of all items excluding two items regarding evaluation of dyadic coping scale. A total score on the DCI <111 is an indication of a below average couple's

joint coping efforts, between 111-145 is normal couple's joint coping efforts, and >145 is above average couple's joint coping efforts. The DCI has good psychometric properties (7, 18) and has been used in patients and partners with advanced cancer previously (19-22).

Covariates

Relationship satisfaction was assessed using the Dyadic Adjustment Scale (23), on which patients and partners could indicate their degree of happiness in their relationship on a 7-point Likert scale ranging from "very unhappy" to "perfect". Scores were transformed to a 0-100 scale.

Illness appraisal of patients was assessed with the validated 8-item Brief Illness Perception Questionnaire (24). One item was excluded due to its inappropriateness for this study population, namely "How long do you think your illness will continue?". A sum score was calculated with a higher score reflecting a more threatening view of the illness, ranging from 0 to 70.

Physical functioning of patients was assessed with the 4-item physical functioning scale of the EORTC QLQ-C30 questionnaire. The four-point Likert scale ranged from 1 "Not at all" to 4 "Very much", where higher scores indicate better physical functioning.

In the baseline questionnaire sociodemographic characteristics including age, gender, education (low, medium, high), and relationship duration (0-4 years or ≥ 5 years) were self-administered. Additionally, partners reported if they were an informal caregiver of the patient and patients reported the cancer treatments they received in the past three months prior to the questionnaire on self-administered items. Patients' physical comorbidities were assessed by the Self-Administered Comorbidity Questionnaire (25). Clinical patient data were obtained from the Netherlands Cancer Registry (NCR), including primary tumor and date of primary diagnosis.

Statistical analysis

Descriptive statistics were used to describe the sociodemographic and clinical characteristics. Mean scores on dyadic coping scales were calculated for patients and partners. Interdependence between patients and partners regarding their coping was calculated by means of Pearson's correlations. According to Cohen's guidelines a correlation of .20 is considered small, a correlation of .50 is medium, and a correlation of .80 is large (26).

We used the actor-partner interdependence model (APIM) (27). The Actor-partner interdependence model is developed to analyze dyadic processes and shows the association between own dyadic coping and (1) own emotional functioning score (actor effect), and (2) emotional functioning of the partner (partner effect). Data of patients and partners are likely to be dependent of each other. Multilevel modeling with a pairwise dataset accounts for this inter-dependence within couples and is considered one of the best methods to examine effects in the APIM (27, 28). The univariate Pearson correlations between patients and partners indicated that the APIM was appropriate to use and there was no presence of multicollinearity. We controlled for gender, age, education (low, medium, high), being a caregiver (partners only). We also controlled for a-priori defined factors associated with dyadic coping based on previous studies among couples coping with cancer (13, 29-31), including relationship satisfaction and the patients' physical functioning. As only 1% of respondents reported a relationship duration of 0-5 years, this variable was not suitable for the APIM.

Illness perception is known to be predictive of coping (32) and therefore the patient's illness perception was also included. Multiple imputation was applied to handle missing data (missing data ranged between 0.5-11.1% for patients and 0.4-8.7% for partners) because missings were not

at completely at random (MCAR). A sensitivity analysis showed that results of the regression analyses did not change after imputation of data. A p-value <.05 was considered significant. Effect sizes for each significant continuous variable were calculated. In accord with the APIM model, these are partial correlations following the formula: $r = \sqrt{t^2 / (t^2 + df)}$ (27). All statistical analyses were conducted in STATA version 16.0.

Results

Of the 566 couples, most couples were together for more than five year (99%) and fourteen were same-sex couples. About half of the patients and partners were male (56% and 45% respectively) and the mean age of both groups was 65 years (Table 1). Most patients and partners had a medium level of education (40% and 45% respectively). Most patients were diagnosed with lung cancer (28%) or colorectal cancer (19%) and the majority of patients (82%) was diagnosed with their primary cancer tumor in the past five years. The mean score of emotional functioning was 77.3 (SD 21.3) for patients and 69.4 (SD 21.7) for partners. The mean score on happiness in the partnered relationship was 4.1 (SD 1.1) for patients and 4.0 (SD 1.2) for partners. The mean score of patients on illness perceptions was 33.1 (SD 13.8) and their physical functioning score was 70.7 (SD 22.3).

Table 1. Sociodemographic and clinical characteristics of patients with advanced cancer (n=566) and their partners (n=566).

	Patients with advanced cancer	Partners
	n (%)	n (%)
Gender		
Male	318 (56)	256 (45)
Female	248 (44)	310 (55)
Age		
Mean (SD), range	65 (9.1), 29-88	65 (9.6), 18-87
Education ^a		
Low	161 (28)	160 (28)
Medium	227 (40)	254 (45)
High	172 (30)	147 (26)
Duration of relationship		
0-5 years	8 (1)	8 (1)
>5 years	558 (99)	558 (99)
Primary tumour		-
Lung	155 (28)	
Colorectal	107 (19)	
Breast	72 (13)	
Prostate	77 (14)	
Other	155 (28)	
Time since primary diagnosis		-
<1 year	184 (33)	
1-3 years	274 (49)	
>3 years	101 (18)	
Treatments in the prior three months ^c		-
None	142 (25)	
Chemotherapy	174 (31)	
Radiotherapy	44 (8)	
Surgery	104 (19)	
Immunotherapy	132 (24)	
Other	124 (22)	
Number of comorbidities ^b		-
None	240 (42)	
1	199 (35)	
>1	127 (22)	

Missing data: did not exceed 5%. Responses of the other person was used to handle missings regarding relationship duration..

^aEducational levels are categorized according to International Standard Classification of Education guidelines.

^bComorbidities defined as physical conditions from the Self-administered Comorbidities Questionnaire (25).

^cTreatments were self-reported. Patients could receive more than one treatment modality, the percentages do not sum up to 100%.

Dyadic coping

Most patients (81%) and partners (75%) rated their total dyadic coping efforts as normal or above average, total dyadic coping effort scores in patients and partners were in the normal range (74.4 and 72.3 respectively, Table 2). Negative dyadic coping (i.e., hostile, ambivalent or superficial responses) was most often used by both patients and partners, respectively 88 and 86. Common dyadic coping was rated (i.e., working together to handle stress) the lowest (both 66). Correlations showed small to moderate interdependence between patients and partners, ranging between .27 for delegated dyadic coping and .56 for total dyadic coping score. Patients were more satisfied with their coping as a couple compared to their partner, respectively 86 and 79 ($p<.001$).

Association between dyadic coping and emotional functioning

Results of the multivariable linear regression analysis showed that the positive association between satisfaction with dyadic coping and emotional functioning was stronger for partners compared to patients ($B=.40$ and $B=.03$ respectively, $p<.001$) (Table 3). The positive association between satisfaction with dyadic coping of the other person was more strongly associated with emotional functioning in patients compared to partners ($B=.23$ and $B=.02$, $p=.04$). The perception on supportive dyadic coping was negatively associated with emotional functioning in partners, but not in patients ($B=-.34$ and $B=.06$, $p=.003$). The perception on negative dyadic coping was positively associated with emotional functioning and this relationship was stronger for patients compared to partners ($B=.37$ and $B=.13$, $p=.04$). The perception of the other person on negative dyadic coping was positively associated with emotional functioning in both patients and partners ($B=.17$, $p<.05$). The perception of the other person on supportive dyadic coping was negatively

associated with emotional functioning in patients, but not in partners ($B=-.31$ and $B=.07$, $p=.03$).

Table 2. Mean crude scores on dyadic coping of couples ($n=566$) confronted with advanced cancer including their interdependence.

	Patients with advanced cancer	Partners	Interdependence
	Mean (SD)	Mean (SD)	r
Satisfaction with dyadic coping (0-100)	86.1 (14.0), $n=515$	79.4 (16.1), $n=531$.31*
Total dyadic coping (0-100)	74.4 (9.0), $n=510$	72.3 (9.5), $n=527$.56*
	n (%)	n (%)	
below average	9 (52)	17 (98)	
normal	65 (368)	64 (364)	
above average	16 (90)	11 (65)	
missing	10 (56)	7 (39)	
	Mean (SD)	Mean (SD)	
Dyadic coping styles (0-100)			
Common dyadic coping	66.1 (16.0) $n=511$	66.0 (16.9), $n=527$.45*
Supportive dyadic coping	75.4 (10.7) $n=511$	72.8 (12.0), $n=529$.49*
Own supportive dyadic coping	71.6 (12.4), $n=511$	75.5 (12.0), $n=532$.26*
Other supportive dyadic coping	78.9 (12.4), $n=521$	70.0 (16.4), $n=531$.30*
Negative dyadic coping	87.7 (11.5) $n=508$	85.8 (12.3), $n=527$.44*
Own negative dyadic coping	86.6 (12.9), $n=503$	87.0 (13.2), $n=517$.26*
Other negative dyadic coping	89.1 (12.9), $n=511$	85.3 (13.7), $n=527$.40*
Delegated dyadic coping	71.0 (11.6) $n=503$	67.2 (12.0), $n=522$.27*
Own negative dyadic coping	65.0 (16.8), $n=507$	74.7 (13.3), $n=529$.05
Other negative dyadic coping	76.8 (16.2), $n=516$	59.6 (18.8), $n=528$	-.15*
Stress communication (0-100)	67.3 (11.0), $n=517$	64.7 (10.8), $n=532$.40*
Own stress communication	73.0 (13.2), $n=524$	61.2 (13.6), $n=531$.16*
Other stress communication	61.6 (14.6), $n=515$	68.1 (14.0), $n=534$.07

Notes: The sample size per outcome measure or subscale varied from 503 to 566 for patients and 522 to 541 for partners due to missings. Interdependence was measured with pearson correlations. * $p<.001$.

Table 3. Multivariable linear regression results according to Actor-partner interdependence model of the association between dyadic coping and emotional functioning of patients with advanced cancer and their partners (n=566)

Variables	Mean difference (b)	SE	CI 95%	p-value	t	Effect size
Satisfaction with DC						
Own satisfaction with DC (actor effect)	.40	.07	.26 to .54	<.001**	5.71	.17
Own satisfaction with DC (actor effect) * role	-.37	.11	-.58 to -.16	<.001**	-3.36	.10
Other satisfaction with DC (partner effect)	.02	.07	-.13 to .16	.83	.29	.01
Other satisfaction with DC (partner effect) * role	.21	.10	.01 to .41	.04*	2.10	.06
Supportive DC						
Own supportive DC (actor effect)	-.34	.11	-.57 to -.12	.003*	-3.09	.09
Own supportive DC (actor effect) *role	.40	.17	.07 to .74	.02*	2.35	.07
Other supportive DC (partner effect)	.07	.13	-.18 to .32	.58	.54	.02
Other supportive DC (partner effect) * role	-.38	.17	-.71 to -.04	.03*	-2.36	.07
Negative DC						
Own negative DC (actor effect)	.13	.08	-.03 to .29	.12	1.63	.05
Own negative DC (actor effect) *role	.24	.12	.01 to .48	.04*	2.00	.06
Other negative DC (partner effect)	.17	.08	.00 to .33	.05*	2.13	.06
Delegated DC						
Other delegated DC (partner effect)	.15	.09	-.02 to .33	.07	1.67	.05
Stress communication						
Own stress communication (actor effect)	.18	.10	-.01 to .37	.06	1.80	.05
Between dyads covariates						
Illness perception (patient variable) (actor effect)	-.19	.06	-.32 to -.07	.002*	-3.17	.09
Illness perception (patient variable) (partner effect) * role	-.21	.08	-.38 to -.05	.01*	-2.63	.08
Physical functioning (patient variable) (actor effect)	.09	.04	.01 to .17	.03*	2.25	.07
Physical functioning (patient variable) (partner effect) * role	.18	.05	.07 to .28	.001*	3.60	.11
Being a caregiver (partner variable)	-5.10	1.72	-8.46 to -1.73	.003*	-2.97	.09
Being a caregiver (partner variable) (partner effect) * role	5.27	2.32	.73 to 9.81	.02*	2.27	.07
Other covariates (actor effects)						
Happiness in the relationship	-.27	.84	-1.91 to 1.38	.75	-.32	.01
Happiness in the relationship * role	2.67	1.16	.39 to 4.95	.02*	2.30	.07
Age	.38	.09	.21 to .55	<.001**	4.22	.13
Age * role	-.22	.12	-.46 to .02	.07	-1.8	.05
Education				.58		
low	1					
medium	-1.70	1.88	-5.38 to 1.98	.37	.90	.03
high	-2.07	2.21	-6.40 to 2.25	.35	.94	.03
Education * role				.05*		
low	1					
medium	5.98	2.69	.71 to 11.25	.03*	2.22	.07
high	6.43	3.04	.48 to 12.39	.03*	2.12	.06
Role						
partner	1					
patient	14.12	15.59	-16.43 to 44.67	.37	.91	.03

Notes: DC = dyadic coping. The regression model included all scales of the Dyadic Coping Inventory reported by patients and partners (continuous variables). Interaction terms were added between those items and role. Interaction term between role and covariates were also included in the regression model. Between dyads covariates were assessed in either patients or their partners. Multiple imputations were applied to handle missing data. Only significant associations are shown. Variance inflation factor (VIF) values were <5, confirming the absence of multicollinearity. Only significant associations are presented. *p<.05, **p<.001.

Discussion

Our study shows that the vast majority of patients with advanced cancer and their partners have a normal to above average level of dyadic coping efforts. Negative dyadic coping (i.e., hostile, ambivalent or superficial responses) was most common in both groups, while common dyadic coping (i.e., working together to handle stress) was least often used by both. There was a small to moderate interdependence between patients and partners regarding their dyadic coping efforts. Compared to partners, patients were more satisfied with dyadic coping, but their satisfaction with dyadic coping was not as strongly associated with emotional functioning (e.g., feeling tense, worried, irritable or down). Satisfaction with dyadic coping of the other person was more strongly associated with the emotional functioning of patients compared to partners. We also found positive actor and partner associations for negative dyadic coping in both patients and partners. Supportive dyadic coping as perceived by the partner was negatively associated with the emotional functioning of both.

Some findings deserve particular attention. First, most patients and partners in our study had a normal to above average level of dyadic coping efforts. This is in line with a previous study among couples with breast cancer showing similar scores on the total DCI (33). However, that study also showed lower scores for negative dyadic coping: raw scores were 26 and 24 for respectively patients and partners compared to 35 and 34 in our study (33). The greater frequency of perceived negative dyadic coping in our study compared to this group might be due to the larger sample size, older age and more advanced cancer in our study. Metastatic cancer comes with a great threat to life, higher symptom burden, and the requirement of advance care planning and end-of-life care. These challenges in advanced cancer may be associated with greater feelings of uncertainty and helplessness, which may lead to more negative dyadic

coping, as observed in our study. However, the previous study was consistent with our finding that patients and partners rate their coping efforts as a couple equally high (33).

Negative dyadic coping was the most common coping style used by patients with advanced cancer and their partners in our study. A previous study of dyadic coping among patients with metastatic breast cancer showed that patients used more positive common dyadic coping than negative common dyadic coping (10). However, this study used a modified version of the Dyadic Coping Questionnaire (FDCT-N) to measure common negative dyadic coping ("When we are both stressed, we withdraw and avoid each other") and three items accounted for positive common dyadic coping. The we-approach to measure negative dyadic coping in this study differs from the individual approach on negative coping in the DCI (e.g., "I blame my partner for not coping well enough with stress"), which limits the comparability of the findings. Common dyadic coping seems more beneficial for couples, as it appears to strengthen the feelings of "we-ness" in the relationship (34). However, common dyadic coping was least often used by the couples in our study. In addition to distress related to the advanced cancer diagnosis, couples may experience distress related to the relative lack of "we-ness" in the relationship and adequate dyadic coping. Such coping strategies may be amenable to psychological treatment, such as cognitive behavioral therapy (35).

Our results also show that satisfaction with dyadic coping in partners was positively related to their own and to the patients' emotional functioning. Sparla et al (2016) showed, with their qualitative research on couples facing advanced cancer, that partners can experience feelings of helplessness regarding the patients' deterioration (36) which adversely affect their emotional functioning. Satisfaction from coping together as a

unit may reduce feelings of helplessness in partners and improve their emotional functioning by fostering the sense of “we-ness”. This positive effect may affect the emotional functioning of patients because caregiver mastery (i.e. the feeling of being in control and not helpless) has been associated with better patient outcomes (37). Remarkably, patients' satisfaction with dyadic coping and their perception on dyadic coping styles were not related to their own or their partners' emotional functioning. Most likely, in patients with advanced cancer, other factors are more strongly related to their emotional functioning, such as their physical functioning and symptoms or cancer treatment.

Limitations

To our knowledge, this is the first study of dyadic coping in advanced cancer based on a large sample of patients and their partner. However, there are some limitations to the findings of this study. The validated questionnaire for dyadic coping (DCI) was developed to measure dyadic coping in case of stress in general, not stress specifically related to health or cancer (7), although it has been widely used in healthcare settings. We did not control for the duration of the dyadic relationship, which was measured categorically and most couples were together for more than five years. However, based on our results and previous studies (29-31, 38, 39) the quality of the relationship may be more important than the duration in assessing dyadic coping. The effect sizes of our results were rather small, indicating that the magnitude of the association between dyadic coping and emotional functioning may not be clinically relevant. Finally, this cross-sectional analysis could not determine causality of effects. It remains unclear, therefore, whether satisfaction with dyadic coping has a causal effect on the emotional functioning of patients and their partners. Longitudinal follow-up of the couples in our study is expected to provide more insight into the directionality of these effects.

Clinical implications and future research

This study highlights the important relationship between dyadic coping in couples confronted with advanced cancer and their emotional functioning. The findings suggest that the emotional functioning and dyadic coping of patients and partners are interrelated. Health care professionals should be aware of the social context of patients and address how couples cope as a unit. They should also pay attention to the perspective of partners on dyadic coping and perceive them as a source of support for patients as well as individuals in need of support for themselves. Future research should explore factors that contribute to dyadic coping in couples confronted with advanced cancer and how this may evolve over time and at what point in the trajectory individual and/or couple-based support may be most needed and most effective. Also, future research should utilize a shortened version of the DCI, as the length of this questionnaire may become too burdensome for patients nearing death.

Conclusions

The present study demonstrates an association of dyadic coping with the emotional functioning of patients with advanced cancer and their partners. The partners' perspective on dyadic coping appears to be particularly related to their own emotional functioning and that of the patient. These findings highlight the potential importance of dyadic functioning for the wellbeing of patients with advanced cancer and their partners but also identifies differences in these domains between patients and their partners. Future research is needed to understand these relationships and the potential benefit of interventions directed to improve dyadic coping in couples with advanced cancer.

References

1. Hagedoorn M, Sanderman R, Bolks HN, Tuinstra J, Coyne JC. Distress in couples coping with cancer: a meta-analysis and critical review of role and gender effects. *Psychol Bull.* 2008;134(1):1-30.
2. Northouse L, Williams AL, Given B, McCorkle R. Psychosocial care for family caregivers of patients with cancer. *J Clin Oncol.* 2012;30(11):1227-34.
3. Hotopf M, Chidgey J, Addington-Hall J, Ly KL. Depression in advanced disease: a systematic review Part 1. Prevalence and case finding. *Palliat Med.* 2002;16(2):81-97.
4. Streck BP, Wardell DW, LoBiondo-Wood G, Beauchamp JES. Interdependence of physical and psychological morbidity among patients with cancer and family caregivers: Review of the literature. *Psychooncology.* 2020;29(6):974-89.
5. Jacobs JM, Shaffer KM, Nipp RD, Fishbein JN, MacDonald J, El-Jawahri A, et al. Distress is Interdependent in Patients and Caregivers with Newly Diagnosed Incurable Cancers. *Ann Behav Med.* 2017;51(4):519-31.
6. Lau BH, Wong DFK, Fung YL, Zhou J, Chan CLW, Chow AYM. Facing death alone or together? Investigating the interdependence of death anxiety, dysfunctional attitudes, and quality of life in patient-caregiver dyads confronting lung cancer. *Psychooncology.* 2018;27(8):2045-51.
7. Bodenmann G. Dyadisches Coping Inventar: Testmanual[Dyadic Coping Inventory: Testmanual]. Bern, Switzerland: Huber. 2008.
8. Nipp RD, El-Jawahri A, Fishbein JN, Gallagher ER, Stagl JM, Park ER, et al. Factors associated with depression and anxiety symptoms in family caregivers of patients with incurable cancer. *Ann Oncol.* 2016;27(8):1607-12.
9. Harding R, Higginson IJ, Donaldson N. The relationship between patient characteristics and carer psychological status in home palliative cancer care. *Support Care Cancer.* 2003;11(10):638-43.

10. Badr H, Carmack CL, Kashy DA, Cristofanilli M, Revenson TA. Dyadic coping in metastatic breast cancer. *Health Psychol.* 2010;29(2):169-80.
11. McLean LM, Walton T, Matthew A, Jones JM. Examination of couples' attachment security in relation to depression and hopelessness in maritally distressed patients facing end-stage cancer and their spouse caregivers: a buffer or facilitator of psychosocial distress? *Support Care Cancer.* 2011;19(10):1539-48.
12. von Heymann-Horan A, Bidstrup PE, Johansen C, Rottmann N, Andersen EAW, Sjogren P, et al. Dyadic coping in specialized palliative care intervention for patients with advanced cancer and their caregivers: Effects and mediation in a randomized controlled trial. *Psychooncology.* 2019;28(2):264-70.
13. Ernst J, Hinz A, Niederwieser D, Dohner H, Honig K, Vogelhuber M, et al. Dyadic coping of patients with hematologic malignancies and their partners and its relation to quality of life - a longitudinal study. *Leuk Lymphoma.* 2017;58(3):655-65.
14. van de Poll-Franse LV, Horevoorts N, van Eenbergen M, Denollet J, Roukema JA, Aaronson NK, et al. The Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship registry: scope, rationale and design of an infrastructure for the study of physical and psychosocial outcomes in cancer survivorship cohorts. *Eur J Cancer.* 2011;47(14):2188-94.
15. van Roij J, Zijlstra M, Ham L, Brom L, Fransen H, Vreugdenhil A, et al. Prospective cohort study of patients with advanced cancer and their relatives on the experienced quality of care and life (eQuiPe study): a study protocol. *BMC Palliat Care.* 2020;19(1):139.
16. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QOL-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst.* 1993;85(5):365-76.
17. Kohler N, Perner A, Anders D, Brahler E, Papsdorf K, Gotze H. [Family caregivers of palliative cancer patients: health-related quality of life and care-related burden]. *Psychother Psychosom Med Psychol.* 2012;62(5):157-62.

18. Ledermann T BG, Gagliardi S, Charvoz L, Verardi S, Rossier J, Bertoni A, & lafrate R. Psychometrics of the Dyadic Coping Inventory in three language groups. *Swiss Journal of Psychology / Schweizerische Zeitschrift für Psychologie / Revue Suisse de Psychologie*. 2010;69(4):201-12.
19. Li Q, Xu Y, Zhou H, Loke AY. A couple-based complex intervention for Chinese spousal caregivers and their partners with advanced cancer: an intervention study. *Psychooncology*. 2015;24(11):1423-31.
20. Rottmann N, Hansen DG, Larsen PV, Nicolaisen A, Flyger H, Johansen C, et al. Dyadic coping within couples dealing with breast cancer: A longitudinal, population-based study. *Health Psychol*. 2015;34(5):486-95.
21. Northouse LL, Mood DW, Schafenacker A, Kalemkerian G, Zalupski M, LoRusso P, et al. Randomized clinical trial of a brief and extensive dyadic intervention for advanced cancer patients and their family caregivers. *Psychooncology*. 2013;22(3):555-63.
22. Badr H, Smith CB, Goldstein NE, Gomez JE, Redd WH. Dyadic psychosocial intervention for advanced lung cancer patients and their family caregivers: results of a randomized pilot trial. *Cancer*. 2015;121(1):150-8.
23. Spanier GB. Measuring dyadic adjustment: New scales for assessing the quality of marriage and similar dyads. *Journal of Marriage and Family*. 1976;38:15-28.
24. Weinman J PK, Moss-Morris R, Horne R. The Illness Perception Questionnaire: a new method for assessing the cognitive representation of illness. *Psychol Health*. 1996;11(431-445).
25. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis Rheum*. 2003;49(2):156-63.
26. JW. C. Statistical power analysis for the behavioral sciences. Hillsdale: Lawrence Erlbaum Associates. 1988:284-7.

27. Kenny D, Kashy, DA, & Cook, WL. *Dyadic Data Analysis*. New York: The Guilford Press. 2006.
28. Schellekens MPJ, Karremans JC, van der Drift MA, Molema J, van den Hurk DGM, Prins JB, et al. Are Mindfulness and Self-Compassion Related to Psychological Distress and Communication in Couples Facing Lung Cancer? A Dyadic Approach. *Mindfulness* (N Y). 2017;8(2):325-36.
29. Meier F, Cairo Notari S, Bodenmann G, Revenson TA, Favez N. We are in this together - Aren't we? Congruence of common dyadic coping and psychological distress of couples facing breast cancer. *Psychooncology*. 2019.
30. Traa MJ, De Vries J, Bodenmann G, Den Ouden BL. Dyadic coping and relationship functioning in couples coping with cancer: a systematic review. *Br J Health Psychol*. 2015;20(1):85-114.
31. Pankrath AL, Weissflog G, Mehnert A, Niederwieser D, Dohner H, Honig K, et al. The relation between dyadic coping and relationship satisfaction in couples dealing with haematological cancer. *Eur J Cancer Care (Engl)*. 2018;27(1).
32. Magsamen-Conrad K, Checton MG, Venetis MK, Greene K. Communication Efficacy and Couples' Cancer Management: Applying a Dyadic Appraisal Model. *Commun Monogr*. 2015;82(2):179-200.
33. Cai T, Qian J, Huang Q, Yuan C. Distinct dyadic coping profiles in Chinese couples with breast cancer. *Support Care Cancer*. 2021.
34. G. B. Dyadic coping and its significance for marital functioning, in *Couples Coping With Stress: Emerging Perspectives on Dyadic Coping*. eds Revenson T A, Kayser K, Bodenmann G (Washington, DC: American Psychological Association;). 2005;33–49. 10.
35. Greer S. CBT for emotional distress of people with cancer: some personal observations. *Psychooncology*. 2008;17(2):170-3.
36. Sparla A, Flach-Vorgang S, Villalobos M, Krug K, Kamradt M, Coulibaly K, et al. Individual difficulties and resources - a qualitative analysis in patients with advanced lung cancer and their relatives. *Patient Prefer Adherence*. 2016;10:2021-9.

37. Boele FW, Given CW, Given BA, Donovan HS, Schulz R, Weimer JM, et al. Family caregivers' level of mastery predicts survival of patients with glioblastoma: A preliminary report. *Cancer*. 2017;123(5):832-40.
38. Regan TW, Lambert SD, Kelly B, McElduff P, Girgis A, Kayser K, et al. Cross-sectional relationships between dyadic coping and anxiety, depression, and relationship satisfaction for patients with prostate cancer and their spouses. *Patient Educ Couns*. 2014;96(1):120-7.
39. R OTF. Relationship Between Dyadic Coping and Marital Quality in Women With Breast Cancer in Shiraz. *Iranian Quarterly Journal of Breast Disease*. 2018;10(4).

CHAPTER 9

Sexual health and closeness in couples coping with advanced cancer: Results of a multicenter observational study (eQuiPe)

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Abstract

Background: Cancer and its treatment can severely affect sexual health. It is unknown how this may relate to the feelings of closeness between patients and their partners.

Aim: To assess the association between sexual health and closeness in the relationship in couples coping with advanced cancer.

Design: This study was part of a prospective multicentre longitudinal observational cohort study on experienced quality of care and quality of life in patients with advanced cancer and their relatives (eQuiPe).

Setting/participants: Baseline data regarding sexual health and closeness in people with advanced cancer and their partners.

Results: Out of the 566 dyads, 14 were same-sex couples. Especially male partners showed an interest in sex, but more than half of all patients and partners were not sexually active. Approximately one third experienced sexual dysfunction to be a problem but did not seek specialized support (<10%). There was a positive association between own sexual satisfaction and feelings of closeness in the relationship, which was stronger for partners compared to patients ($p < 0.001$). Sexual satisfaction of the other person was also related to own feelings of closeness ($p = 0.003$).

Conclusions: Couples coping with advanced cancer clearly face challenges regarding sexual health but are not likely to seek specialized support. When discussing sexual health, it is crucial that health care professionals pay attention to the aspects of sexual health that may contribute to feeling close to each other and suggest specialized care if necessary.

Background

Cancer and its treatment can severely affect sexual health of people with advanced cancer.^{1–5} It is estimated that sexual problems and dysfunction after cancer treatment ranges from 40% and up to 100%.^{6,7} Research has shown that the impact of cancer on sexual health and satisfaction is more severe in people with advanced disease compared to patients with early-stage cancer.^{8,9}

For people with advanced cancer, the emotional connection with their partner arising from sexual relationships such as intimacy, belonging, bonding, and mutuality seems more important than the physical sexual experience.^{2,10} Previous research has also shown that people sometimes develop closer relationships or improved intimacy when diagnosed with advanced cancer^{10–12} while other research suggest that relationship functioning in couples coping with cancer is impaired due to the disease.^{13–15}

While the act of sex usually involves two people, research on sexual health and intimacy in partners of people with advanced cancer is scarce. Some qualitative studies among partners have reported that a diminished sexual relationship may result in disappointment, anger, sadness, and feelings of rejection among these partners.^{16–18} This may be due to disease progression and changing roles and responsibilities of the partner and anticipatory loss and grief in patient-partner dyads.^{19–21}

Sexual health and intimacy in advanced cancer are often unspoken topics in clinical practice. In a survey among hospitalized people with cancer receiving palliative consultation, the vast majority of patients (92%) reported that they had not been asked about the impact of cancer on intimacy, while almost half (48%) of the patients reported that their intimate life was negatively impacted by their disease.²² Another study

showed that a vast majority of people with advanced cancer experience an impaired sex life and more than half of them experience unmet needs for support related to this from their healthcare professionals.⁷

Wang et al.²³ have conducted a narrative literature review and concluded that there is limited understanding of patients' and partners' concerns regarding sexual health and intimacy in the context of advanced cancer and minimal incorporation of sexual health care in palliative care. Understanding sexual health and identifying potential unmet needs and could improve quality of life of patients and partners. Therefore, the aim of this study was to assess sexual health and its association with intimacy in couples coping with advanced cancer. We hypothesized that sexual activity and satisfaction are positively associated with feelings of closeness for both patients and partners. We expected that sexual health may differ for males and females irrespective of role (e.g. being a patient or partner) and included gender in our analysis.

Methods

Study design

A prospective, longitudinal, multicentre, observational study on the experienced quality of care and quality of life in patients with advanced cancer and their relatives was conducted in the Netherlands. The study was assessed by the Medical Research Ethics Committee of the Antoni van Leeuwenhoek hospital (METC17.1491) and is registered as NTR6584 in the Netherlands Trial Register. Details of the study have been reported elsewhere.²⁴

Study population and recruitment

People with advanced cancer were asked to participate in this study between November 2017 and January 2020 by their treating physician from 40 participating hospitals in the Netherlands or they self-enrolled.

People with advanced cancer, defined as having a solid primary tumor with metastases, and their relatives were eligible to participate. Additional inclusion criteria were defined for people with breast or prostate cancer to exclude inclusion of patients with a relatively good prognosis. People diagnosed with breast cancer were eligible when their metastases were located in multiple organ systems. People suffering from prostate cancer were eligible when their cancer was metastasized and castrate-resistant. Relatives had to be 18 years or older and able to complete a Dutch questionnaire. All patients who were interested in participation in the study were further informed by phone by the research team to discuss participation. All patients were also asked if they had a relative (i.e. partner, child, other family, or friend) who would like to participate in the study. After giving written informed consent, patients and relatives completed a questionnaire every 3 months till the patient's death. Questionnaires were completed on paper or online via the Patient Reported Outcomes Following Initial treatment and Long-term Evaluation of Survivorship (PROFILES) registry.²⁵ For this study, baseline data of patients and their partners (e.g. both patient and partner participating) was used, resulting in 566 patientpartner couples.

Measures

Feelings of closeness in the relationship was assessed with a single item from the Social Wellbeing subscale of the validated Functional Assessment of Cancer Therapy General (FACT-G)²⁶: "I feel close to my partner." A fourpoint Likert scale ranged from not at all to very much.

Sexual interest, sexual activity, satisfaction with sex life, and joy during sex in the past week were assessed by four items derived from the European Organisation for Research and Treatment of Cancer questionnaires (EORTC) Quality of Life Group Item Library.^{27,28} A four-point Likert scale was used ranging from not at all, a little, quite a bit, and very much.

A single item of the validated Body Image Scale (BIS)²⁹ was used to assess feelings of being less sexually attractive. The BIS has been validated in people with cancer³⁰ and has previously been used in people with advanced cancer.³¹ Partners were asked to rate on a five point Likert scale ranging from “never” to “very often” whether they had experienced physical intimacy using a single item of the Self-Care Practices Scale (SCPS).³²

Four items of the validated Problems and Needs in Palliative Care (PNPC) questionnaire were used³³ to assess experienced problems regarding sexual health (“Do you experience sexual dysfunction to be a problem?”) and within the relationship (“Do you experience problems in the relationship with your life companion?”) (the latter only in patients) and to assess related unmet health care needs (“Do you need (extra) professional attention for sexual dysfunction/the relationship”). Healthcare use of patients and partners was assessed with two self-developed items: “Did you contact a sexologist/psychologist in the past month?” (yes/no).

Sociodemographic variables

Socio-demographic variables (i.e. age, gender, educational level, duration of partnered relationship) were collected via self-administered questionnaires. Also comorbidities in patients were self-reported, by using the Self-administered Comorbidity Questionnaire (SCQ).³⁴ Primary tumor type and time since primary diagnosis of patients were extracted from the Netherlands Cancer Registry (NCR).

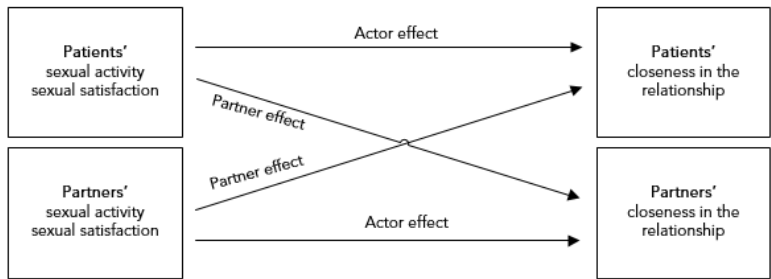
Statistical analysis

Descriptive statistics were used to describe the sociodemographic characteristics and the outcome measures. An Actor-Partner Interdependence Model (APIM) was used to assess whether sexual health was related to intimacy for patients and partners. The APIM takes the dependency between patients and partners into account by treating data

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as nested within the couple.³⁵ Before using the APIM model,³⁵ interdependence between patients and their partners on sexual activity, sexual satisfaction, and feelings of closeness was examined by calculating Pearson's correlations.³⁶ The univariate correlations ranged between 0.04 and 0.45 indicating that the APIM was appropriate to use and there was no presence of multicollinearity. The APIM was applied by means of a multilevel mixed linear regression as presented in Figure 1. Maximum likelihood was used to estimate actor (i.e. own score) and partner effects (the score of the other dyad member) of sexual activity and sexual satisfaction of patient-partner dyads in relation to their feelings of closeness in the relationship (continuous outcome measure). Scores on closeness, sexual activity, and sexual satisfaction (continuous) were linearly transformed to 0–100, where higher scores indicated more closeness, more activity, or higher satisfaction. Role (e.g. being a patient or partner) and gender (categorical) were included in the model, while age, education, and relationship duration were not included in the model because they did not correlate significantly with closeness (dependent variable) ($p > 0.10$). We re-ran the multilevel mixed linear regression analysis after trimming non-significant interaction terms to provide more stable estimates for the main effects, which showed similar findings compared to the full model for each predictor regarding direction and significance. We calculated the High Variance Inflation Factor (VIF) to assess multicollinearity in our multivariable APIM. All statistical analyses were performed using STATA version 16.

Figure 1. The Actor-Partner Interdependence model of the association of sexual activity and sexual satisfaction with closeness in the relationship.



Note: the actor effect is the own score of a dyad member on the independent variable, the partner effect is the score of the other dyad member on the independent variable.

Results

Most patients were male (56%) and most partners were female (55%). Out of the 566 dyads, 14 were same-sex couples. Most patients (41%) and partners (45%) had a medium educational level and were on average 65 years old. Twenty-eight percent of the patients were diagnosed with lung cancer, were diagnosed within the last 5 years (78%), and 58% of the patients reported physical comorbidities. Most couples (93/98%) were in a long-term relationship (5 years or longer) (Table 1).

Table 1. Socio-demographic and clinical characteristics of people with advanced cancer and their partners (n=566)

	People with advanced cancer (n=566)	Partners of patients with advanced cancer (n=566)
	n (%)	n (%)
Gender		
Male	318 (56)	256 (45)
Female	248 (44)	310 (55)
Age (in years) mean (SD), range	65 (9.1), 29-88	65 (9.6), 18-87
Education		
Low	161 (28)	160 (29)
Medium	227 (41)	254 (45)
High	172 (31)	147 (26)
Years in relationship		
Five years or longer	529 (93)	561 (98)
Less than five years	7 (1)	8 (1)
missing	35 (6)	2 (0)
Primary tumor		
Lung	155 (28)	-
Colorectal	107 (19)	-
Breast	72 (13)	-
Prostate	77 (14)	-
Other	157 (27)	-
Time since primary diagnosis		
0-2 years	178 (31)	-
2-5 years	267 (47)	-
>5 years	121 (21)	-
Number of physical comorbidities		
0	240 (42)	-
1	199 (35)	-
>1	127 (22)	-

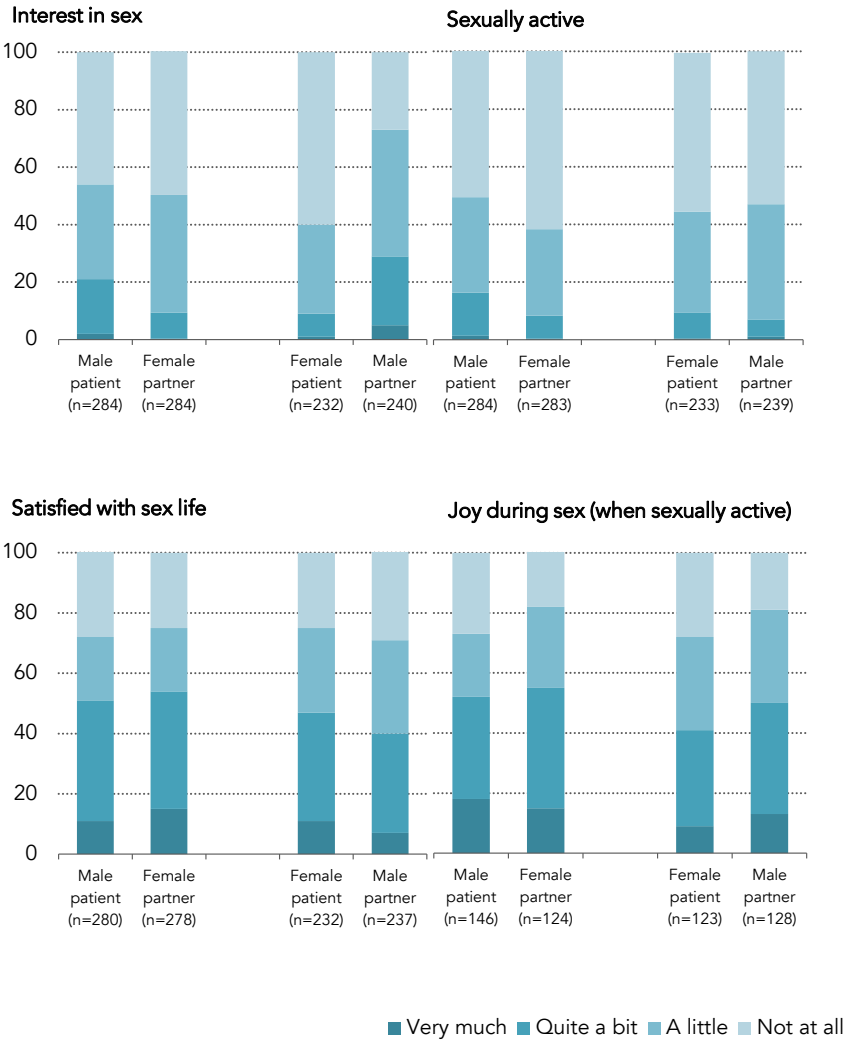
Abbreviations: SD: standard deviation.

Notes: There were 14 same-sex couples. Missing data were <5% unless stated otherwise.

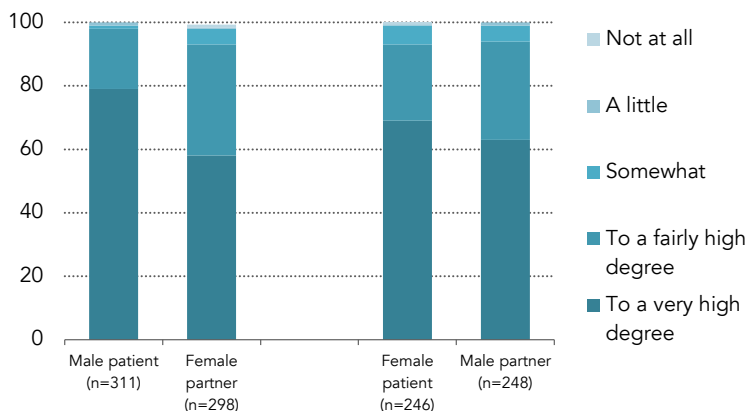
Sexual health and closeness in patientpartner dyads

A large majority of the patients and partners felt close to their partner, patients reported somewhat higher scores on "feelings close" compared to their partners (92 and 88 respectively, $p < 0.001$). Half of male and female patients (respectively 54% and 40%) and female partners (50%) experienced an interest in sex, whereas male partners experienced more interest in sex (73%). More than half of all participants reported not to be sexually active (51% for male and 55% for female patients, 53% for male and 62% for female partners, respectively). Between 25% and 29% of patients and partners reported not to be satisfied with their sex life (Figure 2). More female patients (56%) found themselves less attractive due to their illness or its treatment compared to male patients (34%, $p < 0.001$). Furthermore, more male partners (31%) stated that they rarely or never experienced physical intimacy compared to female partners (24%, $p < 0.001$) (Supplemental Material 1).

Figure 2. Sexual health and feelings of closeness in the relationship reported by people with advanced cancer and partners (n=566) sorted by gender



Closeness in relationship



Unmet needs and health care use related to sexual health and relationship quality

Male patients reported most problems regarding sexual dysfunction (36%) but were least likely to want more attention for their problems (11%). Female partners experienced the least problems regarding sexual dysfunction (21%) whereas male partners most often (32%) wanted more attention for their problems (Table 2). Sixteen percent of male patients and 20% of female patients reported that they experienced problems in the relationship with their life companion, of whom 29% and 25%, respectively wanted more attention for their problems (Table 2). A minority of patients (8%) and partners (7%) had been in contact with a sexologist or a psychologist in the last month.

Table 2. Frequencies of problems in sexual health and relationship of people with advanced cancer and their partners (n=566)

	Male patients (n=318)	Female patients (n=248)	Male partners (n=256)	Female partners (n=310)
	n (%)	n (%)	n (%)	n (%)
Do you experience sexual dysfunction to be a problem?				
Yes	113 (36)	78 (31)	80 (31)	67 (21)
No	174 (55)	146 (59)	158 (62)	207 (66)
Missing	31 (10)	-	18 (7)	36 (12)
Do you need (extra) professional attention for sexual dysfunction?* (n=113)				
Yes, more	12 (11)	18 (23)	25 (32)	10 (15)
As much as now	28 (25)	15 (19)	21 (27)	19 (29)
No	71 (63)	42 (54)	32 (41)	37 (56)
Do you experience problems in the relationship with your life companion?				
Yes	49 (16)	48 (20)	-	-
No	266 (84)	193 (80)		
Do you need (extra) professional attention for your relationship with your life companion?* (n=49)				
Yes, more	14 (29)	12 (25)	-	-
As much as now	19 (39)	17 (35)		
No	12 (24)	18 (38)		
Missing	4 (8)	1 (2)		

Note: missing data <5% were omitted from the table.

*These are conditional items which were answered by patients or partners who experience problems in their sexuality or relationship.

Actor-Partner Interdependence Model of sexual health on relationship closeness

Results of the linear regression model showed that the positive association between own sexual satisfaction and feelings of closeness in the relationship was stronger for partners compared to patients ($B = 0.15$ and $B = 0.03$ respectively, $p < 0.001$). Sexual satisfaction of the other was positively associated with closeness in the relationship ($B = 0.05$, $p =$

0.003), irrespective of role (i.e. being a patient or partner) or gender. Own sexual activity was negatively associated with feelings of closeness in the relationship and this was stronger for females compared to males ($B = -0.19$ and $B = -0.05$ respectively, $p = 0.001$) (Table 3).

Table 3. Results of the mixed linear regression analysis of actor and partner effects of sexual satisfaction and sexual activity on closeness in the relationship among dyads ($n=471$).

Variables	Mean difference (b)	SE	CI 95%	p-value
Own sexual satisfaction (actor effect)	.15	.02	.11 to .19	<.001**
Own sexual satisfaction (actor effect) * role	-.12	.03	-.17 to -.06	<.001**
Other sexual satisfaction (partner effect)	.05	.02	.02 to .08	.003*
Own sexual activity (actor effect)	-.05	.03	-.11 to .01	.086
Own sexual activity (actor effect) * gender	-.14	.04	.06 to .22	.001*
Other sexual activity (partner effect)	.01	.02	-.04 to .06	.696
Gender				
male	1	-		
female	-6.09	1.17	-8.39 to -3.79	<.001**
Role				
partner	1			
patient	9.27	1.54	6.25 to 12.28	<.001**

* $p < .05$, ** $p < .001$.

Notes: The initial regression model included own and other sexual satisfaction and sexual activity (continuous variables). Interaction terms were added between those items and role and gender. An interaction term between role and gender was also included in the initial model. Interaction terms were trimmed sequentially by excluding the interaction with the highest nonsignificant p-value. Variance inflation factor (VIF) values were <4 , confirming the absence of multicollinearity.

Discussion

Main findings

This study showed that almost all people with advanced cancer and their partners felt close to each other. Half of all patients and partners generally showed interest in sex, but more than half was not sexually active. About a third of the patients and partners were not satisfied with their sex life and results showed that own sexual satisfaction was positively associated to feelings of closeness, especially for partners. Sexual satisfaction of the other was also important for patients and partners to feel close to each other in the relationship. Male patients and partners, and females even more so, felt less close to their partner when they were more sexually active.

We found that males were more interested in sex compared to females, irrespective of role (patient vs partner). The sexual disinterest in female patients and partners and male patients was much higher compared to the general population, where 49% of the males and 75% of the females between 60 and 69 years of age have no interest in sex.³⁷ Regarding sexual activity, Bond et al.⁷ found that 60% of people with advanced cancer were not sexually active which is in line with our findings. Patients and partners in our study were more sexually active compared to the general population, where 37% of the males and 23% of the females between 60 and 69 years of age were sexually active.³⁷ About 72%–81% of the sexually active patients and partners in our study experienced joy during sex. This is lower compared to 90% in the general population.³⁸ A decrease in sexual interest, activity, and joy do not necessarily impact satisfaction with sex life for patients and partners. However, about one fourth of the male patients and partners and one third of the female patients and partners were not satisfied with their sex life. This may

indicate a need for helping patients and partners with how they can become more satisfied with their sex life.

We found that about a third of the patients and partners experience problems regarding sexual health and/or in their relationship but were not likely to seek specialized support. A recent study by Krouwel et al.³⁹ among oncologists found that sexual health was discussed with less than half of the people with cancer. Patients and partners might expect that healthcare professionals will initiate the conversation if it is important.⁴⁰ A recent survey among people who had been diagnosed with cancer in the Netherlands showed that 27% thought there was no solution to their sexual problems and they did not know where to get support. Moreover, almost a quarter of people with cancer (24%) were too afraid to talk about sexual health.⁴¹ Barriers for discussing sexual health among oncologists include lack of time, lack of training, and finding it difficult to discuss the topic, especially with older patients or patients treated without curative intent.³⁹ Other known barriers are embarrassment of health care professionals when discussing sexual health and intimacy,⁴² fear of causing distress or offense, misconceptions regarding sexual health, perception that it is the responsibility of another healthcare professional, limited confidence in communication, or a lack of privacy.^{43,44} Due to all these barriers, sexual health often remains unspoken for couples coping with advanced cancer.

Results from our APIM model indicated that sexual satisfaction of oneself and the other was associated with higher levels of closeness in the relationship for patients and even more so for partners. Unexpectedly, own sexual activity was negatively related to feelings of closeness, especially in females. It is possible that, when regular sexual intercourse is limited by physical functioning, sexual activity may become a source of discomfort and stress for couples. For instance, patients may feel guilty

for not being able to please their partner as they used to or partners may find the patient less attractive due to changes in appearance following cancer treatment. These changes challenge couples to seek alternative ways to have sex (oral sex, masturbation, toys) to maintain intimacy. Such flexibility in couples' definitions of sexual activity is associated with better adjustment to cancer.⁴⁵ The negative association of sexual activity with closeness in the relationship in our study suggest that emotional connection may be achieved via other ways than the physical act of having sex together.³⁴

Strengths and weaknesses

To our knowledge, this is the first study among a large sample with a high response rate to examine the association between sexual health on relationship closeness in couples coping with advanced cancer and using a dyadic approach. Some limitations of this study need to be addressed. First, information regarding the experiences of sexual health and relationship quality among patients and partners prior to the advanced cancer diagnosis is lacking. Therefore, it is not possible to assess whether it is the advanced cancer that has impacted sexual health and relationship quality in dyads included in this study (crosssectional data). Second, selection bias might be present as most ill people with advanced cancer or patients and partners with the most concerns regarding their relationship may not have participated. For instance, 42% of our patients did not have any comorbid conditions. Therefore, the results may underestimate prevalence of issues with sexual health and relationship quality among people with advanced cancer and their partners. Lastly, we used single items in study to measure our outcomes. While the use of single items in research is common practice, they are often not validated as such. Also, validated multi-item measurement instruments generally have greater reliability and validity compared to single items. Closeness

was measured with one item from the social wellbeing scale of the validated FACT-G questionnaire. Because the questionnaire from the eQuiPe study was already extensive, an entire validated questionnaire on closeness would have increased the administration burden for patients and relatives even more. We also used single items of the EORTC item bank to measure sexual health. While these are validated items, the EORTC has recently developed and validated a questionnaire to measure sexual health in people with cancer, the EORTC SHQ-2246,⁴⁷ which also includes the four items used in our study.

What this study adds

Healthcare professionals caring for people with advanced cancer should be aware that it is important to assess both the patient and partner perspectives on sexual health because their experiences regarding sexual health impact each other and they are both the focus of palliative care.⁴⁸ Instead of focusing on sexual activity, discussing alternative ways to maintain or regain closeness within the relationship may be effective in fostering the partnered relationship. Special attention should go out to male partners because their sexual problems appear to be highly common and may be overlooked as they often do not seek support. Normalizing sexual problems and being transparent about supportive care options might reduce the barriers patients, partners, and health care professionals may experience. Stimulating open communication between partners may also support their ability to adjust to changes in their sexual functioning and can enhance feelings of closeness.^{49–51}

Conclusions

People with advanced cancer and their partners clearly face challenges regarding their sexual health but are not likely to seek specialized support. Feelings of closeness is an important emotional need for people with advanced cancer and their partner. Feeling close to each other is

positively related to sexual satisfaction in patients and partners, while sexual activity is negatively related to closeness. When discussing sexual health, it is crucial that health care professionals are aware that sexual activity may change due to advanced cancer and alternative ways to adjust to these changes may be beneficial for couples to feel close to each other while dealing with advanced cancer.

References

1. Mercadante S, Vitrano V and Catania V. Sexual issues in early and late stage cancer: a review. *Support Care Cancer* 2010; 18(6): 659–665.
2. Lemieux L, Kaiser S, Pereira J, et al. Sexuality in palliative care: patient perspectives. *Palliat Med* 2004; 18(7): 630–637.
3. McClelland SI, Holland KJ and Griggs JJ. Vaginal dryness and beyond: the sexual health needs of women diagnosed with metastatic breast cancer. *J Sex Res* 2015; 52(6): 604–616.
4. McClelland S. “I wish I’d known”: patients’ suggestions for supporting sexual quality of life after diagnosis with metastatic breast cancer. *Sex Relation Ther* 2016; 31: 414–431.
5. Janecki M, Kaptacz I, Janecka Z, et al. A pilot study on the quality of sexual life of patients receiving home palliative care in Poland. *Sexes* 2021; 2(2): 174–182.
6. PDQ Supportive and Palliative Care Editorial Board. Sexuality and Reproductive Issues (PDQ®): health professional version. 2013 Sep 4. In: PDQ cancer information summaries [Internet]. Bethesda, MD: National Cancer Institute (US), 2002.
7. Bond CB, Jensen PT, Groenvold M, et al. Prevalence and possible predictors of sexual dysfunction and self-reported needs related to the sexual life of advanced cancer patients. *Acta Oncol* 2019; 58(5): 769–775.
8. Ananth H, Jones L, King M, et al. The impact of cancer on sexual function: a controlled study. *Palliat Med* 2003; 17(2): 202–205.
9. Vitrano V, Catania V and Mercadante S. Sexuality in patients with advanced cancer: a prospective study in a population admitted to an acute pain relief and palliative care unit. *Am J Hosp Palliat Care* 2011; 28(3): 198–202.
10. Taylor B. Experiences of sexuality and intimacy in terminal illness: a phenomenological study. *Palliat Med* 2014; 28(5): 438–447.
11. Flynn KE, Jeffery DD, Keefe FJ, et al. Sexual functioning along the cancer continuum: focus group results from the Patient-Reported

Outcomes Measurement Information System (PROMIS®).
Psychooncology 2011; 20(4): 378–386.

12. van Roij J, Brom L, Youssef-El Soud M, et al. Social consequences of advanced cancer in patients and their informal caregivers: a qualitative study. *Support Care Cancer* 2019; 27(4): 1187–1195.
13. Ell K, Nishimoto R, Mantell J, et al. Longitudinal analysis of psychological adaptation among family members of patients with cancer. *J Psychosom Res* 1988; 32(4–5): 429–438.
14. Badr H, Herbert K, Reckson B, et al. Unmet needs and relationship challenges of head and neck cancer patients and their spouses. *J Psychosoc Oncol* 2016; 34(4): 336–346.
15. Karraker A and Latham K. In sickness and in health? Physical illness as a risk factor for marital dissolution in later life. *J Health Soc Behav* 2015; 56(3): 420–435.
16. Gilbert E, Ussher JM and Hawkins Y. Accounts of disruptions to sexuality following cancer: the perspective of informal carers who are partners of a person with cancer. *Health (London)* 2009; 13(5): 523–541.
17. Gilbert E, Ussher JM and Perz J. Renegotiating sexuality and intimacy in the context of cancer: the experiences of carers. *Arch Sex Behav* 2010; 39(4): 998–1009.
18. Hawkins Y, Ussher J, Gilbert E, et al. Changes in sexuality and intimacy after the diagnosis and treatment of cancer: the experience of partners in a sexual relationship with a person with cancer. *Cancer Nurs* 2009; 32(4): 271–280.
19. Carlson LE, Bultz BD, Specia M, et al. Partners of cancer patients: part 1. Impact, adjustment, and coping across the illness trajectory. *J Psychosoc Oncol* 2000; 18: 39–57.
20. Tan A, Zimmermann C and Rodin G. Interpersonal processes in palliative care: an attachment perspective on the patient-clinician relationship. *Palliat Med* 2005; 19(2): 143–150.
21. Manne S and Badr H. Intimate relationships and cancer. In: Sullivan K and Davila J (eds) *Support processes in intimate relationships*. New York, NY: Oxford University Press, 2010, pp.240–264.

22. Kelemen A, Cagle J, Chung J, et al. Assessing the impact of serious illness on patient intimacy and sexuality in palliative care. *J Pain Symptom Manage* 2019; 58(2): 282–288.
23. Wang K, Ariello K, Choi M, et al. Sexual healthcare for cancer patients receiving palliative care: a narrative review. *Ann Palliat Med* 2018; 7(2): 256–264.
24. van Roij J, Zijlstra M, Ham L, et al. Prospective cohort study of patients with advanced cancer and their relatives on the experienced quality of care and life (eQuiPe study): a study protocol. *BMC Palliat Care* 2020; 19(1): 139.
25. van de Poll-Franse LV, Horevoorts N, van Eenbergen M, et al. The patient reported outcomes following initial treatment and long term evaluation of survivorship registry: scope, rationale and design of an infrastructure for the study of physical and psychosocial outcomes in cancer survivorship cohorts. *Eur J Cancer* 2011; 47(14): 2188–2194.
26. Cella DF, Tulsky DS, Gray G, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *J Clin Oncol* 1993; 11(3): 570–579.
27. European Organisation for Research and Treatment of Cancer questionnaires. EORTC items on sexuality, <https://qol.eortc.org/questionnaires/> (accessed 21 October 2019).
28. European Organisation for Research and Treatment of Cancer questionnaires (EORTC) Quality of Life Group (QLG), item library, <https://qol.eortc.org/item-library/> (accessed 6 November 2019).
29. Hopwood P, Fletcher I, Lee A, et al. A body image scale for use with cancer patients. *Eur J Cancer* 2001; 37(2): 189–197.
30. van Verschuer VM, Vrijland WW, Mares-Engelberts I, et al. Reliability and validity of the Dutch-translated Body Image Scale. *Qual Life Res* 2015; 24(7): 1629–1633.
31. Diaz-Frutos D, Baca-Garcia E, Garcia-Foncillas J, et al. Predictors of psychological distress in advanced cancer patients under palliative treatments. *Eur J Cancer Care (Engl)* 2016; 25(4): 608–615.
32. Lee JJ, Bride B and Miller SE. Development and initial validation of the self-care practices scale (SCPS). Poster session presented at the

meeting of the society for social work and research, Washington, DC, 2016.

33. Osse BH, Vernooij MJ, Schade E, et al. Towards a new clinical tool for needs assessment in the palliative care of cancer patients: the PNPC instrument. *J Pain Symptom Manage* 2004; 28(4): 329–341.
34. Sangha O, Stucki G, Liang MH, et al. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis Rheum* 2003; 49(2): 156–163.
35. Kenny D, Kashy DA and Cook WL. *Dyadic data analysis*. New York, NY: The Guilford Press, 2006.
36. Alferes VR and Kenny DA. SPSS programs for the measurement of nonindependence in standard dyadic designs. *Behav Res Methods* 2009; 41(1): 47–54.
37. van de Poll-Franse LV, Mols F, Gundy CM, et al. Normative data for the EORTC QLQ-C30 and EORTC-sexuality items in the general Dutch population. *Eur J Cancer* 2011; 47(5): 667–675.
38. (IKNL) TNCCO. Kankerzorg in beeld: over leven met en na kanker, <https://shop.iknl.nl/shop/oncologische-zorg/rapporten-kankerzorg>.
39. Krouwel EM, Albers LF, Nicolai MPJ, et al. Discussing sexual health in the medical oncologist's practice: exploring current practice and challenges. *J Cancer Educ* 2020; 35: 1072–1088.
40. Hordern AJ and Street AF. Constructions of sexuality and intimacy after cancer: patient and health professional perspectives. *Soc Sci Med* 2007; 64(8): 1704–1718.
41. (NFK) DPFoCPONFvKo. Wat is er nodig om het onderwerp seksualiteit bespreekbaar te maken? <https://nfk.nl/onderzoeken/wat-is-er-nodig-om-het-onderwerp-seksualiteitbespreekbaar-te-maken> (2020, accessed 30 June 2020).
42. Cort E, Monroe B and Oliviere D. Couples in palliative care. *Sex Relation Ther* 2004; 19: 337–354.
43. Cort E. Let's talk about sex: tackling embarrassing issues. *Nurs Pract* 2003; Nov/Dec: 79–84.

44. White K. Chapter 17. Sexuality and body image. In: O'Connor MM and Aranda S (eds) Palliative care nursing: a guide to practice. Boca Raton, FL: Routledge, 2003, pp.245–258.
45. Beck AM, Robinson JW and Carlson LE. Sexual values as the key to maintaining satisfying sex after prostate cancer treatment: the physical pleasure-relational intimacy model of sexual motivation. *Arch Sex Behav* 2013; 42(8): 1637–1647.
46. Oberguggenberger AS, Nagele E, Inwald EC, et al. Phase 1-3 of the cross-cultural development of an EORTC questionnaire for the assessment of sexual health in cancer patients: the EORTC SHQ-22. *Cancer Med* 2018; 7(3): 635–645.
47. Greimel E, Nagele E, Lanceley A, et al. Psychometric validation of the European Organisation for Research and Treatment of Cancer-Quality of Life Questionnaire Sexual Health (EORTC QLQ-SH22). *Eur J Cancer* 2021; 154: 235–245.
48. WHO. Definition palliative care, <http://www.who.int/cancer/palliative/definition/en/> (2002, accessed 23 November 2016).
49. Badr H and Taylor CL. Sexual dysfunction and spousal communication in couples coping with prostate cancer. *Psychooncology* 2009; 18(7): 735–746.
50. Bois K, Bergeron S, Rosen N, et al. Intimacy, sexual satisfaction, and sexual distress in vulvodynia couples: an observational study. *Health Psychol* 2016; 35(6): 531–540.
51. Manne S and Badr H. Intimacy processes and psychological distress among couples coping with head and neck or lung cancers. *Psychooncology* 2010; 19(9): 941–954.

Supplement 1. Feeling attractive and physical intimacy in patients with advanced cancer and their partners (n=566)

	Male patients (n=318)	Female patients (n=248)	Male partners (n=256)	Female partners (n=310)	p-value
	n (%)	n (%)	n (%)	n (%)	
Feeling less sexually attractive due to illness/treatment					
Not at all	189 (59)	103 (42)	-	-	<.001
A little	66 (21)	69 (28)			
Very much	25 (8)	40 (16)			
A lot	6 (2)	19 (8)			
missing	32 (10)	17 (7)			
Experienced physical intimacy					
Never	-	-	24 (9)	23 (7)	<.001
Rarely			51 (20)	48 (15)	
Sometimes			94 (37)	121 (39)	
Often			60 (23)	80 (26)	
Very often			16 (6)	19 (6)	
missing			11 (4)	19 (6)	

CHAPTER 10

General discussion

GENERAL DISCUSSION

The population of patients with advanced cancer (i.e., stage IV or metastatic cancer) is growing due to advancements in medical treatments (1). Both patients and relatives are affected by the advanced cancer diagnosis and frequently need support to cope with their situation. Fortunately, there is growing attention and implementation of palliative care in the Netherlands. Palliative care aims to improve quality of life (QoL) of both patients and their relatives. In the Netherlands palliative care is considered generalist care that can be provided by all health care professionals, and supported by specialist palliative care professionals when needed. Up to now, there has been limited knowledge regarding how patients and their relatives experience health care, their QoL during the palliative care trajectory and how their experiences are interrelated. Therefore, the central goal of this thesis was to gain a better understanding of the experiences of patients with advanced cancer and that of their relatives regarding quality of care, and QoL and their interdependent relationship. The three aims were:

1. To explore care experiences and QoL of patients with advanced cancer and that of their relatives.
2. To assess the interdependent relationship between patients' and relatives' care experiences and QoL.
3. To assess relational aspects of couples coping with advanced cancer.

Increasing our knowledge about their experienced quality of care and QoL, including their interdependencies, will ultimately provide opportunities to optimize palliative oncology care and improve QoL in patients with advanced cancer and that of their relatives.

Impact of advanced cancer on patients and their relatives

This thesis shows that advanced cancer has a great impact on patients. As expected, the QoL in patients with advanced cancer is lower compared to the Dutch general population. In light of their medical situation, their QoL was actually relatively high compared to other studies (2, 3). More surprisingly, we found that the emotional functioning of relatives and their satisfaction with care was much lower compared to the patients. Relatives also reported that health care professionals had little attention for their wellbeing. Previous studies have also shown that informal caregivers are often more burdened (4) and experience more (unmet) needs compared to patients (5). Their dissatisfaction with support has previously been associated with higher distress and caregiver burden in relatives (6). Our study supports the view that we need to improve the care for relatives of patients with advanced cancer because their wellbeing still seems to be largely overlooked. Palliative care aims to improve QoL of both patients and relatives. However, for health care professionals to give attention to the wellbeing of relatives requires a paradigm shift as their focus has traditionally been on patients. Although there is limited knowledge regarding effective interventions for relatives of patients with advanced cancer (7, 8), the role family meetings might play seems promising (9). Family meetings are meetings in which healthcare professionals meet with the patient and the patients' family to discuss information about the patient's illness, the response to treatment, and what to expect (10). Family meetings are recommended in the literature for health care professionals because these meetings foster communication and individualized care by discussing care needs and goals with patients and their relatives (10). These meetings must also be used to discuss the wellbeing of relatives and it has already been shown that these meetings reduce distress in relatives and improve quality of care (9, 11). Fortunately,

there are currently multiple projects being conducted in the Netherlands on how to address the wellbeing of relatives in clinical practice (12). For instance, the project "Oog voor naasten" provides a practical guide for health care professionals on how to support relatives before and after the death of the patient. Health care professionals could also recommend the 'Mantelzorgbalans' website to relatives, an eHealth where relatives can learn more about how to support patients and themselves.

A family approach

We found that there is interdependence between care experiences and emotional functioning in patients and relatives. The emotional functioning of patients and their relatives is related, suggesting that there is a social ripple effect where the impact of the advanced cancer diagnosis of the patient creates ripples that impact the patients' social network. We also showed that how relatives perceive the care for the patient is not only related to their own emotional functioning but also to the emotional functioning of the patient. By devoting greater attention to the relative and their perspective on care, health care professionals may be able to impact the wellbeing of both patients and relatives. There is growing evidence that patients with advanced cancer and their relatives suffer in relation to each other (13). Unmet care needs of relatives of patients with advanced cancer may negatively impact their own wellbeing (5, 14, 15) but also the patient health outcome (16). In order to optimize care for both, patients and their relatives should be perceived as one unit or system (17-19). This is in line with the Family Systems Theory which states that any significant change or event in a family member affects all other members of the family (20, 21). Furthermore, in advanced cancer, the diagnosis and illness trajectory of the patient often causes feelings of distress in the whole family (17, 20-23), and increases the risk of psychological morbidity in relatives (24, 25). In this way, the social network

of a patient may be supportive but can become a source of additional distress. The same theory emphasizes the importance of support within a family for each other's wellbeing. Family members' support to each other is of great importance to the individual members of a family but also for the functioning of the family as a whole. Families with high levels of support and cohesion have fewer psychosocial problems and more effective social adjustment compared to families with lower levels of support, during the whole palliative care trajectory and during bereavement (26-28). A previous study among family members of patients with a limited life expectancy receiving palliative home care found that relatives who thought that the patient was supported by other family members felt more supported themselves (29). Also, perceived support from other, more distant, family members and the possibility of respite care when they needed a break were associated with feeling supported (29). Thompson et al (30) recently published the Dyadic Cancer Outcomes Framework to guide future research and intervention development for patients with cancer and their family members. This framework incorporates the relationship processes of the dyad (e.g., coping strategies, communication, caregiving tasks), their social context, and a wide range of dyadic and individual-level characteristics and outcomes (30), and may also be applicable for families coping with advanced cancer.

Research on benefits of a family approach in advanced cancer is scarce and most studies focus on the dyadic relation between patients and their partners. Awareness about this dyadic relationship may have the potential to further optimize the care for patients with advanced cancer and their relatives. Recently, two meta-analyses underpinned this, by showing that interventions using a family or dyadic approach are effective in improving physical and mental health in patients with chronic illness, even more effective than standard treatment for all outcomes (31, 32). One promising

example is the COPE, a cognitive-behavioral problem-solving educational intervention for patients with advanced cancer and their relatives (33). A randomized trial among patients with advanced cancer and their informal caregivers showed that the QoL of the caregivers declined significantly less over time compared to caregivers in the control group (33). However, the QoL of patients in the intervention group did not differ from the QoL of patients in the control group (33). FOCUS is another dyadic intervention that involves regular conversations between patients and relatives with a trained nurse (34). FOCUS showed positive effects on dyads' QoL, emotional and functional well-being, emotional distress, benefits of illness (i.e., perceived benefits arising from the cancer illness), and self-efficacy (34). However, effect sizes of dyadic interventions are small to moderate effects and such interventions are rarely implemented in clinical care (35).

Important elements of care

Patients and relatives have a shared perspective on the elements of care that are important to them. In our qualitative studies we found that besides the medical-technical aspects of care, the organization of care (coordination, continuity, and tailored logistics) and the relational aspects (health care professionals need to be personally engaged, provide support and compassion) were crucial for patients with advanced cancer and their relatives. In our prospective observational study, we found four specific elements of care that were positively associated with the emotional functioning of patients or relatives: 1) general satisfaction with care, 2) clarity about the central health care professional, 3) continuity of care, and 4) continuity of information. In patients, general satisfaction with care and clarity about who their central health care professional is was important for their emotional functioning. The Dutch quality framework for palliative care that was launched in 2017 also recommends that there

should be a central health care professional available for patients (36). For relatives, continuity of care and information about the patient's care was important to their emotional functioning. This is in line with a previous study that stated that the quality of life in relatives was influenced by the relatives' satisfaction with patient care and their own emotional functioning (37-39). In addition to these elements of care, we also found interdependence between patients and relatives; continuity of care as perceived by relatives was positively associated with the patient's emotional functioning. In other words, when relatives perceived the patient's care as complementary, patients feel less tense, worried, irritable or down.

Improving (perceived) continuity of care

As a way to enhance integrated palliative care, 'patient journeys' became a common way to describe cancer care trajectories of patients. By truly envisioning the unique experience of individual patients, we aim to gain a better understanding of the patient experience in order to improve their care experiences and satisfaction. Patient journeys have shown us that care for patients is becoming increasingly complex due to the high prevalence of comorbid psychiatric and medical conditions and polypharmacy (40-42). In addition, relatives may also suffer from comorbid conditions. This complexity might lead to fragmented care as patients and relatives may receive care from multiple health care departments and organizations. To improve continuity of care we may need to look beyond organization walls and prioritize collaborations with other departments and organizations. However, with departments being understaffed and the high workload among health care professionals (43) providing high quality continuity of care may become challenging. A recent study in the Netherlands showed that according to nurses, collaboration between care settings and information exchange in

palliative care is suboptimal (44). In the Netherlands there are 65 regional networks of palliative care to improve collaboration between care providers in the region (45). Palliative care networks are a collaboration between organizations that provide palliative care in a certain region, initiated to stimulate collaboration between organizations to improve the quality of care (45).

Moreover, we may also be able to improve continuity of care by involving relatives more in the patient's care. Relatives spend the most time with the patients and can provide health care professionals with information about the patient's needs or wellbeing in the home setting. Some studies have also shown that relatives who were involved in consultations take better care of patients and feel more confident in their caregiving role compared to relatives who were not involved in consultations (46). It seems also necessary to include relatives in the care and treatment decision making process with patients as a previous study among informal caregivers of terminally ill cancer patients showed that the vast majority (97%) of family members will make end-of-life decisions for patients (47). Although this study was conducted in China, a collectivistic country where individuals' choices are not their own but belong to all family members (47), a systematic review on how family members are involved in the Dutch practice of euthanasia and physician assisted suicide also suggests that decisions in advanced cancer situations are often made together (48). This is especially the case nowadays where discussions regarding the necessity of treatment at the end of life due to rising costs of oncological care (49) and the increased attention for QoL versus life-prolonging treatment (50) are more present than ever. When relatives are involved in cancer treatment decisions, they help patients to manage the information that providers share by translating treatment options into understandable terms to the patient and to weigh treatment options together (51, 52).

However, relatives can have different perception on treatment than patients and this may lead to discussion or conflict. For instance, a cohort study among patients with terminal cancer and their relatives showed that 68% of the relatives supported patients in making their preferences heard, but 32% of the relatives acted against the patient's wishes (53). Disagreement between patients and their relatives occurred in 21% of the cases (53). When health care professionals invite relatives to the decision making process, patients are more likely to have frequent discussions about treatment options with their relatives (54), but patients and relatives may need guidance in their discussions (55).

Involving relatives in the care for the patient is not only beneficial to the patient, but also to the relatives. Relatives may experience more continuity of care and feel more confident in caring for the patient when they are more included in care for the patient by health care professionals (46). Caregiver activation is defined as "the knowledge, skills, and confidence of the informal caregiver to provide care for the patient" (56) and provides the opportunity for relatives to establish a partnership with the patient and health care professionals (56). Establishing a personal relationship between health care professionals and relatives also contributes to perceived continuity of care. Trust and confidence of the patient and family in the health care professionals, as well as coordination of care have been found to be associated with the quality of death (measured with the Good Death Inventory) of patients dying at home with cancer according to bereaved family members (57). When paying attention to the perspective of relatives on care for the patient, they may feel heard and seen by health care professionals and their perspective on continuity of care may change. Previous research also showed that when relatives are involved in care for the patient, they are better prepared for

the death of the patient and this may predict more favorable bereavement outcomes (58-60).

The potential of self-care and resilience in relatives

In addition to a need for greater attention to and involvement of relatives, other aspects can also contribute to the increased wellbeing of relatives of patients with advanced cancer. We found that relatives with a low/medium caregiver burden engaged more in self-care and were more resilient compared to relatives with a high caregiver burden. A previous study found that caregivers of patients with advanced cancer experienced more emotional distress when they were limited in their ability to engage in valued activities and interests regardless of the amount of care they provided (61). However, self-care in relatives of patients with advanced cancer receives little attention in the literature. Relatives in palliative care may prioritize the patient's needs over their own, or may not want to bother health care professionals with their personal struggles (62). Relatives should be made aware that healthcare professionals are available for them and that taking care of themselves will benefit both themselves and their loved one with cancer.

Resilience also appears to be critical to the ability of relatives to manage their stressful situation and provide effective care for the patient (63). Previous studies among relatives of patients with an advanced illness showed that resilience of relatives was associated with a lower risk of distress and burden, more social support, and better adaptation to their situation (64, 65). There are many conceptualizations of resilience in research and often resilience is portrayed as a relatively stable trait. However, it is possible that resilience levels may be positively affected by proper self-care. For instance, previous studies showed that self-care is an important individual approach to promoting resilience in health care

professionals working in palliative care (66, 67). This may also be the case for patients and their relatives. Self-care is conceptualized in many different ways, effective self-care could involve inner self-care (such as self-awareness and self-compassion) and physical and social self-care (68). Avoiding such self-care practices may lead to decreased resilience. A study that is currently being conducted by Limardi et al. may shed more light on the role of resilience in informal caregivers of patients receiving palliative care because the aim of their study is to identify the predictive, mediating and moderating role of resilience in informal end-of-life caregivers regarding psychological, behavioral and healthcare factors (69).

The impact of advanced cancer on the wellbeing of relatives is substantial and deserves sufficient attention from health care professionals. Devoting greater attention to self-care and resilience in relatives of patients with advanced cancer may be beneficial in enhancing their wellbeing and ability to take care for the patient. (70, 71). A previous qualitative study showed that resilience may be enhanced in caregivers of patients with advanced cancer by health care professionals via the establishment of a personal relationship (i.e., being seen and known by health care professionals), the availability of palliative care, the provision of adequate information and communication about the patients' illness, prognosis, and death, and facilitating a good patient-relative relationship (72). Furthermore, the acknowledgement by health care professionals of the relatives' caregiver burden, and also effective symptom management, information provision, and adequate care planning all appear to form important elements of high quality of care.

Methodological considerations

Multiple approaches were used in this thesis including a systematic literature review, a qualitative study, and a quantitative study including

dyadic data analysis to assess the interdependence between patients and their relatives. The eQuiPe study is one of the largest prospective studies that includes both patients with advanced cancer and their relatives and has delivered new insights regarding the quality of care and life of patients and their relatives. However, lessons have been learned and the following improvements should be considered in future studies.

Study population

Large sample of patients with advanced cancer

Large scale studies among patients with advanced cancer and their relatives are scarce. We did not reach the intended sample size of 1500 patients and 1000 relatives in our quantitative study. We included 1106 patients, which is substantial. However, if one intends to perform sub-analyses according to cancer type, a preferentially larger sample should be used. Traditionally, it is challenging to include patients in palliative oncological scientific studies (73). We tried to anticipate this by making clear to health care professionals that all patients with advanced cancer would be eligible to participate in our study. We specifically used objective inclusion criteria (e.g. metastatic cancer, with additional criteria for patients with breast and prostate cancer) because previous studies have shown that the use of subjective criteria such as the 'surprise question' (i.e., where health care professionals ask themselves "would you be surprised if this patient died within the next twelve months") to identify patients in their last year of life would lead to an underestimation, as health care professionals tend to overestimate the survival of patients (74). Our objective criteria were based on a median survival of one year for all primary tumors obtained from the Netherlands Cancer Registry (NKR) data. During our study we found that some patients lived much longer (>2 years) than expected. Unfortunately, NKR does not provide real-life clinical data and we only had information on the first part of the illness

trajectory of patients. Our objective criteria have led to the inclusion of patients with a prognosis >1 year, showing that it remains difficult to define inclusion criteria to include patients in their last year of life. It is possible that this may have led to an overestimation of QoL as previous studies have shown that QoL decreases over time (75).

Patients and relatives are willing to participate

Despite our objective inclusion criteria, health care professionals may have been hesitant to ask patients with an incurable illness to participate in scientific studies and a systematic review showed there are many reasons for this 'gatekeeping' phenomenon (76). This is unfortunate, because patients who are terminally ill are often highly motivated to participate in scientific research as mentioned by patients and relatives in our qualitative study and other studies (77, 78). In fact, patients and relatives may experience benefit from participating in research (79). Patients and relatives are of course also free and capable to decline participation, as we experienced when we contacted them by phone to discuss their participation. Our method of inclusion was highly personal (e.g., we phoned each patient to discuss study participation). Our approach very probably contributed to our high response rate, but was also time consuming. We are aware that our inclusion approach requires a great deal of time and effort on the part of a research team, in which we were fortunate, but this may not be available to other researchers in the field.

Recruitment method

Initially we were focused on including patients via their treating physician in the hospital after receiving their advanced cancer diagnosis. However, during the study we received participation requests from patients (n=48, of whom 36 participated) who had read about our study online. We did not want to exclude these motivated patients from our study but also did

not actively pursue online recruitment any further. However, recruiting via online platforms is an option to consider in future studies in order to reach larger sample sizes. We also collaborated with other large cohort studies (80) so that eligible patients could participate in multiple studies simultaneously while reducing their study participation burden by downsizing our questionnaire to a core set of questions. It was challenging to achieve a well-coordinated workflow for all research teams involved. However, the collaboration with other research teams shows that 'fishing in the same pond' can provide the opportunity for efficient use of research data as QoL data of these patients was collected via one combined questionnaire but used by multiple research teams.

Selection bias in patients and relatives

Selection bias may be present in our study population. In our focus group study, patients with a non-western background were underrepresented in our study. Underrepresentation of patients with a non-western background was also the case in our cohort study. As shown in chapter 6, patients in our study were also generally younger and more highly educated as compared to all patients who died of cancer in the Netherlands (based on Netherlands Statistics (CBS) data). Future studies should therefore consider a population based approach in order to achieve a more representative sample of patients with advanced cancer in the Netherlands.

In addition, while we gave patients the choice to ask any relative to participate in our study, it was mostly partners (74%) of patients who participated. Although partners are probably most affected, other relatives of these patients may also be impacted by the illness but they were not included in our study. We could have actively asked patients to identify multiple relatives. Then we might also have included relatives who were less close to the patient and we would have been able to examine

the full social impact of the advanced cancer diagnosis of the patient. Future research should consider a broader social perspective since the wellbeing of other relatives is also affected by the illness of the patient and their wellbeing may also be of significance to the wellbeing of patients and their partners.

Measurement instruments

Measurement instruments to assess quality of life

Firstly, the EORTC QLQ-C15-PAL questionnaire was the best validated instrument to measure QoL in patients with advanced cancer in our systematic literature review (Chapter 4) but we chose the EORTC QLQ-C30 in our prospective cohort study instead. The EORTC QLQ-C15-PAL was developed to decrease the administration burden for patients. However, we expected patients in our study to be in a relatively good medical condition and this proved to be a good choice in hindsight as patients lived even longer than we expected. We also preferred the EORTC QLQ-C30 rather than the EORTC QLQ-15-PAL because the use of the EORTC QLQ-C30 in our study benefits the comparability of our results with other (international) studies.

To measure the quality of life of relatives of patients with advanced cancer is challenging. Most instruments/measures focus on caregiver burden instead of QoL. We chose to also use the emotional, social, and global functioning scale of the EORTC QLQ-C30 in relatives so their scores could also be compared with patient scores. While the EORTC QLQ-C30 was previously used in relatives, we hope the development and validation of instruments to measure QoL in relatives will receive more attention in future research. For instance, the emotional functioning scale measures anxiety and depressive symptoms but does not assess shame or guilt, which are likely to play a role in the emotional functioning of relatives (81). In hindsight, we find it unfortunate that we did not include other domains

of the QLQ-C30 such as the physical functioning scale because the QoL domains are interrelated and the physical health of relatives may very well be affected due to their situation and their experienced distress. Relatives are actually sometimes referred to as 'hidden patients' since they tend to develop psychological and physical health conditions as a consequence of the advanced cancer diagnosis of the patient (82). It would be of great clinical value to assess which elements during the disease trajectory predict these outcomes in relatives and assess how health care can influence these outcomes in future studies.

Measurement instruments to assess experienced quality of care

It was challenging to find well-validated outcome measures for our cohort study concerning experienced quality of care for patients with advanced cancer. Measurement instruments to assess quality of care in relatives were even more limited. Many instruments did not incorporate important aspects of palliative care such as continuity of care and provision of information, or devoting greater attention to the wellbeing of and support options for relatives while we found that these were important aspects for patients and relatives in our qualitative study. Also, some measurement instruments were focused on informal caregivers or partners of patients with advanced cancer, while we also included relatives in our study who did not always perceive themselves to be an informal caregivers to patients. Therefore, we developed a number of items to assess important aspects of palliative care according to the Dutch Quality Framework of Palliative care (36). The Dutch Quality Framework of Palliative Care is based on the wishes and needs of patients and relatives (83). These self-developed items were tested by means of a short pilot study where we asked several (n=31) patients and relatives to complete our questionnaire and provide us with feedback. Unfortunately, however, these self-developed items were not thoroughly validated. Additional attention

needs to be addressed to the development and validation of instruments to measure experienced quality of care in patients with advanced cancer and their relatives.

Addressing palliative care and death in questionnaires

The measurement instruments in our study did not use a 'one size fits all' approach. We received feedback from a few patients and relatives who felt the questions did not fit their situation, for instance, because patients did not perceive themselves to have been diagnosed with incurable cancer or because relatives were not providing practical care for the patient because the patient was in relatively good health. The feedback could suggest that these patients and relatives may be struggling with the acceptance of the advanced cancer diagnosis which makes it difficult to be confronted with such a questionnaire. The feedback from participants might also indicate that patients and relatives associated palliative care with terminal care. This is in line with a previous study by Collins et al. (84, 85) who showed that there are many misconceptions about the meaning of palliative care among the general population. For instance, patients may associate palliative care with terminal care which explains why patients and relatives in our study might have felt that palliative care was not suitable for them yet. Future studies should be aware of the importance of the language used in questionnaires to describe palliative care. However, it remains difficult to compose a questionnaire that would fit the patients' and relatives' situation at the beginning of the illness trajectory as well as during the last phase of life. Naturally, we could not differentiate between patients in the beginning or end of life phase as it was not possible to foresee their outcome. A more flexible method of measurement such as computer adaptive testing may be more suitable than a standardized questionnaires because it has the ability to select questions that are appropriate to ask based on the situation of the

respondent (being recently diagnosed versus the end of life or being an informal caregiver or a friend of the patient).

Implications for clinical practice

Our findings point to the importance of assessment of quality of life of patients and their relatives, while taking into account their interdependence. Patients with cancer and their relatives experience a great deal of distress, especially when confronted with advanced illness (83-86). Given the impact of advanced cancer on their emotional functioning, their psychosocial needs should be addressed in order to maintain or improve their QoL (5). Despite the efforts of the World Health Organization to include the well-being of family members and caregivers in the concept of palliative care, their needs are rarely assessed systematically (90). Relatives are considered a unit of care in palliative care definitions, whereas the organization of care and financial side of care is often mainly focused on patients (91) and does not yet include a broader social context such as family care. However, health care professionals should be aware that each patient is part of a social context. In order to provide high quality care to patients, health care professionals must pay attention to the relatives' perspective of the patients' care and the emotional functioning of relatives.

Our results suggest that we may be able to improve emotional functioning in patients and their relatives by optimizing (continuity of) care. Some of our significant results had rather small effect sizes, indicating that results may not be of great clinical value. However, the observed positive association between experienced quality of care and emotional functioning is noteworthy because there are many more factors which influence emotional functioning. Furthermore, the time patients and relatives spend with health care professionals is only a fraction of their

available time and activities related to their emotional functioning. Health care professionals should be aware of their potential impact on patients and relatives.

Based on our study, optimizing continuity of current care for patients with advanced cancer and their relatives may be sufficient to improve their emotional functioning. Complex interventions that require more time from health care professionals, interventions that increase health care costs, or interventions that are difficult to implement in clinical practice may not be necessary to improve continuity of care. Continuity of care may be improved by involving relatives in care because they can contribute to continuity of care by providing valuable information regarding the patient and partly coordinate the care. Including relatives in the care of the patient may also contribute to (perceived) continuity of care as relatives may feel more involved and heard by health care professionals. For instance, a recent study showed that inviting relatives to advance care planning conversations were more positive about the patient care and support for relatives in the final days of life (92). This suggests that relatives want to be seen by health care professionals and this can be achieved by a few words or a small gesture (93).

Future directions for research

Future research should focus on subgroup analysis because there may be differences between patients with different primary tumor types or prognoses. Furthermore, at the time of writing this thesis, we could not determine what stage of the disease trajectory patients were in. This means that the variation in time to death may differ between patients and that emotional functioning is likely to be lower in patients who are near death compared to patients with a relatively good prognosis. This may lead to different or more severe problems or care needs in both patients

and their relatives. Assessing these subgroup differences may help us further tailor health care to the specific needs of patients and their relatives.

Future studies should focus on gaining a deeper understanding of the emotional impact on relatives. For instance, this could be done by including other aspects of emotional functioning such as shame and guilt. Concepts such as caregiver self-efficacy and activation may also play a role in the emotional functioning of relatives. Resilience and self-care should receive more attention from researchers, including the association between concepts. Future studies should include the possible benefits of patient empowerment and self-management. Although possibly not achievable for all patients, these aspects may play a role in patients' feeling in control of their care and incurable illness.

Results suggest that we may be able to improve emotional functioning in patients and their relatives by optimizing continuity of care. However, future research is necessary to assess a causal relationship. The eQuiPe study is a longitudinal study which has the opportunity to gain more insight in directional effects as multiple time points will become available. The eQuiPe study also has the potential to examine health care experiences and QoL in relatives after the death of the patient. Care before and after the death of the patient may impact the way in which relatives grieve and adjust. Since the disease burden, health care needs, and coping strategies might change over time, this should be measured repeatedly from the onset of the disease in patients through to bereavement in relatives.

A systematic review stated that continuity of care and involving the relatives of patients with cancer are an international research area of priority (94). We agree that family members or close friends of patients with advanced cancer deserve greater attention in research. It can help us

to identify the extent to which relatives are impacted by the diagnosis of the patient and also to identify relatives who are at risk due to their high psychosocial burden and their unmet needs in order to reduce their distress. It may also give us insight into the social networks surrounding patients and help us discover when social relations are a source of support or additional distress for patients. Finally, the development and validation of questionnaires suitable for a family approach should receive more attention as the burden of care is increasingly being placed on family members of patients and their experiences may impact the patient's wellbeing. To our knowledge there is only one questionnaire to measure QoL in family members of patients with cancer that is not only suitable for partners or informal caregivers, but also for other family members, the Quality of Life Family Version (QoL-FV) (95). The QoL-FV includes four scales physical wellbeing, psychological wellbeing, social concerns, and spiritual wellbeing (95). Unfortunately the QoL-FV is not developed or validated in family members of patients with advanced cancer.

Concluding remarks

There is a growing number of patients with advanced cancer who live longer with their diagnosis due to advances in treatment and improved survival. However, cancer is one of the leading causes of death (96). Fortunately, palliative care is increasingly integrated into oncology care in the Netherlands, through early identification of palliative care needs, advance care planning, and mandatory palliative care teams in all hospitals providing oncology care (SONCOS) (97). We have shown that high quality care is associated with higher emotional functioning of both patients and relatives. Moreover, both the care experiences and QoL of patients and relatives are interdependent, suggesting a ripple effect where the impact of the diagnosis, as well as the impact of care for the patient, affects the partner, daughter or son, or other family members or

friends. Greater attention devoted to the wellbeing of relatives is essential in order to further improve palliative care for patients and relatives since they cannot be seen as separate individuals, but rather as one unit of care. Informing relatives about the importance of proper self-care and resilience may contribute to the wellbeing of relatives. It is also important to include relatives in the care of the patient to improve the (perceived) continuity of care for patients which may benefit both patients and relatives. Future studies should assess causal effects between care elements and QoL of patients and relatives and further unravel their interdependencies.

References

1. IKNL. Uitgezaaide kanker in beeld. 2020.
2. Duimering A, Turner J, Chu K, Huang F, Severin D, Ghosh S, et al. Informal caregiver quality of life in a palliative oncology population. *Support Care Cancer*. 2020;28(4):1695-702.
3. Dionne-Odom JN, Azuero A, Lyons KD, Hull JG, Tosteson T, Li Z, et al. Benefits of Early Versus Delayed Palliative Care to Informal Family Caregivers of Patients With Advanced Cancer: Outcomes From the ENABLE III Randomized Controlled Trial. *J Clin Oncol*. 2015;33(13):1446-52.
4. Chang YJ, Kwon YC, Lee WJ, Do YR, Seok LK, Kim HT, et al. Burdens, needs and satisfaction of terminal cancer patients and their caregivers. *Asian Pac J Cancer Prev*. 2013;14(1):209-16.
5. Chua GP, Pang GSY, Yee ACP, Neo PSH, Zhou S, Lim C, et al. Supporting the patients with advanced cancer and their family caregivers: what are their palliative care needs? *BMC Cancer*. 2020;20(1):768.
6. Dumont S, Turgeon J, Allard P, Gagnon P, Charbonneau C, Vezina L. Caring for a loved one with advanced cancer: determinants of psychological distress in family caregivers. *J Palliat Med*. 2006;9(4):912-21.
7. Ahn S, Romo RD, Campbell CL. A systematic review of interventions for family caregivers who care for patients with advanced cancer at home. *Patient Educ Couns*. 2020;103(8):1518-30.
8. Lee JZJ, Chen HC, Lee JX, Klainin-Yobas P. Effects of psychosocial interventions on psychological outcomes among caregivers of advanced cancer patients: a systematic review and meta-analysis. *Support Care Cancer*. 2021;29(12):7237-48.
9. Powazki RD, Walsh D, Aktas A, Hauser K. Palliative Medicine Family Conferences Reduce Spokesperson Distress and Enhance Communication in Advanced Cancer. *J Palliat Med*. 2018;21(8):1086-93.
10. Moneymaker K. The family conference. *J Palliat Med*. 2005;8(1):157.

11. Hudson P, Quinn K, O'Hanlon B, Aranda S. Family meetings in palliative care: Multidisciplinary clinical practice guidelines. *BMC Palliat Care*. 2008;7:12.
12. ZonMw. Ondersteuning van mantelzorgers: hoe pak je dat als zorgverlener aan? https://publicatieszonmw.nl/mantelzorg-in-de-palliatieve-fase/ondersteunen-van-mantelzorgers-hoe-pak-je-dat-als-zorgverlener-aan/?utm_source=linkedin&utm_medium=interview&utm_campaign=pz. last accessed on 19th November 2021.
13. Witkamp E, Droger M, Janssens R, van Zuylen L, van der Heide A. How to Deal With Relatives of Patients Dying in the Hospital? Qualitative Content Analysis of Relatives' Experiences. *J Pain Symptom Manage*. 2016;52(2):235-42.
14. Lund L, Ross L, Petersen MA, Groenvold M. Cancer caregiving tasks and consequences and their associations with caregiver status and the caregiver's relationship to the patient: a survey. *BMC Cancer*. 2014;14:541.
15. Kim Y, Kashy DA, Spillers RL, Evans TV. Needs assessment of family caregivers of cancer survivors: three cohorts comparison. *Psychooncology*. 2010;19(6):573-82.
16. Lambert SD, Harrison JD, Smith E, Bonevski B, Carey M, Lawsin C, et al. The unmet needs of partners and caregivers of adults diagnosed with cancer: a systematic review. *BMJ Support Palliat Care*. 2012;2(3):224-30.
17. Carolan CM, Smith A, Forbat L. Conceptualising psychological distress in families in palliative care: Findings from a systematic review. *Palliat Med*. 2015;29(7):605-32.
18. Lo C, Hales S, Braun M, Rydall AC, Zimmermann C, Rodin G. Couples facing advanced cancer: examination of an interdependent relational system. *Psychooncology*. 2013;22(10):2283-90.
19. Northouse LL, Mood DW, Schafenacker A, Kalemkerian G, Zalupski M, LoRusso P, et al. Randomized clinical trial of a brief and extensive dyadic intervention for advanced cancer patients and their family caregivers. *Psychooncology*. 2013;22(3):555-63.

20. Mehta A, Cohen SR, Chan LS. Palliative care: a need for a family systems approach. *Palliat Support Care*. 2009;7(2):235-43.
21. Wright LM LM. Nurses and families: A guide to family assessment and intervention. 5th ed Brantford: W Ross MacDonald School Resource Services Library. 2009.
22. Krikorian A, Limonero JT, Mate J. Suffering and distress at the end-of-life. *Psychooncology*. 2012;21(8):799-808.
23. Milberg A, Wahlberg R, Jakobsson M, Olsson EC, Olsson M, Friedrichsen M. What is a 'secure base' when death is approaching? A study applying attachment theory to adult patients' and family members' experiences of palliative home care. *Psychooncology*. 2012;21(8):886-95.
24. Rumpold T, Schur S, Amering M, Kirchheiner K, Masel EK, Watzke H, et al. Informal caregivers of advanced-stage cancer patients: Every second is at risk for psychiatric morbidity. *Support Care Cancer*. 2016;24(5):1975-82.
25. Grov EK, Dahl AA, Moum T, Fossa SD. Anxiety, depression, and quality of life in caregivers of patients with cancer in late palliative phase. *Ann Oncol*. 2005;16(7):1185-91.
26. Kissane DW, Bloch S, Dowe DL, Snyder RD, Onghena P, McKenzie DP, et al. The Melbourne Family Grief Study, I: Perceptions of family functioning in bereavement. *Am J Psychiatry*. 1996;153(5):650-8.
27. Kissane DW, McKenzie M, McKenzie DP, Forbes A, O'Neill I, Bloch S. Psychosocial morbidity associated with patterns of family functioning in palliative care: baseline data from the Family Focused Grief Therapy controlled trial. *Palliat Med*. 2003;17(6):527-37.
28. Siminoff LA, Wilson-Genderson M, Baker S, Jr. Depressive symptoms in lung cancer patients and their family caregivers and the influence of family environment. *Psychooncology*. 2010;19(12):1285-93.
29. Milberg A, Liljeroos M, Wahlberg R, Krevers B. Sense of support within the family: a cross-sectional study of family members in palliative home care. *BMC Palliat Care*. 2020;19(1):120.

30. Thompson T, Ketcher D, Gray TF, Kent EE. The Dyadic Cancer Outcomes Framework: A general framework of the effects of cancer on patients and informal caregivers. *Soc Sci Med*. 2021;287:114357.
31. Hartmann M, Bazner E, Wild B, Eisler I, Herzog W. Effects of interventions involving the family in the treatment of adult patients with chronic physical diseases: a meta-analysis. *Psychother Psychosom*. 2010;79(3):136-48.
32. Hu Y, Liu T, Li F. Association between dyadic interventions and outcomes in cancer patients: a meta-analysis. *Support Care Cancer*. 2019;27(3):745-61.
33. Meyers FJ, Carducci M, Loscalzo MJ, Linder J, Greasby T, Beckett LA. Effects of a problem-solving intervention (COPE) on quality of life for patients with advanced cancer on clinical trials and their caregivers: simultaneous care educational intervention (SCEI): linking palliation and clinical trials. *J Palliat Med*. 2011;14(4):465-73.
34. Titler MG, Visovatti MA, Shuman C, Ellis KR, Banerjee T, Dockham B, et al. Effectiveness of implementing a dyadic psychoeducational intervention for cancer patients and family caregivers. *Support Care Cancer*. 2017;25(11):3395-406.
35. Badr H, Bakhshaie J, Chhabria K. Dyadic Interventions for Cancer Survivors and Caregivers: State of the Science and New Directions. *Semin Oncol Nurs*. 2019;35(4):337-41.
36. Palliatief TNCCOI. Kwaliteitskader palliatieve zorg Nederland. 2017.
37. Addington-Hall JM, O'Callaghan AC. A comparison of the quality of care provided to cancer patients in the UK in the last three months of life in in-patient hospices compared with hospitals, from the perspective of bereaved relatives: results from a survey using the VOICES questionnaire. *Palliat Med*. 2009;23(3):190-7.
38. Morishita M, Kamibeppu K. Quality of life and satisfaction with care among family caregivers of patients with recurrent or metastasized digestive cancer requiring palliative care. *Support Care Cancer*. 2014;22(10):2687-96.

39. Lee YJ, Kim JE, Choi YS, Hwang IC, Hwang SW, Kim YS, et al. Quality of life discordance between terminal cancer patients and family caregivers: a multicenter study. *Support Care Cancer*. 2016;24(7):2853-60.
40. Miovic M, Block S. Psychiatric disorders in advanced cancer. *Cancer*. 2007;110(8):1665-76.
41. LeBlanc TW, McNeil MJ, Kamal AH, Currow DC, Abernethy AP. Polypharmacy in patients with advanced cancer and the role of medication discontinuation. *Lancet Oncol*. 2015;16(7):e333-41.
42. Sogaard M, Thomsen RW, Bossen KS, Sorensen HT, Norgaard M. The impact of comorbidity on cancer survival: a review. *Clin Epidemiol*. 2013;5(Suppl 1):3-29.
43. Dijkhoorn AQ, Brom L, van der Linden YM, Leget C, Raijmakers NJ. Prevalence of burnout in healthcare professionals providing palliative care and the effect of interventions to reduce symptoms: A systematic literature review. *Palliat Med*. 2021;35(1):6-26.
44. Engel M, van der Ark A, Tamerus R, van der Heide A. Quality of collaboration and information handovers in palliative care: a survey study on the perspectives of nurses in the Southwest Region of the Netherlands. *Eur J Public Health*. 2020;30(4):720-7.
45. Fibula. Netwerken Palliatieve Zorg. <https://www.stichtingfibula.nl/aandachtsgebieden/ondersteuning-samenwerkingsverbanden-palliatieve-zorg/netwerken-palliatieve-zorg>. Last accessed on 15 December 2021.
46. Given BA, Given CW, Sherwood P. The challenge of quality cancer care for family caregivers. *Semin Oncol Nurs*. 2012;28(4):205-12.
47. Gu X, Chen M, Liu M, Zhang Z, Cheng W. End-of-life decision-making of terminally ill cancer patients in a tertiary cancer center in Shanghai, China. *Support Care Cancer*. 2016;24(5):2209-15.
48. Roest B, Trappenburg M, Leget C. The involvement of family in the Dutch practice of euthanasia and physician assisted suicide: a systematic mixed studies review. *BMC Medical Ethics* 2019; 20 (23).
49. Voda AI, Bostan I. Public Health Care Financing and the Costs of Cancer Care: A Cross-National Analysis. *Cancers (Basel)*. 2018;10(4).

50. De Snoo-Trimp JC, Brom L, Pasman HR, Onwuteaka-Philipsen BD, Widdershoven GA. Perspectives of Medical Specialists on Sharing Decisions in Cancer Care: A Qualitative Study Concerning Chemotherapy Decisions With Patients With Recurrent Glioblastoma. *Oncologist*. 2015;20(10):1182-8.
51. Amalraj S, Starkweather C, Nguyen C, Naeim A. Health literacy, communication, and treatment decision-making in older cancer patients. *Oncology (Williston Park)*. 2009;23(4):369-75.
52. Palmer NR, Tooze JA, Turner AR, Xu J, Avis NE. African American prostate cancer survivors' treatment decision-making and quality of life. *Patient Educ Couns*. 2013;90(1):61-8.
53. Hauke D, Reiter-Theil S, Hoster E, Hiddemann W, Winkler EC. The role of relatives in decisions concerning life-prolonging treatment in patients with end-stage malignant disorders: informants, advocates or surrogate decision-makers? *Journal of Oncology Practice*; 22(12):2667-2674.
54. Zeliadt SB, Penson DF, Moinpour CM, Blough DK, Fedorenko CR, Hall IJ, et al. Provider and partner interactions in the treatment decision-making process for newly diagnosed localized prostate cancer. *BJU Int*. 2011;108(6):851-6; discussion 6-7.
55. Witkamp E, Droger M, Janssens R, van Zuylen L, van der Heide A. How to Deal With Relatives of Patients Dying in the Hospital? Qualitative Content Analysis of Relatives' Experiences. *Journal of Pain and Symptom Management*, 2016; 52(2):235-42.
56. Hibbard JH, Stockard J, Mahoney ER, Tusler M. Development of the Patient Activation Measure (PAM): conceptualizing and measuring activation in patients and consumers. *Health Serv Res*. 2004;39(4 Pt 1):1005-26.
57. Hamano J, Morita T, Fukui S, Kizawa Y, Tunetou S, Shima Y, et al. Trust in Physicians, Continuity and Coordination of Care, and Quality of Death in Patients with Advanced Cancer. *J Palliat Med*. 2017;20(11):1252-9.
58. Falzarano F, Prigerson HG, Maciejewski PK. The Role of Advance Care Planning in Cancer Patient and Caregiver Grief Resolution: Helpful or Harmful? *Cancers (Basel)*. 2021;13(8).

59. Dumont I, Dumont S, Mongeau S. End-of-life care and the grieving process: family caregivers who have experienced the loss of a terminal-phase cancer patient. *Qual Health Res.* 2008;18(8):1049-61.
60. Treml J, Schmidt V, Nagl M, Kersting A. Pre-loss grief and preparedness for death among caregivers of terminally ill cancer patients: A systematic review. *Soc Sci Med.* 2021;284:114240.
61. Cameron JI, Franche RL, Cheung AM, Stewart DE. Lifestyle interference and emotional distress in family caregivers of advanced cancer patients. *Cancer.* 2002;94(2):521-7.
62. Hudson PL, Aranda S, Kristjanson LJ. Meeting the supportive needs of family caregivers in palliative care: challenges for health professionals. *J Palliat Med.* 2004;7(1):19-25.
63. Dionne-Odom JN AA, Taylor RA, Wells RD, Hendricks BA, Bechthold AC, Reed RD, Harrell ER, Dosse CK, Engler S, McKie P, Ejem D, Bakitas MA & Rosenberg AR Resilience, preparedness, and distress among family caregivers of patients with advanced cancer. *Supportive Care in Cancer.* 2021;29:6913–20.
64. Palacio C, Krikorian A, Limonero JT. The influence of psychological factors on the burden of caregivers of patients with advanced cancer: Resiliency and caregiver burden. *Palliat Support Care.* 2018;16(3):269-77.
65. Sun H, Qin Y, Hengudomsub P. Factors associated with resilience in spousal caregivers of patients with cancer: An integrative review. *Nurs Open.* 2021;8(5):2131-41.
66. Beng TS, Chin LE, Guan NC, Yee A, Wu C, Pathmawathi S, et al. The experiences of stress of palliative care providers in Malaysia: a thematic analysis. *Am J Hosp Palliat Care.* 2015;32(1):15-28.
67. Sanso N, Galiana L, Oliver A, Pascual A, Sinclair S, Benito E. Palliative Care Professionals' Inner Life: Exploring the Relationships Among Awareness, Self-Care, and Compassion Satisfaction and Fatigue, Burnout, and Coping With Death. *J Pain Symptom Manage.* 2015;50(2):200-7.

68. Mills J, Wand T, Fraser JA. Self-Care in Palliative Care Nursing and Medical Professionals: A Cross-Sectional Survey. *J Palliat Med.* 2017;20(6):625-30.
69. Limardi S, Stievano A, Rocco G, Vellone E, Alvaro R. Caregiver resilience in palliative care: a research protocol. *J Adv Nurs.* 2016;72(2):421-33.
70. Heyland DK, Groll D, Rocker G, Dodek P, Gafni A, Tranmer J, et al. End-of-life care in acute care hospitals in Canada: a quality finish? *J Palliat Care.* 2005;21(3):142-50.
71. Dawson NJ. Need satisfaction in terminal care settings. *Soc Sci Med.* 1991;32(1):83-7.
72. Roen I, Stifoss-Hanssen H, Grande G, Brenne AT, Kaasa S, Sand K, et al. Resilience for family carers of advanced cancer patients-how can health care providers contribute? A qualitative interview study with carers. *Palliat Med.* 2018;32(8):1410-8.
73. Chen EK, Riffin C, Reid MC, Adelman R, Warmington M, Mehta SS, et al. Why is high-quality research on palliative care so hard to do? Barriers to improved research from a survey of palliative care researchers. *J Palliat Med.* 2014;17(7):782-7.
74. Moss AH, Lunney JR, Culp S, Auber M, Kurian S, Rogers J, et al. Prognostic significance of the "surprise" question in cancer patients. *J Palliat Med.* 2010;13(7):837-40.
75. Raijmakers NJH, Zijlstra M, van Roij J, Husson O, Oerlemans S, van de Poll-Franse LV. Health-related quality of life among cancer patients in their last year of life: results from the PROFILES registry. *Support Care Cancer.* 2018;26(10):3397-404.
76. Kars MC, van Thiel GJ, van der Graaf R, Moors M, de Graeff A, van Delden JJ. A systematic review of reasons for gatekeeping in palliative care research. *Palliat Med.* 2016;30(6):533-48.
77. Terry W, Olson LG, Ravenscroft P, Wilss L, Boulton-Lewis G. Hospice patients' views on research in palliative care. *Intern Med J.* 2006;36(7):406-13.
78. van Esch HJ, van Zuylen L, Geijteman ECT, Oomen-de Hoop E, Huisman BAA, Noordzij-Nooteboom HS, et al. Effect of Prophylactic

- Subcutaneous Scopolamine Butylbromide on Death Rattle in Patients at the End of Life: The SILENCE Randomized Clinical Trial. *JAMA*. 2021;326(13):1268-76.
79. Hudson P. The experience of research participation for family caregivers of palliative care cancer patients. *Int J Palliat Nurs*. 2003;9(3):120-3.
 80. Coebergh van den Braak RRJ, van Rijssen LB, van Kleef JJ, Vink GR, Berbee M, van Berge Henegouwen MI, et al. Nationwide comprehensive gastro-intestinal cancer cohorts: the 3P initiative. *Acta Oncol*. 2018;57(2):195-202.
 81. Ochoa CY, Buchanan Lunsford N, Lee Smith J. Impact of informal cancer caregiving across the cancer experience: A systematic literature review of quality of life. *Palliat Support Care*. 2020;18(2):220-40.
 82. Kristjanson LJ, Aoun S. Palliative care for families: remembering the hidden patients. *Can J Psychiatry*. 2004;49(6):359-65.
 83. van der Velden A EY, Nanninga M, Francke A, Fritsma J, Boddaert M, Krabbe P, van der Heide A, Reyners A. What Matters Most for the Dutch Public in Palliative Care: A Survey. *Journal of Pain and Symptom Management* (Abstract only) DOI:<https://doi.org/10.1016/j.jpainsymman.2018.10.358>. 2018;56(6).
 84. Collins A, McLachlan SA, Philip J. Community knowledge of and attitudes to palliative care: A descriptive study. *Palliat Med*. 2020;34(2):245-52.
 85. Hudson P, Collins A, Boughey M, Philip J. Reframing palliative care to improve the quality of life of people diagnosed with a serious illness. *Med J Aust*. 2021;215(10):443-6.
 86. Oechsle K. Current Advances in Palliative & Hospice Care: Problems and Needs of Relatives and Family Caregivers During Palliative and Hospice Care-An Overview of Current Literature. *Med Sci (Basel)*. 2019;7(3).
 87. Sklenarova H, Krumpelmann A, Haun MW, Friederich HC, Huber J, Thomas M, et al. When do we need to care about the caregiver? Supportive care needs, anxiety, and depression among informal

caregivers of patients with cancer and cancer survivors. *Cancer*. 2015;121(9):1513-9.

88. Doubova SV, Aguirre-Hernandez R, Infante-Castaneda C, Martinez-Vega I, Perez-Cuevas R. Needs of caregivers of cancer patients: validation of the Mexican version of the Support Person Unmet Needs Survey (SPUNS-SFM). *Support Care Cancer*. 2015;23(10):2925-35.
89. van Ryn M, Sanders S, Kahn K, van Houtven C, Griffin JM, Martin M, et al. Objective burden, resources, and other stressors among informal cancer caregivers: a hidden quality issue? *Psychooncology*. 2011;20(1):44-52.
90. Osse BH, Vernooij-Dassen MJ, Schade E, Grol RP. Problems experienced by the informal caregivers of cancer patients and their needs for support. *Cancer Nurs*. 2006;29(5):378-88; quiz 89-90.
91. (NZA) NZ. Registreren en declareren van behandelingen. Last accessed 1 December 2021. <https://www.nza.nl/zorgsectoren/medisch-specialistische-zorg/registreren-en-declareren-van-behandelingen>
92. Hjorth NE, Hufthammer KO, Sigurdardottir K, Tripodoro VA, Goldraij G, Kvikstad A, et al. Hospital care for the dying patient with cancer: does an advance care planning invitation influence bereaved relatives' experiences? A two country survey. *BMJ Support Palliat Care*. 2021.
93. J O. Tussenland: Over leven met de dood in je schoenen. Uitgeverij de Graaff, 2021.
94. Hasson F, Nicholson E, Muldrew D, Bamidele O, Payne S, McIlpatrick S. International palliative care research priorities: A systematic review. *BMC Palliat Care*. 2020;19(1):16.
95. Ferrell B GM. Quality of life family version (QOLFV). National Medical Center And Beckman Research Institute. 2005.
96. WHO. Leading cause of death. <http://www.who.int/mediacentre/factsheets/fs297/en/> Last accessed 4 August 2020.

97. SONCOS. Normeringsrapport 2021.
<https://www.soncos.org/kwaliteit/normeringsrapport/> Last accessed
23 December 2021.

CHAPTER 11

Summary

(in English and Dutch)

Summary

Chapter 1 provides an overview of current palliative oncology care practice and its challenges. Palliative care improves quality of life (QoL) but often its provision is too little and too late for patients with advanced cancer and their relatives. Fortunately, (inter)national guidelines have been developed to further improve the integration of palliative care in oncological care. Previous studies on palliative care often focus on patients with advanced cancer or on their relatives, separately. Yet little is known about the interdependence between patients with advanced cancer and their relatives regarding their care experiences and QoL. Patients and their relatives coping with advanced cancer face many challenges together and we need to further unravel their interdependence in order to provide optimal palliative care.

The central goal of this thesis is to gain a better understanding of the experiences of patients with advanced cancer and that of their relatives in the Netherlands and their interdependent relationship regarding quality of care and QoL. The three aims are:

1. To explore care experiences and QoL of patients with advanced cancer and that of their relatives.
2. To assess the interdependent relationship between patients' and relatives' care experiences and QoL.
3. To assess relational aspects of couples coping with advanced cancer.

Part 1: Quality of care and life concept inventory

Chapter 2 shows that the social consequences of advanced cancer for patients and their relatives are significant. We conducted a qualitative focus group study in which 18 patients and 15 of their relatives mentioned

three major consequences in their social lives due to advanced cancer. The first theme was social engagement: patients and relatives experienced many barriers in continuing life as it has been prior to the diagnosis. The second theme was social identity: patients and their relatives experienced feelings of isolation and felt that others identified them with their cancer. The third theme was social network: patients and their relatives experienced positive and negative changes in their network, such as an increase or decrease in the number of social relations, more clarity regarding the value of their social relations, and a change in value of certain social relationships.

Chapter 3 provides an overview of the aspects of care that are essential to patients with advanced cancer and their relatives. We conducted a qualitative focus group study and found that there were similar essential aspects of care mentioned by patients (n=18) and their relatives (n=15). Two main themes arose from the data of which the first was 'relation'. Patients and relatives found it essential that health care professionals were personally engaged and provided support and compassion. The second theme was 'organization of care' because patients and relatives found it important that the coordination, continuity, and logistical organization of care was tailored to their needs and personal situation.

Chapter 4 includes the results of a systematic literature review on measurement instruments for QoL used in patients with advanced cancer. Sixty-nine articles relating to 39 measurement instruments were included. Results showed that validation research of QoL measurement instruments in this population is incomplete and none of the instruments included in our systematic literature review performed sufficiently on all measurement properties. Based on the studies included we concluded that the EORTC QLQ-C15-PAL and the EORTC QLQ-BM22 had adequate measurement properties to measure QoL in patients with advanced cancer.

Part 2: Assessing quality of life and care experiences

Chapter 5 presents the study protocol of the eQuiPe study. This prospective longitudinal multicenter observational study assesses the experienced quality of care and QoL in patients with advanced cancer and their relatives in the Netherlands. For this study we collaborated with more than 40 hospitals in the Netherlands. Between November 2017 and March 2020 patients with advanced cancer (having metastases from (a solid) cancer) were asked to participate in the study by their treating physician. Patients identified relatives who were also willing to participate in the study. After giving informed consent, patients and relatives received questionnaires regarding their experienced quality of care and QoL every three months until death. In this thesis we have used the baseline questionnaires of both patients and relatives who participated in the eQuiPe study.

Chapter 6 describes the experiences with regard to health care and QoL in patients with advanced cancer and their relatives who participated in the eQuiPe study, a prospective multicenter observational study. The QoL scores of the 1,103 participating patients were much lower compared to a gender and age matched normative population, respectively 78 vs 87 for emotional functioning ($p < .001$). In total, also 831 relatives were included. Relatives experienced even lower emotional functioning compared to patients, respectively 69 vs 78 ($p < .001$), and were also less satisfied with care compared to patients, respectively 74.4 vs 58.7 ($p < .001$). Being more satisfied with care in general (OR=1.13 (95%CI:1.00-1.27), $p < .05$) and feeling clarity about who their central health-care professional is (OR=3.16 (95%CI:1.14-8.75), $p < .05$) was positively associated with high emotional functioning in patients. Experienced continuity of care (OR=1.10 (95%CI:1.03-1.18), $p < .01$) and information for the patient (OR=1.08 (95%CI:1.01-1.15), $p < .05$) was positively associated

with high emotional functioning in relatives. Results also showed that high emotional functioning in patients was positively associated with the emotional functioning of relatives and vice versa ($p < .001$). Finally, how relatives perceive continuity of care for the patient was of importance for the patients' ($OR = 1.13$ (95%CI:1.04-1.23), $p < .01$) and their own ($OR = 1.07$ (95%CI:1.00-1.15), $p < .05$) emotional functioning.

Chapter 7 describes the caregiver burden of relatives of patients with advanced cancer. Most of the relatives who participated in this study were the patient's partner (78%, $n = 746$). Fifty-four percent of the relatives reported that they were an informal caregiver of the patient and the median hours of caregiving a week was 15. Most relatives of patients with advanced cancer experienced moderate caregiver burden and 11% of the relatives experienced high caregiver burden. Results of this study also show that relatives of patients with advanced cancer engaged less in self-care activities and were less resilient compared to the general population ($p < .001$). Relatives with a high caregiver burden were younger ($OR = .96$), highly educated ($OR = 2.08$), often reported to be an informal caregiver of the patient ($OR = 2.24$), and less well informed about the importance of self-care ($OR = .39$) compared to relatives with low/medium caregiver burden. Moreover, engaging in self-care activities ($OR = .87$) and being resilient ($OR = .76$) were associated with lower caregiver burden.

Part 3: A dyadic perspective among couples

Chapter 8 gives an overview of how 566 couples cope with advanced cancer together (dyadic coping). Patients with advanced cancer and their partners had normal joint dyadic coping efforts (i.e., efforts regarding stress communication and coping with stress together). Patients and their partners most often used negative dyadic coping (i.e., hostile, ambivalent or superficial responses) and least often use common dyadic coping (i.e.,

working together to handle stress). There was a small to moderate interdependence between the perspectives of patients and partners regarding their dyadic coping efforts (.27-.56). Patients were more satisfied with their coping as a couple (86 and 79 respectively, $p < .001$) compared to partners, but their satisfaction was less strongly associated with their own emotional functioning ($B = .40$ and $B = .03$ respectively, $p < .001$). Satisfaction with dyadic coping of the other person was more strongly associated with higher emotional functioning of patients than with higher emotional functioning of partners ($B = .23$ and $B = .02$, $p = .04$). Negative dyadic coping in both patients and partners was associated with their own emotional functioning ($B = .37$ and $B = .13$, $p = .04$) and the emotional functioning of the other person (both $B = .17$, $p < .05$). Supportive dyadic coping as perceived by the partner was negatively associated with their own emotional functioning ($B = -.34$, $p = .003$) and with the emotional functioning of the patient ($B = -.31$, $p = .03$).

Chapter 9 shows that, among 566 couples, more than half of all patients with advanced cancer and their partners were interested in sex (especially male partners), although more than half of the patients and partners were not sexually active. Furthermore, the majority of female patients (56%) felt less sexually attractive due to their illness or its treatment. Between 25 and 29% of patients and partners were not satisfied with their sex life and only one third of these experienced unmet care needs regarding their sexual health or relationship. However, only a few patients and partners (<10%) had contacted a sexologist or psychologist. Fortunately, most patients and partners felt close to their significant other in the relationship with patients reporting somewhat higher scores on 'feelings close' compared to their partners (92 and 88 respectively, $p < .001$). Satisfaction with sex life of both partners appeared to be positively associated with their own feelings of closeness in their partnered relationship and the

effect was stronger for partners ($B=.15$ and $B=.03$ respectively, $p<.001$). Sexual satisfaction of the other person was also related to their own feelings of closeness ($B=.05$, $p=.003$), irrespective of role (i.e. being a patient or partner) or gender.

Chapter 10 contains the general discussion of the key findings of this thesis, the methodological considerations, future directions for research and implications for clinical practice. We emphasize that a family approach in palliative oncology care for patients with advanced cancer and their relatives may have great potential to promote, on the one hand, greater attention devoted to the wellbeing of relatives and, on the other hand, to further improve the patient's wellbeing. Such a family approach may also lead to increased involvement of relatives in the care of patients with advanced cancer in order to improve continuity of care which is highly important for both patients and relatives. The care experiences and the QoL of patients with advanced cancer and their relatives are interdependent: taking this 'ripple effect' into account may ultimately further optimize palliative oncology care.

Samenvatting

Hoofdstuk 1 geeft een inleiding in de huidige praktijk van palliatieve zorg en de uitdagingen daarbij. Palliatieve zorg verbetert de kwaliteit van leven, vermindert de symptoomlast en zorgt voor minder ongewenste zorg in de laatste levensfase. Ondanks deze positieve effecten wordt palliatieve zorg vaak te weinig en te laat verleend aan patiënten met gevorderde kanker en hun naasten. Gelukkig zijn er (inter)nationale richtlijnen ontwikkeld om de integratie van palliatieve zorg in de oncologische zorg verder te verbeteren. Patiënten en hun naasten die te maken hebben met gevorderde kanker staan samen voor vele uitdagingen. Eerdere studies naar palliatieve zorg richtten zich vaak op patiënten met gevorderde kanker of op naasten. Er is weinig bekend over de onderlinge afhankelijkheid tussen patiënten met gevorderde kanker en hun naasten met betrekking tot hun zorgervaringen en kwaliteit van leven. Het onderzoeken van de onderlinge afhankelijkheid van de ervaringen van patiënten én naasten is nodig om aanknopingspunten te vinden om de zorg beter te laten sluiten op hun beider ervaringen en behoeften. Daarom is het doel van dit proefschrift om meer inzicht te krijgen in de ervaringen van patiënten met gevorderde kanker én hun naasten met betrekking tot kwaliteit van zorg, kwaliteit van leven en hun onderlinge afhankelijkheid. De drie doelen zijn:

1. Het onderzoeken van zorgervaringen en kwaliteit van leven van patiënten met gevorderde kanker en hun naasten.
2. Het analyseren van de onderlinge relatie tussen zorgervaringen en kwaliteit van leven van patiënten met gevorderde kanker en hun naasten.
3. Het analyseren van relationele aspecten van patiënt-partnerkoppels die geconfronteerd zijn met gevorderde kanker.

Deel 1: Kwaliteit van zorg en leven: concept inventarisatie

In **hoofdstuk 2** laten we zien dat de sociale gevolgen van gevorderde kanker groot zijn voor zowel patiënten als hun naasten. In onze kwalitatieve focusgroep studie benoemden 18 patiënten met gevorderde kanker en 15 naasten drie belangrijke thema's met betrekking tot de gevolgen van gevorderde kanker voor hun sociale leven. Het eerste thema was sociale betrokkenheid: patiënten en naasten ervoeren veel belemmeringen in het voortzetten van het leven zoals voorafgaand aan de diagnose van gevorderde kanker. Het tweede thema was sociale identiteit: patiënten en hun naasten ervoeren gevoelens van isolatie en hadden het gevoel dat anderen hen vooral identificeerden met hun kanker. Het derde thema was sociaal netwerk: patiënten en hun naasten ervoeren positieve en negatieve veranderingen in hun sociale netwerk. Voorbeelden hiervan waren een toename of afname van het aantal sociale relaties, meer duidelijkheid over de waarde van hun sociale relaties en een veranderende waarde van bepaalde sociale relaties.

De uitkomsten van een kwalitatieve focusgroep studie onder 18 patiënten met gevorderde kanker en 15 naasten naar zorgaspecten die essentieel zijn voor hen worden beschreven in **hoofdstuk 3**. Patiënten en naasten benoemden los van elkaar veel dezelfde essentiële aspecten van zorg: Uit de focusgroepen kwamen twee hoofdthema's naar voren, waarvan het eerste 'relatie' was. Patiënten en hun naasten vonden het beiden essentieel dat zorgverleners persoonlijk betrokken zijn, steun bieden en compassie hebben. Het tweede thema was 'organisatie van zorg'. Patiënten en hun naasten vonden het belangrijk dat de coördinatie, continuïteit en logistieke organisatie van de zorg zijn afgestemd op hun behoeften en persoonlijke situatie.

Hoofdstuk 4 bevat de resultaten van een systematisch literatuuronderzoek naar instrumenten om de kwaliteit van leven te meten bij patiënten met gevorderde kanker. In deze review werden 69 studies opgenomen die de psychometrie onderzochten van 39 meetinstrumenten voor kwaliteit van leven. Deze studies werden aan de hand van de COSMIN-checklist beoordeeld op verschillende kwaliteitscriteria zoals interne consistentie, betrouwbaarheid, meetfout, verschillende vormen van validiteit en responsiviteit. De resultaten laten zien dat psychometrisch onderzoek in deze populatie onvolledig is. De geïnccludeerde studies bevatten onvoldoende informatie over alle psychometrische eigenschappen van de meetinstrumenten. Op basis van de beschikbare informatie hebben we geconcludeerd dat de EORTC QLQ-C15-PAL en de EORTC QLQ-BM22 adequate psychometrische eigenschappen hebben om kwaliteit van leven te meten bij patiënten met gevorderde kanker.

Deel 2: Beoordeling van kwaliteit van leven en zorgervaringen

We beschrijven in **hoofdstuk 5** het studieprotocol van de eQuiPe-studie. Deze observationele, prospectieve longitudinale studie onderzoekt de ervaren kwaliteit van zorg en leven bij patiënten met gevorderde kanker en hun naasten in Nederland. Voor deze studie werken we samen met 40 ziekenhuizen in Nederland. Tussen november 2017 en maart 2020 werden patiënten met gevorderde kanker (uitgezaaide kanker) door hun behandelend arts gevraagd om deel te nemen aan de studie. Patiënten werden gevraagd of een naaste van hen ook bereid was om deel te nemen aan de studie. Patiënten konden meerdere van hun naasten vragen om deel te nemen aan de studie. Na het geven van schriftelijke toestemming ontvingen patiënten en naasten elke drie maanden een vragenlijst over hun ervaren kwaliteit van zorg en leven tot het moment van overlijden van de patiënt.

In **hoofdstuk 6** maakten we gebruik van de vragenlijsten die 1103 patiënten en 831 naasten invulden op het eerste meetmoment (baseline) van de eQuiPe studie en beschrijven we hun ervaringen met betrekking tot de ervaren zorg en kwaliteit van leven. Patiënten hadden een lagere kwaliteit van leven dan mannen en vrouwen met een zelfde leeftijd in de algemene bevolking, namelijk 78 vs. 87 voor emotioneel functioneren ($p < .001$). Naasten hadden een nog minder goed emotioneel functioneren in vergelijking met de patiënten (69; $p < .001$) en waren ook minder tevreden met de zorg dan patiënten (59 vs 74; $p < .001$). Meer tevreden zijn met de zorg in het algemeen ($OR = 1.13$ (95%CI:1.00-1.27)) en duidelijkheid voelen over wie de centrale zorgverlener is ($OR = 3.16$ (95%CI:1.14-8.75)) was positief geassocieerd met een hoog emotioneel functioneren bij patiënten. Ervaren continuïteit van zorg ($OR = 1.10$; 95%CI:1.03-1.18)) en continuïteit van informatie over zorg voor de patiënt ($OR = 1.08$; 95%CI:1.01-1.15)) was positief geassocieerd met een hoog emotioneel functioneren bij naasten. De resultaten toonden ook aan dat het emotioneel functioneren van patiënten positief geassocieerd was met het emotioneel functioneren van naasten en vice versa ($p < .001$). Tenslotte was hoe naasten continuïteit van zorg voor de patiënt ervoeren positief geassocieerd met het emotioneel functioneren van de patiënt ($OR = 1.13$ (95%CI:1.04-1.23)) en van henzelf ($OR = 1.07$ (95%CI:1.00-1.15)).

De zorglast (de last voortkomend uit zorgen voor de patiënt) van naasten van patiënten met gevorderde kanker wordt in **hoofdstuk 7** beschreven. Er is één naaste per patiënt random geselecteerd, resulterend in 746 naasten. De meeste naasten waren de partner van de patiënt (78%), de overige naasten waren kinderen, andere familieleden of een goede vriend(in). Ruim de helft (54%) van de naasten was mantelzorger van de patiënt en besteedde 15 uur per week aan mantelzorg (mediaan). Elf procent van de naasten ervoer een hoge zorglast, 31% ervoer een matige

zorglast en 54% ervoer een lage zorglast. Naasten van patiënten met gevorderde kanker ondernamen minder zelfzorgactiviteiten en waren minder veerkrachtig dan mannen en vrouwen met een zelfde leeftijd in de algemene bevolking ($p < .001$). Naasten met een hoge mantelzorglast waren jonger (OR = .96, 95%CI .95-.99), hoger opgeleid (OR = 2.08, 95%CI 1.00–4.32), beschouwden zichzelf vaker een mantelzorger van de patiënt (OR = 2.24, 95%CI 1.28-3.93), en waren minder goed geïnformeerd over het belang van zelfzorg (OR = .39, 95%CI 0.21-0.73) in vergelijking met naasten met een lagere zorglast. Bovendien hing het doen van zelfzorgactiviteiten (OR = .87, 95%CI 0.82-0.92) en veerkrachtig zijn (OR = .76, 95%CI 0.65-0.89) samen met minder zorglast.

Deel 3: Een dyadisch perspectief bij patiënt-partnerkoppels

In **hoofdstuk 8** geven we een overzicht van hoe patiënt-partnerkoppels ($n=566$) samen omgaan met gevorderde kanker (dyadische coping). Patiënten met gevorderde kanker en hun partners hadden volgens afkapwaarden van de vragenlijst over dyadische coping normale gezamenlijke dyadische coping inspanningen (inspanningen met betrekking tot stresscommunicatie en het samen omgaan met stress). Patiënten en hun partners gebruikten het vaakst negatieve dyadische coping (d.w.z. vijandige, ambivalente of oppervlakkige reacties) (gemiddelde score respectievelijk 88 en 86) en het minst vaak gemeenschappelijke dyadische coping (samenwerken om stress te hanteren) (gemiddelde score voor zowel patiënten en partners was 66). De samenhang tussen het perspectief van patiënten en partners over hun dyadische coping was klein tot gemiddeld (.27-.56). Patiënten waren meer tevreden over hun coping als koppel (respectievelijk 86 en 79, $p < .001$) dan hun partners, maar hun tevredenheid was minder sterk geassocieerd met hun eigen emotioneel functioneren ($B = .40$ en $B = .03$ respectievelijk, $p < .001$). Tevredenheid van de ander over dyadische

coping was positief sterker geassocieerd met het emotioneel functioneren van patiënten dan dat van partners ($B=.23$ en $B=.02$, $p=.04$). We vonden ook positieve associaties tussen negatieve dyadische coping van patiënten en partners op het emotioneel functioneren van hunzelf ($B=.37$ en $B=.13$, $p=.04$) en van de ander (beide $B=.17$, $p<.05$). Steunende dyadische coping zoals ervaren door de partner was negatief geassocieerd met hun eigen emotioneel functioneren ($B=-.34$, $p=.003$) en met het emotioneel functioneren van de patiënt ($B=-.31$, $p=.03$).

Uit **hoofdstuk 9** blijkt dat onder patiënt-partnerkoppels ($n=566$) meer dan de helft van alle patiënten met gevorderde kanker en hun partners geïnteresseerd was in seks (vooral mannelijke partners), hoewel meer dan de helft van de patiënten en partners niet seksueel actief was. De meerderheid van de vrouwelijke patiënten (56%) voelde zich minder seksueel aantrekkelijk als gevolg van hun ziekte of de behandeling ervan. Tussen 25-29% van zowel patiënten als partners was niet tevreden met hun seksleven en een derde ervoer onvervulde zorgbehoeften met betrekking tot hun seksuele gezondheid of relatie. Minder dan 10% van alle patiënten en partners rapporteerde dat zij contact hadden opgenomen met een seksuoloog of psycholoog. De meeste patiënten en partners voelden zich nauw verbonden met elkaar, waarbij patiënten hogere scores voor verbondenheid rapporteerden dan hun partners (respectievelijk 92 vs. 88, $p<.001$). Tevredenheid over het seksleven van beide partners hing positief samen met eigen gevoelens van verbondenheid in hun partnerrelatie en deze relatie was sterker in partners dan in patiënten, respectievelijk $\beta=0.15$ en $\beta=0.03$ (beide $p<.001$). Tevredenheid over het seksleven van de ander hing ook samen met eigen gevoelens van verbondenheid ($\beta=.05$, $p=.003$), ongeacht rol (d.w.z. patiënt of partner zijn) of geslacht.

Hoofdstuk 10 bevat de belangrijkste bevindingen van dit proefschrift, de methodologische overwegingen van de verschillende studies, suggesties voor toekomstig onderzoek en implicaties voor de klinische praktijk. We benadrukken hierin dat een familiebenadering in de palliatieve oncologische zorg voor patiënten met gevorderde kanker en hun naasten grote potentie heeft om enerzijds het welzijn van de patiënt verder te verbeteren en anderzijds de aandacht voor het welzijn van naasten te bevorderen. Een dergelijke familiebenadering kan ook leiden tot meer betrokkenheid van naasten bij de zorg voor patiënten met gevorderde kanker. Dit kan bijdragen aan betere continuïteit van zorg, wat weer van groot belang is voor zowel patiënten als hun naasten. De zorgervaringen en de kwaliteit van leven van patiënten met gevorderde kanker en hun naasten zijn wederzijds van elkaar afhankelijk. Door rekening te houden met dit sociale 'rimpeleffect' kan de palliatieve oncologische zorg verder worden verbeterd.

"I alone cannot change the world, but I can cast a stone across the waters to create many ripples."

- Mother Teresa

APPENDICES

Words of Appreciation

List of Publications

About the Author

Words of Appreciation

eQuiPe is Frans voor 'team'. Een passende naam, want dit onderzoek was er niet geweest zonder de inzet van vele betrokkenen. Van patiënten en naasten tot artsen, verpleegkundigen en onderzoekers: iedereen werkte samen. Samen zorgden we dat de eQuiPe studie niet alleen een succes werd, maar ook tot vele nieuwe initiatieven leidde die bijdragen aan integratieve palliatieve zorg voor patiënten en naasten.

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List of Publications

This Thesis

van Roij, Fransen, van de Poll-Franse, Zijlstra, Raijmakers. Measuring health-related quality of life in patients with advanced cancer: a systematic review of self-administered measurement instruments. *Quality of Life Research*, 2018.

van Roij, Brom, Youssef-El Soud, van de Poll-Franse, Raijmakers. Social consequences of advanced cancer in patients and their informal caregivers: a qualitative study. *Supportive Care in Cancer*, 2018.

van Roij, Zijlstra, Ham, Brom, Fransen, Vreugdenhil, Raijmakers, van de Poll-Franse. Prospective cohort study of patients with advanced cancer and their relatives on the experienced quality of care and life (eQuiPe study): a study protocol. *BMC Palliative Care*, 2020.

van Roij, de Zeeuw, Zijlstra, Claessens, Raijmakers, van de Poll-Franse, Brom. Shared Perspectives of Patients With Advanced Cancer and Their Informal Caregivers on Essential Aspects of Health Care: A Qualitative Study. *Journal of Palliative Care*, 2021.

van Roij, Brom, Sommeijer, van de Poll Franse, Raijmakers. Self care, resilience, and caregiver burden in relatives of patients with advanced cancer: results from the eQuiPe study. *Supportive Care in Cancer*, 2021.

van Roij, Raijmakers, Ham, van den Beuken-van Everdingen, van den Borne, Creemers, Hunting, Kuip, van Leeuwen, van Laarhoven, Mandigers, Nieboer, van der Velden, van Zuylen, Gelissen, Zijlstra, Brom, Fransen, van de Poll-Franse. Quality of life and quality of care as experienced by patients with advanced cancer

and their relatives: a multicenter observational cohort study (eQuiPe). *European Journal of Cancer*, 2022.

van Rooij, Raijmakers, Johnsen, Bang Hansen, Thijs-Visser, van de Poll-Franse. Sexual health and closeness in couples coping with advanced cancer: Results of a multicenter observational study (eQuiPe). *Palliative Medicine*, 2022.

van Rooij, Raijmakers, Kloover, Kuip, Smilde, van der Velden, Rodin, van de Poll-Franse L. Dyadic coping and its association with emotional functioning in couples confronted with advanced cancer: Results of the multicenter observational eQuiPe study (submitted).

Other Publications

Raijmakers, Zijlstra, van Rooij, Husson, Oerlemans, van de Poll-Franse. Health-related quality of life among cancer patients in their last year of life: results from the PROFILES registry. *Supportive Care in Cancer*, 2018.

de Rooij, Thong, van Rooij, Bonhof, Husson, Ezendam. Optimistic, realistic and pessimistic illness perceptions, quality of life and survival among 2,457 cancer survivors - the population-based PROFILES registry. *Cancer*, 2018.

Kroon, van Rooij, Korfage, Reyners, van den Beuken-van Everdingen, den Boer, Creemers, de Graeff, Hendiks, Hunting, de Jong, Kuip, van Laarhoven, van Leeuwen, van Lindert, Mandigers, Nieboer, van der Padt-Pruijsten, Smilde, Sommeijer, Thijs, Tiemessen, Vos, Vreugdenhil, Werner, van Zuylen, van de Poll-Franse, Raijmakers. Perceptions of involvement in advance care planning

and emotional functioning in patients with advanced cancer.
Journal of Cancer Survivorship, 2020.

van Roij, Kieffer, van de Poll-Franse, Husson, Raijmakers, Gelissen.
Assessing measurement invariance in the EORTC QLQ-C30.
Quality of Life Research, 2021.

Damen, Visser, van Laarhoven, Leget, Raijmakers, van Roij, Fitchett.
Validation of the FACIT-Sp-12 in a Dutch cohort of patients with
advanced cancer. Psycho-Oncology, 2021.

Damen, Raijmakers, van Roij, Visser, van den Beuken-Everdingen, Kuip,
van Laarhoven, van Leeuwen-Snoeks, van der Padt-Pruijsten,
Smilde, Leget, Fitchett. Spiritual well-being and associated
factors in Dutch patients with advanced cancer. Journal of Pain
and Symptom management, 2021.

Ham, Fransen, van den Borne, Hendriks, van Laarhoven, van der Padt-
Pruijsten, Raijmakers, van Roij, Sommeijer, Vriens, van Zuylen,
van de Poll – Franse. Bereaved relatives' quality of life before
and during the COVID-19 pandemic: Results of the prospective,
multicenter, observational eQuiPe study. Palliative Medicine,
2021.

About the Author

Janneke van Roij was born on 12 October 1984 in Tilburg, the Netherlands. After graduating preuniversity education at the Paulus Lyceum in Tilburg in 2002, she did a bachelor Human Resource Management at Fontys applied university in Tilburg, the Netherlands. After graduating her bachelor's degree in 2010, she started a bachelor Psychology at Tilburg University, the Netherlands.



She graduated Cum Laude in 2013. She then followed a two-year master program in Medical psychology with a clinical internship at Elisabeth-TweeSteden hospital in Tilburg. In 2016, she completed her master with distinction and also completed most courses from the Research Master Social and Behavioral Sciences at Tilburg University. Subsequently, she started her PhD research at the Netherlands Comprehensive Cancer Organisation (IKNL). Her research focused on care experiences and quality of life of patients with advanced cancer and their relatives. As part of her PhD training, she did a two month research internship at Bispebjerg Hospital in Copenhagen, Denmark. Currently, she is working as a psychologist and has the ambition to further pursue a career in research.

