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Support and wellbeing for people with serious illness and their family caregivers

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“The closest thing to being cared for is to care for someone else.”

- Carson McCullers

Table of contents

Chapters II - VI are based on the following publications:

Chapter II

Matthys, O., Dierickx, S., Deliens, L., Lapeire, L., Hudson, P., Van Audenhove, C., De Vleminck, A., & Cohen, J. (2022). How are family caregivers of people with a serious illness supported by healthcare professionals in their caregiving tasks? A cross-sectional survey of bereaved family caregivers. *Palliative medicine*, *36(3),* 529–539. https://doi.org/10.1177/02692163211070228

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Chapter IV

Matthys, O., De Vleminck, A., Dierickx, S., Deliens, L., Van Goethem, V., Lapeire, L., Groenvold, M., Lund, L., Arnfeldt, C. M., Sengeloev, L., Pappot, H., Johnsen, A. T., Guerin, S., Larkin, P. J., Jordan, C., Connolly, M., D'Alton, P., Costantini, M., Di Leo, S., Guberti, M., … Cohen, J. (2021). Effectiveness of a nurse-delivered (FOCUS+) and a web-based (iFOCUS) psychoeducational intervention for people with advanced cancer and their family caregivers (DIAdIC): study protocol for an international randomized controlled trial. *BMC palliative care*, *20*(1), 193. https://doi.org/10.1186/s12904-021-00895-z

Chapter V

Matthys, O., Dierickx, S., Van Goethem, V., Deliens, L., Lapeire, L., De Pauw, A., Hudson, P., Vulsteke, C., Geboes, K., De Waele, S., Spoormans, I., Di Leo, S., Guberti, M., Schmidt, U. S., Scott, D., Harding, R., Witkamp, E., Connolly, M., DIAdIC team, De Vleminck, A., Cohen, J. Sexual satisfaction and its predictors in patients with advanced cancer and their family caregivers in six European countries: Baseline data from the DIAdIC study (Submitted - Minor revisions).

Chapter VI

Matthys, O., Turola, E., Dierickx, S., Dombrecht, L., Van Goethem, V., Deliens, L., Lapeire, L., Hudson, P., Eecloo, K., Brazil, K., Groenvold, M., Di Leo, S., van der Heide, A., Normand, C., Harding, R., Pilch, M., Northouse, L., DIAdIC team, De Vleminck, A., Cohen, J. The DIADIC advanced cancer psychoeducational intervention RCT: impact on emotional function and self-efficacy (ready for submission).

List of abbreviations

ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
CASE	Cancer Self-efficacy Scale
CCM	Communal Coping Model
CI	Confidence Interval
CONSORT	Consolidated Standards of Reporting Trials
COPD	Chronic Obstructive Pulmonary Disease
CQOLC	Caregiver Quality of Life Index-Cancer
DIAdIC	Dyadic Interventions for people with Advanced cancer and their Informal Caregiver
DCCM	Developmental-Contextual Coping Model
EORTC	European Organisation for Research and Treatment of Cancer
EORTC QLQ-C15-PAL	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 15 Palliative Care
EORTC QLQ-C30	European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire
EF10	Emotional functioning short form
FACT-G	Functional Assessment or Cancer Therapy-General
FCS	Fully Conditional Specification
FS	Fixed Sequence
GDPR	General Data Protection Regulation
GP	General practitioner
ITT	Intention-To-Treat
MANCOVA	Multivariate Analysis of Covariance
MNCAR	Missing Not Completely at Random
NA	Negative Affect
NPT	Normalization Process Theory
PA	Positive Affect
PANAS	Positive and Negative Affect Schedule
PIPFLA	Participatory and Iterative Process Framework for Language Adaptation
PP	Per-Protocol
QoL	Quality of Life
RA	Research Assistant
RCCM	Relational-Cultural Coping Model
RFM	Relationship-Focused model
RCT	Randomized Controlled Trial
SD	Standard Deviation
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
SPSS	Statistical Package for the Social Sciences
STM	Systemic-Transactional Model
STROBE	Strengthening of the Reporting of Observational studies in Epidemiology
TIDieR	Template for Intervention Description and Replication
WHO	World Health Organisation

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Chapter I
General introduction

Introduction

Receiving a cancer diagnosis can bring about many different emotions such as shock, disbelief, anxiety, and depression, making it challenging to go about everyday tasks. The symptoms of advanced cancer can greatly impact the patient's quality of life[1]. But when someone is diagnosed with advanced cancer, it's not just their own life that is affected, but also the lives of those closest to them, especially family caregivers. Family caregivers often describe cancer as an emotionally and physically demanding condition[2,3]. The interrelatedness between the patient and their family caregiver creates a dynamic where the wellbeing of each person is intricately linked to the other, where each person affects the other[4].

Individuals who are in the advanced stage of cancer and their family caregivers often have many psychosocial needs that remain unmet[5–10]. Due to advancements in medical treatments for cancer[11], causing people to live longer with the illness, there is a growing need for supportive care to address the specific needs of this population. Programs or interventions that address these needs (e.g. by providing information, skills and support) can alleviate the burden they face when dealing with advanced cancer, and enhance the quality of life for both patients and family caregivers[12–14].

The present doctoral thesis zooms in on the challenges a serious illness such as advanced cancer imposes on patients and their family caregivers, as well as the support that is available for them that can address these challenges.

Context to some concepts

In this dissertation, there are three recurring concepts that require clarification and interpretation within the specific context of this thesis. These are discussed below.

Family caregiver

A family caregiver is any relative, partner, friend or neighbor who has a significant personal relationship with, and provides a broad range of assistance for, an older person or an adult with a chronic or disabling condition. Despite the word ‘family’ in the concept, in the context of this dissertation, family caregivers can also be non-family members.

Self-efficacy

Self-efficacy serves as a central concept in the DIAdIC study and is extensively examined throughout this dissertation. Both the DIAdIC study and the referenced FOCUS studies used the Lewis Cancer Self-Efficacy Scale to measure self-efficacy, which encompasses patients' and family caregivers' confidence in managing cancer-related challenges, such as supporting loved ones through illness ('I am confident that I have what it takes to help my family through this illness'). This concept spans various domains, including symptom management, communication with healthcare professionals, navigating uncertainty, and addressing the impact on social relationships.

Serious illness

Chapters II and III focus on the family caregivers of patients with serious illnesses, broadly defined to include cancer, heart conditions, strokes, lung conditions (e.g., COPD), diabetes, kidney or liver diseases, dementia, and more. Chapters IV, V, and VI, narrow their focus to examine the unique challenges encountered by patients specifically coping with advanced cancer, a subset within the broader category of serious illnesses explored in the earlier chapters.

The impact of advanced cancer on patients and family caregivers

Cancer impacts around 10 million individuals in Europe, and it is expected that its prevalence will double over the next decade[15]. In 2018, the comprehensive expenditure of cancer in Europe amounted to €199 billion. These included health expenses for cancer care totaling €103 billion, €32 billion allocated to cancer drugs, and €26 billion associated with informal care costs[16]. With the European population reaching older ages and increasing longevity[17], healthcare resource scarcity[18], and a shortage of healthcare workforce[19], the demand for informal care is expected to continue to rise significantly.

There is ample research on the negative effect of advanced cancer on patients. In this dissertation, advanced cancer is considered an incurable illness which is still responsive to life-prolonging treatments[20]. The symptoms in advanced cancer patients typically differ from those in early stage cancer[21]. According to multiple studies, over half (54.6%) of patients with advanced cancer report feeling pain[22], while 60% to 70% experience nausea, 30% deal with vomiting[23,24], 60.6% suffer from fatigue[25], and between 39% and 82% report serious weight loss[26].

In addition to the physical symptom burden, patients also have psychosocial care needs. Patients with advanced cancer report having feelings of anxiety, fear, sadness and uncertainty[27,28], which all result in a decline in patients' quality of life[29]. A study on symptom distress in advanced cancer patients found that 37% of patients reported a depressive mood and 44% reported anxiety[30]. Patients also report existential distress attributed to loss of meaning-making and finding a purpose in life[31].

The impact of advanced cancer doesn't stop with the patient, but often extends to the family caregiver. A family caregiver is '*an unpaid, informal provider of care who has a personal connection to the patient (a friend, partner, ex-partner, sibling, parent, child, or other blood or non-blood relative) and provides one or more physical, social, practical, and emotional tasks'*[32]. The number of family caregivers in Europe is estimated at about 10-25% of the entire population[33].

The percentage of family caregivers that reports psychological distress ranges from 41% to 62%, and this psychological distress gets worse when the performance status of the patient is declining and the patient loses autonomy[34]. Family caregivers also encounter health and emotional issues[35–37], and these difficulties become worse when the person they are caring for is nearing the end-of-life[38,39]. The progression to an advanced stage of the illness may lead family caregivers to worry about what the future will look like for the patients they are caring for and themselves[40].

Another domain of quality of life that is affected by advanced cancer is sexuality. Cancer can disrupt interpersonal and sexual relationships[41,42]. Prevalence of sexual dysfunction in cancer patients varies between 20% and 90%, depending on the cancer diagnosis, cancer stage and treatment[43]. Sexual dysfunction occurs in all sexes and on all levels (biological, psychological and social)[44] with complications such as decreased sexual arousal, vaginal dryness, dyspareunia and erectile dysfunction[45–48]. Cancer treatments can change one's physical appearance, resulting in body image dissatisfaction[49], such as after a mastectomy[50]. Additionally, chemotherapy can cause tiredness and nausea, which negatively impacts sex drive[48]. Unfortunately, sexuality is rarely discussed in patients with advanced cancer, as healthcare professionals often falsely assume that patients in the advanced stage of cancer are 'asexual'[48] and healthcare professionals are more comfortable addressing treatment outcomes[51]. Sexuality is another example of a domain affected by cancer with impact extending to the partner. One study found that spouses more frequently report sexual function issues after cancer treatment than patients[52]. In another study with prostate cancer couples, partners reported that the patients were less able to gain an erection and to have sexual intercourse, causing them distress[53]. A study with partners of people with cancer found that approximately 19% of women and 14% of men renegotiated their sexual relationship by introducing sexual activities outside of sexual intercourse and other forms of intimacy[54].

The impact of other serious chronic illnesses

Serious chronic illness is the primary global cause of death, with a majority due to cardiovascular disease, cancer, chronic respiratory disease and diabetes[55]. Multiple studies have shown that individuals with cancer and other chronic illnesses experience similar symptom burdens[56–60]. A cross-sectional study found that both cancer and non-cancer patients exhibited comparable levels of depression and fatigue[61]. As found for cancer patients, the immediate family is impacted by the chronic illness as well[62]. Family members do not only worry about the wellbeing of the patient, but also about the impact on their own life[63]. They report feeling as if they lose their autonomy by taking on the responsibility of caring for an ill individual[64]. Relationships and sexual satisfaction in patients and their partners are also often affected, either because of the illness itself, or because of the treatment[65].

The critical role of family caregivers in end-of-life care

Family caregivers take up a wide range of caregiving tasks such as emotional support, transportation to medical appointments, monitoring symptoms, and managing the household[66]. In end-of-life care, the caregiver's responsibilities and tasks also tend to accumulate and intensify over time[67]. However, many family caregivers report feeling unprepared for their caregiving tasks[68]. They need professional support when it comes to handling practical caregiving tasks[69]. In a qualitative study, family caregivers of chronically ill patients report that they need assistance for example physical care tasks and require informational support[70]. The latter study also found that these family caregivers would opt for telephone-based support by a professional in this if it would be available.

Considering their close relationship with the patient, family caregivers have unique and valuable knowledge that make them part of the care team[71]. A review showed that family caregivers take on many collaborative roles, such as participant in decision making, spokesperson of the family; protector of vulnerable family members and "experts" on health care[72]. In a study by Vermorgen, family caregivers state that opportunities for effective collaboration are frequently missed when it comes to providing end-of-life care[73]. The critical involvement of family caregivers in cancer care emphasizes the necessity for healthcare professionals to provide support, coordination, and communication to enable family caregivers to carry out their tasks effectively[74].

Theories on coping with cancer

The cognitive model by Lazarus and Folkman[75] initially served as a framework to understand how people cope with cancer. The framework states that several personal, social, and illness-related factors determine how patients and family caregivers perceive cancer and manage the challenges that are associated with the illness. Research shows that these factors serve as key predictors of psychosocial outcomes in patients and family caregivers[76]. However, later on the model by Lazarus and Folkman has been criticized for its individual perspective as couples' stress should be considered a dyadic experience rather than an individual one[77]. This perspective underscores the interdependence of partners' stress and situates the coping process within the relational context, where partners respond to both individual and shared stressors[78].

Based on this shift in perspective several dyadic coping models have emerged, that are applicable to coping with a serious illness such as cancer (referred to in each model as 'a stressor'). A first model is the Congruence Model (CM), which focuses on the interaction between how partners individually cope with their own stressors, while disregarding combined strategies to deal with shared stressors[78]. Another model is the relationship-focused model (RFM), which acknowledges relationship-focused strategies that are '*aimed at managing, regulating or preserving relationships during stressful periods'*[79]. There also is the Communal Coping Model (CCM), that postulates that individuals view stress as something that affects 'us' collectively (a social appraisal) rather than as 'mine' or 'yours' individually (an individualistic appraisal), which refers to a collaborative, communal coping process[80]. A fourth model is the Systemic-Transactional Model (STM), that argues that when people encounter stress, they employ both individual and dyadic coping strategies, and additionally look for support resources outside of the dyadic relationship[81]. An expansion of the STM is the Relational-Cultural Coping Model (RCCM), that also focuses on the cultural and relational factors that contribute to people's coping strategies[82]. A final model is the Developmental-Contextual Coping Model (DCCM), which centers on the partner's reactions to stressors, which highlights that dyadic coping can vary throughout a lifespan, during specific time periods and during the various stages of dealing with a serious illness. The DCCM acknowledges that how people cope can even vary on a daily basis through interactions about certain stressors between partners[83].

All listed theoretical models recognize that dyads' experiences of stress and their coping are interrelated in response to stressors[78]. Each model can therefore be regarded as complementary, as they emphasize different coping mechanisms and account for various influencing variables. By recognizing the ways people navigate the challenges of cancer, these models offer a comprehensive understanding that can inform supportive strategies.

Support for patients and family caregivers to mitigate the consequences of advanced cancer

There is consensus that both patients and family caregivers have high support needs and could benefit from palliative care[7]. The World Health Organisation (WHO) defines palliative care as '*an approach that improves the quality of life of patients (adults and children) and their families who are facing problems associated with life-threatening illness*[84]*. It prevents and relieves suffering through the early identification, correct assessment and treatment of pain and other problems, whether physical, psychosocial, or spiritual'*. Even though the vision of palliative care also entails support and care for the family of the patient, in practice this isn't always offered in an optimal manner[85].
Literature shows that both patients and family caregivers report having many support needs that remain unmet[86]. Supportive care needs encompass a wide range of aspects, from managing physical symptoms to addressing psychological issues like anxiety, depression, and feelings of isolation[87]. A quantitative study with patients with advanced cancer showed that there are five problems they encounter for which they report unmet support needs: informational needs, coping with the unpredictability of the future, fear of metastases, fear of physical suffering, and difficulties remembering what was told during consultations[88]. As family caregivers frequently prioritize the needs of the person they are caring for, they often neglect or disregard their own needs[89]. A review among family caregivers even found more than 200 unmet needs in caregiving responsibilities, mostly in social and emotional domains, which could be addressed in palliative care models[90].

Psychoeducational interventions

Psychoeducational interventions can serve as a valuable support strategy for individuals facing advanced cancer and their family caregivers to acquire knowledge, coping strategies, and emotional support. A psychoeducational intervention is defined as '*a therapeutic approach that involves information giving and receiving, discussion of concerns, problem solving, coping skills training, expression of emotion, and social support*'[91]. Multiple reviews have demonstrated that psychoeducational interventions can improve both psychological and physical health outcomes in patients with cancer[12,92–94].

Another recent review evaluated the effectiveness of psychoeducational interventions aimed at family caregivers of cancer patients on several outcome measures[13]. Three studies found a significant reduction in anxiety[14,95,96] and four studies found a significant relief of depression in the family caregiver, all immediately after the intervention[14,96–98]. Other short term positive effects were found for relieving caregiver burden, improving quality of life and self-efficacy[13]. Positive effects on longer term (at least three months post-intervention) were found in two studies for improved physical health of the family caregiver[99,100].

Psychoeducational interventions can take on many formats[101]. Some are delivered face-to-face, while others take place online or via phone (or as a combination). They can either take place in the home of the patient and/or family caregiver, or in a clinical setting. The interventions can be delivered by a nurse, a social worker, or a psychologist (or a combination of healthcare professionals). A review of psychoeducational programs found that telephone-based interventions resulted in the best outcomes for patients and family caregivers[102]. Another review of psychoeducational interventions aimed at gynecological cancer patients found that nurses are the most suitable provider of psychoeducational interventions, but found no consistent trend in regard to the most effective format (individual, group or couple) of psychoeducational programs[12].

Dyadic interventions

Literature shows that there is an interdependence between several health aspects within the patient-family caregiver dyad. When individuals with advanced cancer report a decline in physical functioning, there is a corresponding decline in the physical health of their family caregivers[103,104]. A survey study among patients diagnosed with a solid organ cancer or lymphoma and their family caregivers found that when the needs of patients diminished, their family caregivers reported a reduced perceived burden of family caregiving[105]. Research also indicates that patients and their partners affect each other's adjustment to the cancer and its treatment, and each other's emotional wellbeing[106]. Furthermore, patients depend on their family caregivers not only for emotional, but also practical support and they collaborate in making treatment decisions[107,108].

A dyadic intervention is 'an intervention that is offered to cancer patients and their family caregivers together as a unit of care'[109]. The benefits of dyadic interventions compared to single target intervention (i.e. aimed at either the patient or the family caregiver alone) are numerous. First, a review of dyadic psychosocial interventions for chronic illnesses shows that outcomes of such interventions result in better outcomes for both patient and family caregiver[110]. Second, the burden of cancer patients and their family caregivers is affected by the interplay between the patients' symptoms and the challenges experienced by the family caregivers themselves[111]. By addressing the issues of patients and family caregivers simultaneously, this interaction between both parties can be considered. Third, dyadic interventions have the potential to be more cost-effective in the long run, when we compare them with interventions aimed at individuals seperately[110].

The position and impact of the FOCUS interventions

Two dyadic psychoeducational interventions that are highly relevant for patients and family caregivers are the face-to-face FOCUS intervention and the web-based FOCUS intervention, developed by Northouse and colleagues in the United States[112,113]. The face-to-face FOCUS intervention is a dyadic program that was developed for patients with cancer and their family caregivers to enable them to cope with the effects of the illness[112].

FOCUS is an acronym that stands for the five core components that are addressed in the intervention: Family involvement, Optimistic attitude, Coping effectiveness, Uncertainty reduction and Symptom management. The program thus focuses on enhancing effective communication between patients and family caregivers, sustaining hope, employing active coping strategies, acquiring information related to the illness, and managing symptom distress. Patients and their family caregivers are invited for three home visits, each lasting approximately one and a half hours, spread over a period of three months. Each session was structured to address the five core content areas of the FOCUS program, following an extensive intervention protocol manual with checklist format. While the manual detailed the main content of the FOCUS program, there was still room for tailoring the content to meet the needs of each dyad. For instance, some dyads might require more support in coping with the uncertainty the illness brings, while others needed more support with managing their symptoms.

Northouse has conducted several randomized controlled trials that have evaluated the effectiveness of the FOCUS intervention. The p-values and effect sizes (when available) for patients and family caregivers can be found in Table 1 and Table 2, respectively. A first longitudinal RCT included dyads of women with recurrent breast cancer and their family caregiver[99]. Results showed that patients assigned to the intervention group showed a decrease in negative appraisal of illness (p=.04) and hopelessness (p=.002) three months after baseline. Likewise, family caregivers reported a significant decrease in negative appraisal of caregiving (p=.04) at the same time point. A second longitudinal RCT included dyads of prostate cancer patients and their spouses[114]. Patients in the intervention group showed less uncertainty (p=.03) and more communication (p=.03) compared to patients in the control group at 4 months. Spouses in the intervention group reported higher appraisal of caregiving (p=.002), self-efficacy (p=.02), communication (p=.002), mental quality of life (p=.03) and general quality of life (p=.004), and lower levels of uncertainty (p=.009), hopelessness (p=.03), and symptom distress (p=.006) at 4 months. Some of these significant improvements in spouses remained at 8 and 12 months. A third longitudinal RCT included dyads with advanced breast, prostate, lung and colorectal cancer patients and their family caregiver and compared a brief (3 sessions) and an extensive (6 sessions) version of the FOCUS program to a control group[109]. The findings showed that dyads in the intervention group reported improvements in coping (p<.001), self-efficacy (p=.024), social quality of life (p=.002), and healthy lifestyle (p=.031). The effects differed based on the intervention dose and different timepoints.

Later on, the ‘F’ component (representing Family involvement) of FOCUS program was converted into a web-based format and was evaluated in a feasibility study[113]. Improvements were found for quality of life ($p<.05$), emotional distress ($p<.05$), perceived benefits of illness/caregiving ($p<.01$) in both patients and family caregivers. Additionally, an increase was found in family caregiver’s self-efficacy ($p<.05$).

Aforementioned studies highlight the effectiveness of the FOCUS intervention in American populations. However, the effect of the FOCUS intervention is yet to be determined in a European context and the European healthcare systems. The DIAdIC trial adapted the FOCUS interventions and evaluated their effectiveness. The adaptation process is extensively described by van der Wel[115] and can be found in Appendix A27.

Table 1: Patient effect size and p-value for FOCUS program in three Randomized Controlled Trials

Outcome (instrument)	**BREAST RCT[99]**		**PROSTATE RCT[114]**						**TRIAGE RCT[109]**
	p-value		**Effect size**			**p-value**			**p-value**
	3 mos	6 mos	4 mos	8 mos	12 mos	4 mos	8 mos	12 mos	Group x time
Appraisal									.46
Appraisal of illness (*Appraisal of illness scale[116])*	.04	.13	-.10	-.03	.04	.22	.81	.74	
Uncertainty (*Mishel Uncertainty in Illness Scale[117])*	.83	.49	-.22	-.06	.01	.03	.57	.97	
Hopelessness (*Beck Hopelessness Scale[118]*)	.002	.19	-.17	-.02	.01	.07	.88	.67	
Efficacy									.024
Self-efficacy (*Lewis Cancer Self-efficacy Scale[119]*)	/	/	.01	-.05	-.07	.98	.68	.57	
Interpersonal relationships									.41
Communication (*Lewis Mutuality and Sensitivity Scale[119]*)	/	/	.22	-.10	.01	.03	.34	.85	
Dyadic support (*Subscale of Social Support Questionnaire[120]*)	/	/	/	/	/	/	/	/	
Coping (*Brief cope[121]*)									.013
Active coping	.99	.77	.05	.08	.20	.69	.34	.14	.28
Avoidant coping	.64	.37	.07	.18	.20	.53	.14	.15	.039
Healthy lifestyle (*Researcher developed*)	/	/	/	/	/	/	/	/	.031
Quality of life									
Mental (*Medical Outcomes Study 12-item short form[122]*)	.92	.79	.08	-.06	-.07	.53	.69	.96	/
Physical (*Medical Outcomes Study 12-item short form*)	.48	.19	-.02	-.05	.03	.96	.80	.88	.33
General quality of life (*Fact-G[123]*)	/	/	.16	.01	.03	.10	.89	.77	
Social (*Fact-G*)	/	/	/	/	/	/	/	/	.002
Functional (*Fact-G*)	/	/	/	/	/	/	/	/	.84
Emotional (*Fact-G*)	/	/	/	/	/	/	/	/	.52
Symptoms									
Symptom distress (*Symptom Scale of the Omega Screening Questionnaire[124]*)	/	/	-.06	.08	.06	.60	.45	.59	/
Urinary (*Expanded Prostate Cancer Index Composite[125]*)	/	/	.19	.10	.05	.09	.32	.67	/
Bowel (*Expanded Prostate Cancer Index Composite*)	/	/	-.10	.08	-.12	.57	.60	.44	/
Sexual (*Expanded Prostate Cancer Index Composite*)	/	/	-.04	.12	-.04	.72	.24	.71	/
Hormone (*Expanded Prostate Cancer Index Composite*)	/	/	.01	.01	-.13	.95	.97	.36	/

Table 2: Family caregiver effect size and p-value for FOCUS program in three Randomized Controlled Trials

Outcome (instrument)	BREAST RCT[99]		PROSTATE RCT[114]						TRIAGE RCT[109]
	p-value		Effect size			p-value			p-value
	3 mos	6 mos	4 mos	8 mos	12 mos	4 mos	8 mos	12 mos	Group x time
Appraisal									.46
Appraisal of caregiving (*Appraisal of caregiving scale*[116])	.04	.37	-.32	-.16	-.08	.002	.17	.51	
Uncertainty (*Mishel Uncertainty in Illness Scale*[117])	.29	.21	-.28	-.22	-.13	.009	.05	.55	
Hopelessness (*Beck Hopelessness Scale*[118])	.80	.23	-.27	-.06	-.15	.03	.61	.25	
Efficacy									.024
Self-efficacy (*Lewis Cancer Self-efficacy Scale*[119])	/	/	.26	.24	.27	.02	.06	.02	
Interpersonal relationships									.41
Communication (*Lewis Mutuality and Sensitivity Scale*[119])	/	/	.31	.25	.29	.002	.01	.009	
Dyadic support (*Subscale of Social Support Questionnaire*[120])	/	/	/	/	/	/	/	/	
Coping (*Brief cope*[121])									.013
Active coping	.67	.31	.16	.11	.28	.16	.40	.02	.28
Avoidant coping	.43	.37	-.20	-.18	.00	.15	.22	.99	.039
Healthy lifestyle (*Researcher developed*)	/	/	/	/	/	/	/	/	.031
Quality of life									
Mental (*Medical Outcomes Study 12-item short form*[122])	.81	.57	.25	-.12	-.07	.03	.40	.76	/
Physical (*Medical Outcomes Study 12-item short form*)	.91	.48	-.04	.28	.32	.67	.02	.005	.33
General quality of life (*Fact-G*[123])	/	/	.26	.19	.14	.004	.06	.18	
Social (*Fact-G*)	/	/	/	/	/	/	/	/	.002
Functional (*Fact-G*)	/	/	/	/	/	/	/	/	.84
Emotional (*Fact-G*)	/	/	/	/	/	/	/	/	.52
Symptoms									
Symptom distress (*Symptom Scale of the Omega Screening Questionnaire*[124])	/	/	-.34	-.16	-.09	.006	.16	.42	/
Urinary (*Expanded Prostate Cancer Index Composite*[125])	/	/	-.30	-.40	-.18	.04	.009	.25	/
Bowel (*Expanded Prostate Cancer Index Composite*)	/	/	.18	.02	.14	.22	.94	.60	/
Sexual (*Expanded Prostate Cancer Index Composite*)	/	/	-.03	.02	.10	.83	.93	.54	/
Hormone (*Expanded Prostate Cancer Index Composite*)	/	/	-.05	.04	.00	.74	.80	.99	/

Knowledge gaps addressed within this dissertation

This dissertation addresses pertinent gaps in the knowledge on the support and wellbeing for both patients with a serious illness (such as advanced cancer) and their family caregivers.

A lot of research is being done on the physical and psychological challenges family caregivers of seriously ill patients face[90,126–129]. However, little attention has been paid to how family caregivers collaborate with healthcare professionals in the last months of life of the person they are caring for. Research often does not take into account the role of family caregivers in the care team and the professional support they receive during those last months before bereavement. Investigating the collaboration between family caregivers and healthcare professionals can contribute to better practice and guidelines, and consequently enhancing the quality of end-of-life care for patients and enhance the quality of life for both patients and their family caregivers[130,131]. The research conducted as part of this dissertation also highlights the importance of family caregivers in end-of-life healthcare and their role of a partner in care. By conducting one of the first population-based surveys to examine the support given to family caregivers by healthcare professionals at the end-of-life in Flanders, Belgium, valuable insights are gathered that can positively impact the experiences of both family caregivers and healthcare professionals involved in end-of-life care, ultimately leading to improved support, communication, and well-being outcomes for all stakeholders involved.

Secondly, studies in family caregiving and psychoeducation have several shortcomings. A meta-analysis of 27 interventions aimed at family caregivers of cancer patients reviewed multiple interventions that show promising results, but many have small sample sizes, and lack clear effectiveness[132]. The DIAdIC trial is set up to reach a large sample size across six countries and the multisite randomized controlled trial allows for the most favorable design to study effectiveness of the interventions. Additionally, literature further suggests that individually tailored interventions are more likely to be effective than those that are not[133]. Given that the DIAdIC interventions are tailored to the dyad's specific needs, this demonstrates promising potential for effectiveness.

The interventions developed as part of the DIAdIC study have the potential of reaching a large group of people who could benefit from palliative care[134], namely patients with cancer and their family caregivers, as the proportion of deaths due to chronic conditions from cancer compared to non-cancer-related causes is approximately 1 to 2[135]. The trial outcomes can offer valuable insights into the formulation of strategies aimed at improving the wellbeing of both patients and family caregivers. This information can in its turn reduce economic and wider societal burden.

Study objectives and research questions

The main objective of this dissertation is to investigate the support and wellbeing for patients coping with serious illness and their family caregivers across Europe. This objective is guided by the following aims and associated research questions:

The **first aim** is to describe experiences of the population of bereaved family caregivers of people with a serious illness regarding their collaboration with healthcare professionals. The following specific research questions will be answered:

1) How are family caregivers of people with a serious illness supported by healthcare professions in their caregiving tasks?
2) Is pre-bereavement collaboration between family caregivers and healthcare professionals associated with post-bereavement emotional wellbeing?

The **second aim** of this dissertation is to describe the protocol of a randomized controlled trial on the evaluation of two psychoeducational interventions for people with advanced cancer and their family caregiver in six European countries. The following research question will be addressed:

3) What is the design, methodology and procedure for conducting the DIAdIC trial?

The **third aim** is to present the findings resulting from the DIAdIC study. The following research questions will be answered:

4) What are the predictors of sexual satisfaction in patients with advanced cancer and their family caregivers who were recruited for the DIAdIC trial?
5) What is the effect of 1) the face-to-face FOCUS+ intervention and 2) the iFOCUS web-based intervention compared to 3) care as usual on the emotional functioning and self-efficacy of the patients with advanced cancer and their family caregivers?

Methods

To answer the research questions of this dissertation, several methods of data collection were employed. First, we conducted a cross-sectional survey among bereaved family caregivers in Flanders, Belgium on their experience with support from and collaboration with healthcare professionals (**Chapter II** and **III**). Next, we drafted a research protocol to describe all relevant aspects of the DIAdIC trial (**Chapter IV**). To describe sexual satisfaction of patients and family caregivers and the effect of two dyadic interventions on emotional functioning and self-efficacy of patient-caregiver dyads, we conducted a randomized controlled trial in six European countries (**Chapter V** and **VI**). The methods for each study are briefly described in the following paragraphs.

Study 1: A cross-sectional survey of bereaved family caregivers on the collaboration between healthcare professionals and family caregivers of persons with a serious illness (research questions 1 and 2)

Using a population-based cross-sectional survey in Flanders, Belgium, we collected data from bereaved family caregivers of individuals with a serious illness. Participants were identified through records from the three largest health insurers in Flanders, which cover approximately 79% of the population. These health insurers keep records of individuals applying for a care budget for persons with significant care needs ('zorgbudget voor zwaar zorgbehoevenden'), as well as the names of their family caregivers. We conducted a random sampling of 3,000 deceased individuals with a serious illness who had applied for a care budget through one of the participating health insurers. The individual registered in the database as the family caregiver was selected. Questionnaires were then distributed by post between November 2019 and January 2020. The questionnaire included items pertaining to the care provided for the patient during the final three months of their life, including demographic items. The complete questionnaire and information letter of the study can be found in Appendix A1 and A2, respectively. A detailed overview of the method can be found in **Chapter II** and **III**.

Study 2: An international randomized controlled trial on the effectiveness of a nurse-delivered (FOCUS+) and a web-based (iFOCUS) psychoeducational intervention for people with advanced cancer and their family caregivers (DIAdIC) (Research questions 3, 4 and 5)

We conducted an international multicenter trial, the DIAdIC trial, comparing the face-to-face FOCUS+ intervention and the web-based iFOCUS intervention to standard care for patients with advanced cancer and their primary family caregivers. The trial spanned six countries (Belgium, The Netherlands, United Kingdom, Denmark, Italy, and Ireland) and recruited participants between February 2021 and September 2023. Randomization (1:1:1 ratio) assigned participants to one of the three study arms; the iFOCUS intervention, the FOCUS+ intervention, or standard care. Participants in the intervention arms received the FOCUS+ or iFOCUS interventions in addition to standard care and focused on psychoeducation, aiming to teach dyads optimal strategies for jointly managing the implications of advanced cancer and addressing their priority concerns. The interventions were tailored to suit the individual needs and preferences of the patients and family caregivers by taking into account what the dyad shared during each intervention session. FOCUS+ involved home visits and online sessions over 12 weeks, while iFOCUS was a self-managed web-based program. While the FOCUS+ and iFOCUS interventions differ in their modes of delivery (face-to-face vs. web-based), they share the same core content, addressing five essential components: (1) supporting family involvement, communication, and mutual support, (2) fostering outlook and meaning, (3) enhancing coping effectiveness, (4) reducing uncertainty, and (5) teaching symptom management while instilling confidence to handle specific tasks.

Data collection occurred at baseline, at 3 months, and once again at 6 months. The primary outcomes assessed in the study were emotional functioning and self-efficacy. Emotional functioning was measured using a 10-item short form (EF10) based on the European Organisation for Research and Treatment of Cancer (EORTC) EF item bank[136]. Self-efficacy was assessed by 17 items from the Lewis Cancer self-efficacy scale[119]. Data on socio-demographic and clinical characteristics were gathered during enrollment and at baseline. The complete questionnaire for patients and family caregivers can be found in Appendix A3 and A4, respectively. A detailed overview of the method of the DIAdIC trial and the sub study on sexual satisfaction can be found in **Chapter IV**, **V** and **VI**.

Dissertation outline

Chapter I entailed a general introduction on support and wellbeing for patients with serious illness and their family caregivers. **Chapters II - VI** of this thesis are based on articles which have either been published or submitted for publication.

This dissertation consists of three parts, consisting of different chapters that answer specific research questions and aims.

Part I discusses the collaboration between healthcare professionals and bereaved family caregivers of persons with a serious illness. This part answers the first aim of this dissertation and the associated research questions one and two.

Part II focuses on the development and design of the two psychoeducational interventions for people with advanced cancer and their family caregivers as part of a DIAdIC trial. This part answers the second aim of the dissertation with associated research questions three.

Part III describes the main findings of the DIAdIC study, answering the third aim of this dissertation with the associated research questions four and five.

In the concluding **Chapter VII**, the main findings of each study are thoroughly discussed, considering the strengths and weaknesses of their designs. The results of this dissertation are then compared to the current literature on wellbeing and support for patients with a serious illness and family caregivers. Finally, the discussion concludes by outlining how these findings can contribute to shaping future research, policy, and practice.

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PART I
Supporting and empowering family caregivers

Chapter II

How are family caregivers of people with a serious illness supported by healthcare professionals in their caregiving tasks? A cross-sectional survey of bereaved family caregivers

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Abstract

Background: Due to medical advances and an increasingly ageing population, the number of people living with a serious illness is rising. This has major implications for the burden on family members of assisting with care. Support of family caregivers by healthcare professionals is needed to ensure they can provide quality care for people with serious illness.

Aim: To investigate how family caregivers of people with serious illness are supported by healthcare professionals in their caregiving tasks.

Design/Participants: Population-based cross-sectional survey of bereaved family caregivers of people with serious illness (N=3,000) who cared for a person who had died two to six months before the sample was drawn (November 2019), as identified through three sickness funds in Flanders, Belgium. The survey explored support from healthcare professionals for family caregivers three months prior to bereavement.

Results: Response rate was 55.0%. Most family caregivers received support from one or more healthcare professionals for family caregiving tasks, ranging from 71% for promoting social interaction to 95% for managing symptoms. The type of support mostly involved providing information. Use of palliative care services was the strongest predictor of such support across physical, psychosocial, and practical tasks.

Conclusion: Most family caregivers of those with serious illness get some form of support from healthcare professionals for their tasks. However, an empowering support strategy e.g. one aimed at increasing self-efficacy of the family caregiver, is rare, and end-of-life communication between healthcare professionals and family caregivers needs improvement.

Background

People with serious illness are often faced with complex symptoms in the last phase of life[1] which involve needs which cannot be met by healthcare professionals alone. Consequently, family caregivers fulfill a wide range of caregiving tasks e.g. bathing, managing finances and communicating with healthcare professionals, which means they are an essential part of the healthcare team[2–6].

Due to the increasingly ageing population and advances in healthcare, the numbers of people with serious illness are rising and at the same time, resources for professional healthcare are being limited[7] so the need for family caregiver support continues to grow[8,9]. In Europe, the proportion of family caregivers is estimated at 10%-25% of the population, depending on the country and the definition used[10]. However, family caregivers often report feeling unprepared for their role[11,12]. For example they indicate a lack of support from nurses for physical tasks such as going to the bathroom but also report receiving good emotional support from healthcare professionals[13].

The time family caregivers spend on providing end-of-life care is often more than that spent by healthcare professionals[14] and periods without professional contacts show greater needs for both patients and family caregivers. Family caregivers experience health and emotional problems too[15–17], which are particularly challenging at the end-of-life stage[16,18,19]. Supporting them as partners in care, but also supporting them as care clients themselves, facilitating their relationship with the person who is dying, and considering them as experts in care, is recommended[20], in line with the interpretation of palliative care as supporting family caregivers as well as the patient[21].

Previous studies have shown that good collaboration between family caregivers and healthcare professionals in end-of-life care leads to improved patient health outcomes[22] and higher satisfaction with the care received[23]. An interview study found that family caregivers want to be considered as a member of the care team, but rarely feel recognised as such[24]. As the focus is typically on the patient, the support needs of family caregivers are often under-addressed[25,26].

Hitherto research has paid little attention to family caregivers as members of the care team and to the support they receive from healthcare professionals at the end of life. Additionally, most studies recruit family caregivers through professional care services meaning that they are people who have already found their way to professional support, thus resulting in a selection bias; studies are needed using samples that represent the wider population of family caregivers.

This population-based study explored how family caregivers are supported by healthcare professionals in their caregiving tasks for people with a serious illness in the last three months before bereavement.

Five research questions were explored:

1) *What are the caregiving tasks performed by family caregivers of people with a serious illness and which of those tasks would they prefer to have performed by someone else?*
2) *Which healthcare professionals support family caregivers in their caregiving tasks?*
3) *How do family caregivers receive support from healthcare professionals?*
4) *To what extent is support from healthcare professionals considered sufficient?*
5) *What factors are associated with whether or not family caregivers receive support from healthcare professionals?*

Methods

Study design and setting

We conducted a population-based cross-sectional survey among bereaved family caregivers in Flanders, Belgium. In Belgium, people with long term extensive care needs can apply for a monthly care budget that helps cover non-medical care. We used registers of the three largest health insurers (accounting for 79% of the population) in Flanders to identify participants, as they keep records of people who apply for this care budget and of the names of their family caregivers. We applied the Strengthening of the Reporting of Observational studies in Epidemiology (STROBE)[27] statement to describe all relevant aspects of the study.

Participants

We randomly sampled 3,000 deaths of people with a serious illness who had applied for a care budget from one of the participating health insurers and selected the person registered in the database as the family caregiver. The sample was proportionately distributed between the health insurers according to the number of family caregivers meeting the inclusion criteria. Based on recommendations in other studies[28–30], we included people who had provided care to someone who had died between two and six months before inclusion to allow sufficient time for grieving while limiting recall bias. Additional criteria were that their postal address was complete in the database, and that both they and the deceased were at least 18 years old. To answer the research questions accurately, family caregivers were included for analysis if 1) they had contact with the deceased during the last three months of life (question 2 in questionnaire), and if 2) the deceased had had at least one of the listed serious illnesses (question 3 in questionnaire).

Data collection

An independent researcher sent out the questionnaires by post between November 2019 and January 2020. The Dillman's Total Design Method was applied, with the aim of obtaining a higher response to the survey[31]. At the start of data collection (day 1), each person received a questionnaire and information letter which described details of the study, the voluntary nature of their participation, and the option to complete an online version of the questionnaire. In cases of non-response, a reminder letter was sent after two and four weeks (days 15 and 29). After another two weeks (day 45), a non-response questionnaire was sent. The purpose of the non-response questionnaire was to evaluate reasons for non-response and possible response bias.

Measures

No pre-existing validated instruments were identified as appropriate to address our research questions, so we developed items based on the modification of existing instruments and previous qualitative interviews[24]. We tested the questionnaire through two rounds of cognitive interviews with five family caregivers each, recruited through convenience sampling. The cognitive testing resulted in adding questions e.g. question 2 and 4 (Appendix A1), changing the sentence structure of certain items and clarifying certain concepts.

The questionnaire (Appendix A1) consisted of six sections of which we used three. The first contained categorical items about the care situation pre-bereavement, including their relationship to the patient and the illness of the patient. A second section evaluated ten caregiving tasks they had possibly performed during the three months pre-bereavement. For each task, four questions were asked: (1) did you perform this task at least once during the last three months of the patient's life? (yes/no), (2) which healthcare professionals have supported you in this task? (multiple choice), (3) how were you supported in this task by healthcare professionals? (multiple choice) and (4) to what extent was the support of healthcare professionals sufficient in supporting you to perform this task? (4-point scale). The caregiving tasks were based on van den Berg & Spauwen[32], additional literature[33,34] and a preceding interview study[24]. A third section concluded with sociodemographic items.

Statistical analysis

We used descriptive statistics to summarise sociodemographic characteristics, caregiving tasks, healthcare professionals, types of support and evaluation of support.

With the purpose of data reduction for a more condensed presentation of the findings, we performed exploratory factor analysis using Principal Component Analysis (oblique rotation) to explore types (dimensions) of support from healthcare professionals. The selection of components was based on our own theoretical assumptions about the grouping of caregiving tasks and on statistical criteria (scree plot, variance explained by the component, eigenvalues, and Cronbach's alpha). Final components were saved as variables with factor scores (i.e. mean=0 and standard deviation=1). We then performed one-way ANOVA tests to find associations between the caregiving task components and patient and family caregivers characteristics. Additionally, in order to correct these associations for confounding we performed multivariable analysis of variance (only of the main effects) with the caregiving task components as dependent variables and the variables for which the one-way ANOVA analysis indicated statistical significance as independent variables. Missing data were removed listwise and an alternative analysis with simple mean imputation functioned as a sensitivity analysis. Data were analysed using SPSS Statistics 27.

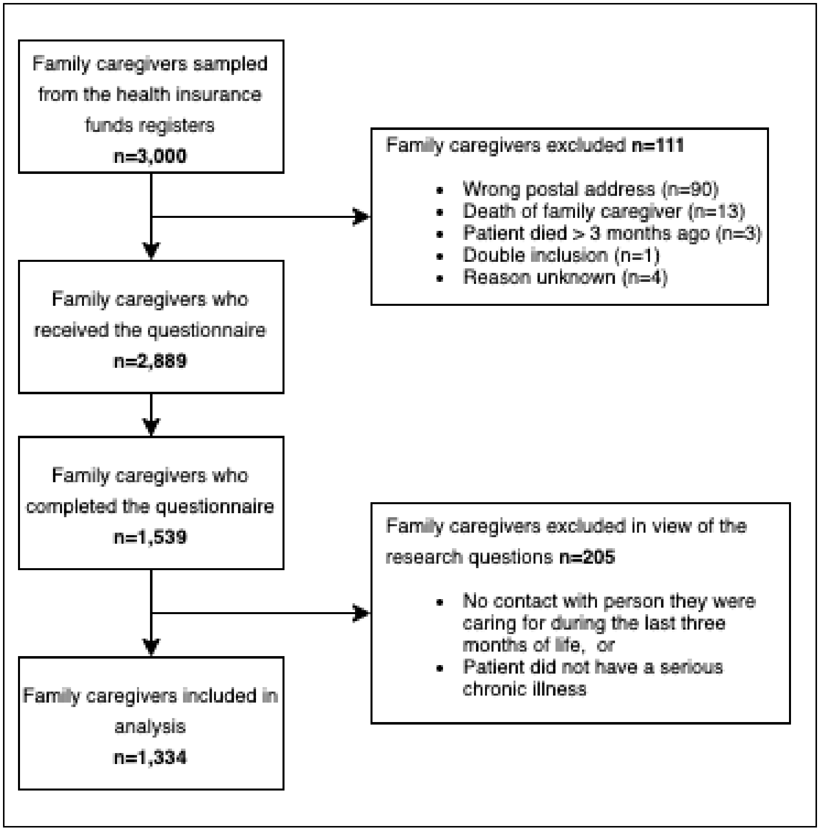
Ethical considerations

The Ethics Commission of Vrije Universiteit Brussel approved the study procedure and materials (approval number B.U.N. 143201940562 on 17/06/2019). This study is performed following the Declaration of Helsinki. Participants were informed that they gave their informed consent implicitly by completing and returning the questionnaire. Participants did not receive any financial compensation for participating in the study. Personal data were processed in line with the General Data Protection Regulation.

Results

Of the 3,000 people sampled, 2,889 received the questionnaire (Figure 1) and 1,539 completed it. The non-response survey was completed by 524 respondents (reasons for non-participation in Table A5 in Appendix) and eliminated the response of another 89 persons. As such the response rate was 55.0%. We included 1,334 respondents for analysis, who were family caregivers of someone with at least one serious illness and had had contact with them during the last three months of life.

Figure 1: Participants flowchart



The majority of these family caregivers were women (68.2%) (Table 1), their average age was 65.5 years; 13.2% had a professional healthcare degree and a majority were either the child (51.7%) or the partner (34.4%) of the seriously ill person with about one third (36.7%) living with them in the last three months of life. The deceased persons had an average age of 78.3 and death was most often with cancer (31.8%) or dementia (30.7%); 36.7% received support from specialised palliative care services and half lived at home for most of the time during their final three months (51.6%).

Table 1: Characteristics of the obtained sample (n = 1,334)

Characteristics of bereaved family caregivers	**N** ***(%)***
Age in years	
18-55	238 *(18.2)*
56-65	488 *(37.3)*
66-75	305 *(23.3)*
76-85	202 *(15.4)*
>85	76 *(5.8)*
Mean *(SD)*	65.5 *(11.96)*
Sex	
Female	892 *(68.2)*
Male	416 *(31.8)*
Educational attainment	
Primary education	212 *(16.2)*
Secondary education	603 *(46.1)*
Bachelor's degree or equivalent	364 *(27.9)*
Master's degree (University)	90 *(6.9)*
None of the above	38 *(2.9)*
Relationship with the deceased, family caregiver is …	
Daughter or son (in law)	687 (51.7*)*
Partner	457 *(34.4)*
Parent	67 *(5.0)*
Sibling	34 *(2.6)*
Other family member	55 *(4.1)*
Not family	29 *(2.2)*
Lived together with deceased loved one in the last three months	478 *(36.7)*
Has a professional healthcare degree	167 *(13.2)*
Employment status	
Retired	612 *(46.9)*
Full-time employed	271 *(20.8)*
Part-time employed	232 *(17.8)*
Homemaker	103 *(7.9)*
Other	58 *(4.4)*
Unemployed	30 *(2.3)*
Characteristics of deceased patient	
Age in years	
18-55	89 *(6.7)*
56-65	181 *(13.9)*
66-75	204 *(15.7)*
76-85	318 *(24.4)*
>85	510 *(39.2)*
Mean *(SD)*	78.34 *(13.79)*
*Serious condition**	
Cancer	424 *(31.8)*

Dementia	410 *(30.7)*
Other	315 *(23.6)*
Heart failure	262 *(19.6)*
Respiratory illness	227 *(17.0)*
Diabetes	195 *(14.6)*
Renal or liver illness (not cancer)	171 *(12.8)*
Stroke (or the consequences thereof)	146 *(10.9)*
Illness of the nervous system other than dementia	95 *(7.1)*
Decisional capacity of patient throughout the last three months	
Yes	529 *(40.2)*
No	430 (*32.7)*
Sometimes / partly	357 *(27.1)*
Specialised palliative care received†	
No	762 (*60.3*)
Yes	464 (*36.7*)
I don't know	38 (*3.0*)
Living at home in the last 3 months	
Most of the time	663 (*51.6*)
Sometimes	124 (*9.6*)
Not at all	499 (*38.8)*

*Percentages do not add up to 100% as multiple answers were possible

†Palliative homecare team, palliative unit in the hospital, palliative support team in the hospital, reference person (palliative care nurse in a retirement home or a palliative daycare center)

Missing values bereaved family caregivers: Age in years: n=25 (1.9%); Sex: n=26 (1.9%); Education: n=27 (2.0%); Relationship with the deceased: n=5 (0.4%); Region: n=25 (1.9%); Living together with deceased loved one in the last three months: n=30 (2.2%); Diploma of doctor, nurse or healthcare professional: n=65 (4.9%); Employment status: n=28 (2.1%)

Missing values deceased patient: Age in years: n=32 (2.4%); Capable of making decisions about his/her care in the last 3 months: n= 18 (1.3%); Specialised palliative care received: n=70 (5.2%); Living at home in the last 3 months: n=48 (3.6%)

Caregiving tasks pre-bereavement

Family caregivers commonly facilitated safe mobility inside or outside the house (85%), talked about emotions (73%), promoted social interaction (73%), assisted with administration (71%), provided physical comfort (72%) and managed symptoms (65%) (Table 2). Less than half (47%) talked about end-of-life preferences or made home adjustments for safety and comfort (39%). The majority of respondents (72-93%) had wanted to perform the caregiving tasks themselves; around 28% of those who provided personal care in the last three months and 23% who took on the task of managing symptoms reported they would have preferred to leave this task to someone else.

Table 2: Caregiving tasks taken on by family caregiver during the last 3 months before the patient's death (n=1,334)

Caregiving task	**Total yes, %**	**Yes, but I would have preferred to leave this activity to someone else, %***	**Yes, and I wanted to take on this activity myself, %***
Providing personal care	54.3	28.2	71.8
Assessing and managing symptoms	65.1	22.8	77.2
Administering medication	56.2	14.0	86.0
Facilitating safe mobility (inside or outside)	84.7	14.3	85.7
Providing physical comfort	71.5	16.6	83.4
Assistance with administration	73.1	12.5	87.5
Making home adjustments for safety and comfort	39.4	7.5	92.5
Talking about emotions	73.3	14.3	85.7
Talking about end-of-life preferences	46.9	14.5	85.5
Promoting social interaction	73.3	6.9	93.1

Percentages are row percentages. Missing values: Providing personal care: n=133 (10%); Assessing and managing symptoms: n=187 (14.0%); Administering medication: n=110 (8.2); Facilitating safe mobility: n=105 (7.9%); Providing physical comfort: n=127 (9.5%); Assistance with administration: n=127 (9.5%); Making home adjustments: n=147 (11.0%); Talking about emotions: n=118 (8.8%); Talking about end-of-life preferences: n=132 (9.9%); Promoting social interaction: n=123 (9.2%)

[*] n=family caregivers who performed the caregiving task

Healthcare professionals supporting family caregivers in different caregiving tasks

Most family caregivers received support from one or more healthcare professionals so they could perform the task themselves, ranging from 71% for promoting social interaction to 95% for managing symptoms (Table 3). The majority of family caregivers received support for making home adjustments (73%) and assistance with administration (72%). Of the family caregivers who didn’t receive support for talking about emotions and end-of-life preferences, one out of five reported that they had needed support.

Home care nurses and GPs most frequently supported family caregivers in their caregiving tasks in the last three months of life. Palliative care nurses or doctors most frequently provided support for talking about end-of-life preferences (37%).

Table 3: Healthcare professionals who provided support to the family caregivers in different family caregiving tasks

	Providing personal care (n=652)	**Assessing and managing symptoms (n=747)**	**Administering medication (n=688)**	**Facilitating safe mobility (n=1041)**	**Providing physical comfort (n=863)**	**Assistance with administration (n=882)**	**Making home adjustments (n=468)**	**Talking about emotions (n=891)**	**Talking about end-of-life preferences (n=564)**	**Promoting social interaction (n=888)**
	%	%	%	%	%	%	%	%	%	%
No support received	10.1	4.7	11.7	21.3	14.0	27.6	27.3	17.9	21.9	28.6
Needed it	15.4	5.7	3.8	6.6	9.4	10.7	7.5	20.0	21.7	8.3
Did not needed it	84.6	94.3	96.2	93.4	90.6	89.3	92.5	80.0	78.3	91.7
Support received	89.9	95.3	88.3	78.7	86.0	72.4	72.7	82.1	78.1	71.4
Support received from different healthcare professionals										
Home care nurse	74.5	58.1	56.5	46.8	56.5	32.1	62.5	39.1	33.2	31.4
Nurse or care worker in hospital or residential care centre	35.0	41.9	28.7	49.6	45.9	n.a.†	n.a.†	42.5	32.0	50.4
GP	42.5	61.1	65.8	19.5	21.6	48.5	29.7	54.6	66.6	28.7
Specialist	11.6	20.7	20.1	4.6	5.9	9.1	2.8	10.9	16.5	4.3
Palliative nurse or doctor	14.2	15.1	15.1	7.6	10.5	10.3	9.4	23.8	36.6	9.7
Pharmacist	n.a.†	n.a.†	23.3	n.a.†	n.a.†	n.a.†	n.a.†	n.a.†	n.a.†	n.a.†
Physiotherapist	n.a.†	n.a.†	n.a.†	21.3	13.7	n.a.†	n.a.†	n.a.†	n.a.†	n.a.†
Social worker	n.a.†	n.a.†	n.a.†	n.a.†	n.a.†	52.0	23.8	13.4	n.a.†	11.7
Psychologist	n.a.†	n.a.†	n.a.†	n.a.†	n.a.†	n.a.†	n.a.†	7.3	n.a.†	n.a.†
Someone close with experience in healthcare	10.4	9.1	7.1	9.7	9.8	9.1	13.8	8.7	10.7	8.7
Other‡	10.7	10.4	12.6	15.0	11.0	15.2	23.1	10.9	0.3	25.9
Number of healthcare professionals of whom support was received from										
1	41.6	31.5	33.3	53.4	53.8	51.9	56.6	36.8	38.3	55.9
2	31.2	35.8	34.0	27.8	27.6	28.1	26.9	33.5	36.3	25.2
3	17.3	21.7	21.1	12.0	11.9	13.7	13.4	18.4	18.9	13.7
4 or more	9.9	10.9	11.6	6.8	6.7	6.4	3.1	11.3	6.5	5.2

Percentages are column percentages.

The n varies for every caregiving task (the number of family caregivers who performed the respective caregiving task in the last three months before the death of the relative varies)

†Not applicable as the respective healthcare professional wasn't an answer option for the task

‡This included for example a pastor (talking about emotions), a notary (Talking about end-of-life preferences), home care story staff (facilitating safe mobility), health insurance funds staff (all tasks).

Missing values: Providing personal care: n=10 (1.5%); Assessing and managing symptoms: n=8 (1.1%); Administering medication: n=22 (3.2); Facilitating safe mobility: n=44 (4.2%); Providing physical comfort: n=29 (3.4%); Assistance with administration: n=35 (4.0%); Making home adjustments: n=28 (6.0%); Talking about emotions: n=27 (3.0%); Talking about end-of-life preferences: n=35 (6.2%); Promoting social interaction: n=48 (5.4%)

Types of support by healthcare professionals

Healthcare professionals mostly explained how family caregivers could perform the task (Table 4). This was the case for assessing and managing symptoms (72%), administering medication (70%), making home adjustments (64%), assistance with administration (57%), providing physical comfort (39%) and providing personal care (35%). Demonstrating how they could perform the task themselves was highest for providing physical comfort (38%), facilitating safe mobility (37%), providing personal care (30%), administering medication (26%) and managing symptoms (24%). For talking about emotions (41%) and end-of-life preferences (54%), healthcare professionals mainly exercised the task with the family caregiver. For making home adjustments, healthcare professionals mainly supported family caregivers by referring them to other services (31%). For promoting social interaction, healthcare professionals stressed the importance of a social life (33%), organised social activities (32%) and encouraged family caregivers to undertake social activities themselves (31%). (Table A6 in Appendix).

Table 4: Types of support delivered to family caregivers

Caregiving tasks*	Explain (%)	Demonstrate (%)	Exercise (%)	Refer to services or information (%)	Other types of support (%)
Providing personal care (n=577)	35.4	30.3	6.6‡	n.a.†	39.9
Assessing and managing symptoms (n=704)	71.9	23.7	4.5‡	n.a.†	15.6
Administering medication (n=588)	70.4	26.0	6.3‡	n.a.†	9.5
Facilitating safe mobility (n=781)	34.3	37.0	7.8‡	n.a.†	24.8
Providing physical comfort (n=717)	39.1	37.5	7.8‡	n.a.†	18.8
Assistance with administration (n=613)	56.6	21.4	29.0§	n.a.†	8.5
Making home adjustments (n=320)	64.1	n.a.†	n.a.†	31.3	11.3
Talking about emotions (n=709)	32.9	n.a.†	41.2§	10.7	28.5
Talking about end-of-life preferences (n=413)	17.9	n.a.†	53.8§	9.4	16.5

Percentages are row percentages. Percentages don't add up to 100% as multiple answers were possible. Missing values: Providing personal care: n=48 (8.3%); Assessing and managing symptoms: n=35 (5.0%); Administering medication: n=33 (5.6%); Facilitating safe mobility: n=75 (9.6%); Providing physical comfort: n=77 (10.7%); Assistance with administration: n=32 (5.2%); Making home adjustments: n=18 (5.6%); Talking about emotions: n=50 (7.1%); Talking about end-of-life preferences: n=21 (5.1%).

*The n for every caregiving tasks is determined by the number of family caregivers who performed the caring activity in the last three months of life of the deceased relative and who received support from at least one healthcare professional

†Not applicable as the respective answer category wasn't an answer option for the task

‡The healthcare professional practice this task with the family caregiver.

§The healthcare professional did this task together with the family caregiver.

Evaluation of support received

The majority of family caregivers indicated they had received sufficient support from healthcare professionals for all caregiving tasks, ranging from 78% for promoting social interaction to 89% for facilitating safe mobility (Table A7 in Appendix). The number of family caregivers who reported not getting enough support was highest for managing symptoms (7%), making home adjustments (7%) and talking about emotions (7%). The number who reported that they got more support than they needed was highest for promoting social interaction (9%), providing personal care (9%) and facilitating safe mobility (7%).

Factors associated with family caregivers receiving support from healthcare professionals

A factor analysis identified three dimensions of support for caregiving tasks, i.e. support for physical, psychosocial and practical tasks (Table A8 in Appendix). One-way ANOVA tests (Table A9 in Appendix) showed that the use of specialised palliative care services is associated with receiving more support across physical (p=0.001), psychosocial (p<0.001) and practical (p<0.001) tasks. To account for confounding, we performed multivariable General Linear Model analyses with the three factors as dependent variables. Family caregivers of people who received specialised palliative care in the last three months received more support from healthcare professionals for physical, psychosocial and practical tasks than those of people who did not receive palliative care (p<0.001, coefficients of 0.388, 0.528 and 0.573, respectively) (Table 5). Family caregivers with a master's degree received less support for psychosocial tasks than those with a secondary degree (B=-0.367, p=0.036). Those between 18 and 55 years received less support for practical caregiving tasks than those between 56 and 65 years (B=-0.385, p=0.004). Family caregivers who were a parent of the patient received less support for practical tasks than those who were the child of the patient (B=-0.728, p=0.008) (Table 5). A sensitivity analysis with mean imputation confirmed these results (i.e. same significant associations, Appendix A10)."

Table 5: Multivariable analysis for factors associated with family caregivers receiving support for physical tasks, psychosocial tasks and practical tasks (n=1,334)

	Support for physical tasks		**Support for psychosocial tasks**		**Support for practical tasks**	
Parameter	Estimate (B)	*p*	Estimate (B)	*p*	Estimate (B)	*p*
Intercept	-,209	,039	-,223	,152	-,204	,086
Decisional capacity of patient throughout the last three months						
Yes	-,131	,277	-,096	,524	/	/
Partly/sometimes	,212	,096	,292	,075	/	/
No	Ref. cat.	.	Ref. cat.	.	/	/
Specialised palliative care received						
Not sure	,206	,473	,678	,018	,388	,307
Yes	,388	,000	,528	,000	,573	,000
No	ref. cat.	.	ref. cat.	.	ref. cat.	.
Educational level of caregiver						
Elementary	/*	/	,019	,898	,320	,060
Secondary	/	/	ref. cat.	.	ref. cat.	.
Bachelor or equivalent	/	/	-,224	,051	-,115	,342
Master/university	/	/	-,367	,036	,110	,607
None of the above	/	/	-,173	,630	,538	,077
Age of the caregiver						
18-55	/	/	/	/	-,398	,004
56-65	/	/	/	/	ref. cat.	.
66-75	/	/	/	/	-,019	,896
76-85	/	/	/	/	,063	,748
86 or over	/	/	/	/	-,050	,855
Relationship of caregiver with patient						
Daughter or son (in law)	/	/	/	/	ref. cat.	.
Partner	/	/	/	/	-,057	,672
Parent	/	/	/	/	-,728	,008
Sibling	/	/	/	/	-,004	,991
Other family member	/	/	/	/	,433	,218
No family	/	/	/	/	-,239	,501

Support for physical, psychosocial and practical tasks are variables based on principal component analysis with the factor scores saved. Estimates represent Standardised mean differences with the reference category (ref. cat).

* Not applicable as the parameter was not included in the multivariate model of the respective task as it was not statistically significant (p>0.05) in one-way ANOVA tests

Discussion

Main findings

This study aimed to investigate how family caregivers of people with serious illness are supported by healthcare professionals in their caregiving tasks. Most take on many different caregiving tasks in the final three months before bereavement and the majority had desired to take them on. Professional support in performing these tasks is mostly provided by GPs and home care nurses, mainly by explaining how they can perform the tasks themselves. The majority of family caregivers evaluated this support as being sufficient. The use of specialised palliative care services was the strongest predictor for receiving more support from healthcare professionals across all caregiving tasks.

Strengths and limitations

Our study has several strengths. Firstly, it is innovative in its focus on support for the family caregiver as a member of the care team, where previous studies have mainly focused on their roles as a provider of care for the patient or as people themselves in need of care. Secondly, our study used a unique sampling frame by combining registers of health insurers thus representing the targeted population more accurately. Our method has distinct advantages in avoiding selection bias compared with most other studies as they recruit family caregivers already using professional services like palliative care. Thirdly, our survey was available both on paper and online to minimise technical barriers, which resulted in a higher response rate (55.0%) compared with other studies with a similar population[35–37].

Our study also has limitations. Firstly, our sample was based on registered family caregivers, so we did not include people who provided family care without being registered by one of the health insurers. This could have introduced some selection bias, excluding those who did not consider themselves a family caregiver. Our selection probably corresponds well with the population recognised by healthcare professionals as family caregivers in serious illness, which limits the inclusion of relatively sudden deaths with little opportunity for family caregiving support. A second limitation is one inherent in the use of self-administered surveys i.e. missing data for certain questions are high, possibly due to the length of the questionnaire. As missings seem random, this is not likely to have had an impact on our findings. Thirdly, the retrospective approach can introduce recall bias, possibly altering the assessment of the support received. However, the time between the activity and the questionnaire completion was a maximum of nine months. Additionally, the death of a loved one is an example of a highly emotional, infrequent life event, which is more easily recalled than a neutral recurring event[38].

Interpretation

Previous studies have demonstrated that family caregivers experience a great impact on their emotional and physical health[39] while taking on a wide range of caregiving tasks[5]. Healthcare professionals can equip them with knowledge and skills and empower them in their role[40]. The results of this study are reassuring as most family caregivers feel sufficiently supported by healthcare professionals. This is in contrast with a part of the literature where bereaved family caregivers report high levels of distress[15–17] and a lack of support[13]. Post-hoc rationalisation could be a possible explanation, i.e. the tendency to retrospectively approve of what happened. Additionally, there are indications that care clients tend to perceive healthcare professionals as someone to only appeal to for tackling acute care needs[41].

Most of the support by healthcare professionals was to inform family caregivers on how they could perform the tasks. An empowering collaborative approach, e.g. the items in the questionnaire referring to healthcare professionals letting family caregivers practise caregiving tasks or doing caregiving tasks together with them, was less frequently reported. Information is an important part of support[42], yet other research has shown that family caregivers prefer a guided learning process[43].

Most family caregivers received support from healthcare professionals, yet only 36.7% received specialised palliative care services. As the involvement of specialised palliative care was associated with more professional support, these findings confirm that palliative care is also intended to support family caregivers[21]. This seems to suggest that integrating palliative care into standard care can lead to a more collaborative and empowering approach towards family caregivers. Research shows that when healthcare professionals involve family caregivers in adequate care planning and acknowledge their burden, the quality of care improves[44,45]. Educational programs aimed at improving the self-efficacy of family caregivers such as the FOCUS program[46,47] are examples of how this can be achieved.

Conclusion

This population-based survey of bereaved family caregivers of people with serious illness provides evidence that they do receive professional support in their caregiving tasks. However, this support mostly concerns provision of information whereas a more empowering approach, i.e. aimed at increasing self-efficacy, is rare. The finding that involvement of specialised palliative care is associated with more professional support for family caregivers for their various tasks indicates a need to diffuse the patient-and-family caregiver approaches of palliative care more widely.

Declarations

Authorship

J.C., A.D.V., L.D., P.H. and C.V. designed the study. O.M., S.D., A.D.V., J.C., L.L., L.D. and P.H. contributed to the interpretation of the results. O.M. wrote the manuscript and all authors critically revised the manuscript and approved the final version.

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Conflicts of interest

The authors declare that there is no conflict of interest.

Data sharing

The datasets are not publicly available to safeguard the privacy of the participants but are available from the corresponding author on reasonable request.

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Chapter III

Is pre-bereavement collaboration between family caregivers and healthcare professionals associated with post-bereavement emotional wellbeing? A population-based survey

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Abstract

Objective: To investigate pre-bereavement collaboration with healthcare professionals and its association with emotional wellbeing of family caregivers of people with serious illness post-bereavement.

Methods: Population-based cross-sectional survey of bereaved family caregivers of people with serious illness (N=3000) who died two to six months before the sample was drawn (November 2019), identified through three sickness funds in Belgium.

Results: Response rate was 55%. As measured by the Positive and Negative Affect Schedule (PANAS), family caregivers scored lower on positive affect (PA) and higher on negative affect (NA) compared to a normative sample. Most family caregivers evaluated the pre-bereavement collaboration with healthcare professionals positively. Family caregivers' evaluation of collaboration with healthcare professionals pre-bereavement was positively associated with PA and negatively with NA, also when controlling for confounding effects of socio-demographic and clinical characteristics of the bereaved family caregiver and the deceased person.

Conclusion: There is a positive association between perceived quality of collaboration at the end of life between healthcare professionals and family caregivers and post-bereavement emotional wellbeing of family caregivers.

Practice implications: Our findings suggest the pertinence of attention from healthcare professionals to effective collaboration with family caregivers.

Background

Due to the increasingly ageing population and the rise in the number of people with a serious medical condition[1], more and more families are required to undertake caregiving during serious illness, including end-of-life care. Caring for a person with a serious illness and experiencing the death of a loved one are recognized as very emotional and distressing life events[2]. At the end of life, many family caregivers have unmet support needs and problems[3], despite the healthcare professionals' policy to support family caregivers[4]. Due to lack of communication and information, family caregivers report feeling uncertain in many areas – including medical (e.g. prognosis), practical (e.g. estate planning) and psychosocial (e.g. changing family dynamics)[5]. When family caregivers do have the required knowledge to carry out certain caregiving tasks, they experience less burden[6].

After death, the operational day-to-day caregiving tasks cease, yet the family caregiver often enters the bereavement phase feeling emotionally exhausted[7]. Bereavement outcomes and their predictors among family caregivers have been widely studied. Schulz et al[8] found that a positive caregiving experience results in higher quality of life, increased social activity, fewer psychological problems, and reduced use of medication post-bereavement. In contrast, family caregivers who experienced a high mental burden before bereavement show higher levels of distress after bereavement[9]. A study among family caregivers of advanced cancer patients showed that those who had to change their employment status as a result of their caregiving role also report higher stress levels post-bereavement[10]. Moreover, many studies have explored the effect of the circumstances of death on bereavement: for example, whether a sudden or unexpected death leads to worse bereavement outcomes than an anticipated death[11,12]. Previous research has also studied the association between quality of care at the end of life and its association with grief and post-bereavement wellbeing. An interview study conducted by Wilson[13] showed that pre-bereavement communication and actions have an impact on the bereavement process – for example, healthcare providers who supported family caregivers before the death of their loved one had a positive influence on the resolution process post-bereavement, whereas unhelpful words from others hindered their bereavement recovery. In a longitudinal study, Garrido and Prigerson[14] found that a better quality of death predicted better quality of life and mental wellbeing in bereaved family caregivers six months post-bereavement.

Examination of the association between quality of care pre-bereavement and the bereavement process suggests that the quality of collaboration with healthcare professionals in their support of family caregivers may play an important role. Collaboration in healthcare is described as two or more individuals from different backgrounds with complementary skills interacting to create a shared understanding that none had previously possessed or could have come to on their own[15]. Collaboration can entail many different aspects, such as family caregivers feeling professionally supported, relationship building with healthcare professionals, and acquiring knowledge [16]. It has been proposed that effective collaboration between healthcare professionals and family caregivers may offer health benefits related to the family caregivers' emotional wellbeing and burden during the caregiving phase[17].

Indeed, one qualitative study found that family caregivers who were well informed by healthcare professionals about the patient's health status coped better with their grief[18]. Hence, collaboration may thus also impact bereavement experiences. However, the relationship between the quality and type of collaboration during family caregiving prior to death and bereavement outcomes is still inadequately studied and poorly understood and needs further investigation[19]. For example, most studies have used a qualitative design and have provided some foundational understanding of the potential existence of such an association[18,20–22], while other studies have explored associations with broad concepts such as quality of life[8,9,23].

Given this background, we investigated the emotional wellbeing of family caregivers of people with a serious illness after bereavement and its association with pre-bereavement collaboration with healthcare professionals. Our research questions were:

1) *What is the emotional wellbeing of family caregivers after bereavement?*
2) *How do family caregivers evaluate the pre-bereavement collaboration with healthcare professionals?*
3) *Is a better evaluated pre-bereavement collaboration between family caregivers and healthcare professionals associated with higher emotional family caregiver wellbeing after bereavement?*

Methods

Study design and setting

We conducted a population-based cross-sectional survey among bereaved family caregivers in Flanders, Belgium. In Belgium, people with long-term extensive care needs can apply for a monthly care budget that helps cover non-medical care. To identify participants, we used registers of health insurers, as they keep records of people who apply for a care budget, including who their family caregiver is. The three largest health insurers in Flanders participated: Christelijke Mutualiteit (Christian), Socialistische Mutualiteit (Socialist), and Liberale Mutualiteit (Liberal), which accounted for 79% (51%, 22%, and 6%, respectively) of the total population in Flanders[24]. We applied the Strengthening of the Reporting of Observational studies in Epidemiology (STROBE)[25] statement to describe all relevant aspects of the study.

Participants

We randomly sampled 3000 deaths of people with a serious illness who applied for a care budget from one of the participating health insurers. For these deaths, the persons who were registered in the database as their primary family caregiver were selected. The sample was proportionally distributed among the health insurers according to the total number of family caregivers meeting the inclusion criteria (Christelijke Mutualiteit n=2,748; Socialistische Mutualiteit n=157; Liberale Mutualiteit n=95). Based on recommendations in other studies[26–28], we included family caregivers who provided care to a person who died at least two months, but no more than six months, prior to inclusion to allow sufficient time for grieving, while limiting potential recall bias. Additional inclusion criteria were that the postal address of family caregivers had to be complete in the database, and the family caregiver and deceased person had to be at least 18 years old.

Data collection

An independent research assistant sent out the questionnaires by post between November 2019 and January 2020. The Dillman's Total Design Method[29] was applied, with the aim of obtaining a higher response to the survey. At the start of data collection (day 1), each family caregiver received a questionnaire and information letter which provided details about the study, the voluntary nature of their participation, and the option to complete an online version of the questionnaire. In case of non-response, a reminder letter was sent after two and four weeks (day 15 and 29). After another two weeks (day 45), a non-response questionnaire was sent. The purpose of the non-response questionnaire was to evaluate reasons for non-response and possible non-response bias.

Measures

The questionnaire consisted of both validated and self-developed items. The emotional wellbeing of family caregivers after bereavement was our primary outcome, the independent variable (exposure variable) of interest was the family caregivers' evaluation of the collaboration with healthcare professionals. Additionally, various socio-demographic characteristics were considered as possible confounders. We tested the questionnaire through two rounds of cognitive interviews with five family caregivers each, recruited through convenience sampling. The cognitive testing resulted in adding questions (e.g., questions 2 and 4 (Appendix A1)), changing the sentence structure of certain items, and clarifying certain concepts.

Emotional wellbeing

We used the Dutch translation of the validated Positive and Negative Affect Schedule (PANAS)[30,31] to measure the family caregivers' emotional wellbeing in the past week. The Dutch version of the PANAS proved to be a reliable and valid measure of self-reported wellbeing. The PANAS contains two sub-scales – positive affect (PA) and negative affect (NA) – with 10 items in each scale. Each item is scored with a minimum of 1 (Very slightly or not at all) and a maximum of 5 (Extremely). Sum scores on both PA and NA range between 10 (Very slightly or not at all) and 50 (Extremely).

Exposure variable: family caregivers' evaluation of collaboration with healthcare professionals

As no pre-existing validated instruments were identified as appropriate to measure the family caregivers' evaluation of collaboration, we developed nine items based on modifying existing instruments[32,33], and preceding qualitative interviews[34]. Items were measured on a 5-point Likert scale, ranging from 1 (totally disagree) to 5 (totally agree) (for the questionnaire, see Appendix A1). These items were face-validated through two rounds of cognitive testing with five family caregivers each, recruited through convenience sampling. The cognitive testing resulted in changing the sentence structure of certain items and clarifying certain concepts.

Possible confounders: socio-demographic characteristics of the family caregiver and the deceased person and illness characteristics of the deceased

We identified a number of possible confounders, i.e., variables that could plausibly (or as identified in published research) influence both the collaboration with healthcare professionals and the emotional wellbeing post-bereavement. These included family caregivers' age, sex, educational attainment, relationship with the deceased, whether the family caregiver lived with the deceased person in the final three months of life, and the patient's age, main illness, and decisional capacity in the last three months. Additionally, the involvement of palliative care services was identified as a potential confounder.

Statistical analysis

To accurately answer the research questions, family caregivers were included for analysis only if 1) they had contact with the person they were caring for during the last three months of life (question 2 in questionnaire, see Appendix A1), and if 2) the deceased person had at least one of the listed serious illnesses (question 3 in questionnaire).

We used descriptive statistics to summarize socio-demographic characteristics, the emotional wellbeing of family caregivers, and the evaluation of collaboration with healthcare professionals. In addition to an exploration of the scree plot, a factor analysis was performed to determine the extent to which each item in the self-developed collaboration scale is associated with the concept of collaboration. The standardized factor scores were saved and used for the analyses.

Next, the Cronbach's alpha was measured to confirm internal consistency within the self-developed collaboration items. The association between family caregivers' evaluation of pre-bereavement collaboration with healthcare professionals and post-bereavement emotional wellbeing was described using Spearman correlation. To correct this association for relevant confounders, we performed a multivariable (i.e., several independent variables) multivariate (i.e., 2 dependent variables, PA and NA sub-scales) analysis of covariance (MANCOVA) – controlling for those confounders that were identified in bivariable analysis as significantly associated with both the exposure variable and the outcome variable. Preliminary MANCOVA assumptions were tested to check for homogeneity of variance and covariance for both PA and NA. A MNCAR assumption was made for missing data, and a simple means imputation for missing values was used for the outcome variable. As is recommended by the STROBE guidance[25], a sensitivity analysis was performed with a MCAR assumption for missing data (i.e., no imputation).
We used SPSS Statistics 27 for data analysis.

Ethical considerations

The Ethics Commission of Vrije Universiteit Brussel approved the study procedure and materials (approval number B.U.N. 143201940562, 17/06/2019). The study was conducted in accordance with the Declaration of Helsinki. Participants were informed that they gave their informed consent implicitly by completing and returning the questionnaire.

Results

Of the 3,000 people sampled, 2,889 received the questionnaire (Figure 1). A non-response survey showed that 89 participants of this sample were ineligible (reasons for non-participation are presented in Table A5 in Appendix), resulting in 2,800 people fitting our sample. In total, 1,539 completed the questionnaire, resulting in a response rate of 55%. In total, 1,334 respondents were included for analysis as per the eligibility criteria described in the methods section.

Sample characteristics

Most family caregivers were women (68.2%) (Table 1). Family caregivers were on average 65.5 years old (standard deviation 12.0) and ranged from 18 to 102 years old. About half of the family caregivers had obtained a secondary education (46.1%), and 13.2% had a professional healthcare degree (e.g., physician, nurse). The majority were child (51.7%) or partner (34.4%) to the deceased person. One out of three (36.7%) lived with the deceased person in the last three months of life. About half (46.9%) of the family caregivers were retired.

The deceased persons ranged in age from 18 to 101, with a mean of 78.3 (standard deviation 13.4). The most common serious illnesses were cancer (31.8%) and dementia (30.7%). Four out of ten deceased persons (40.2%) were capable of making decisions about their care in the last three months of life. A total of 36.7% received support from specialized palliative care services. About half of the deceased persons lived at home for most of the time during the last three months of life (51.6%).

Figure 1: Participants flowchart

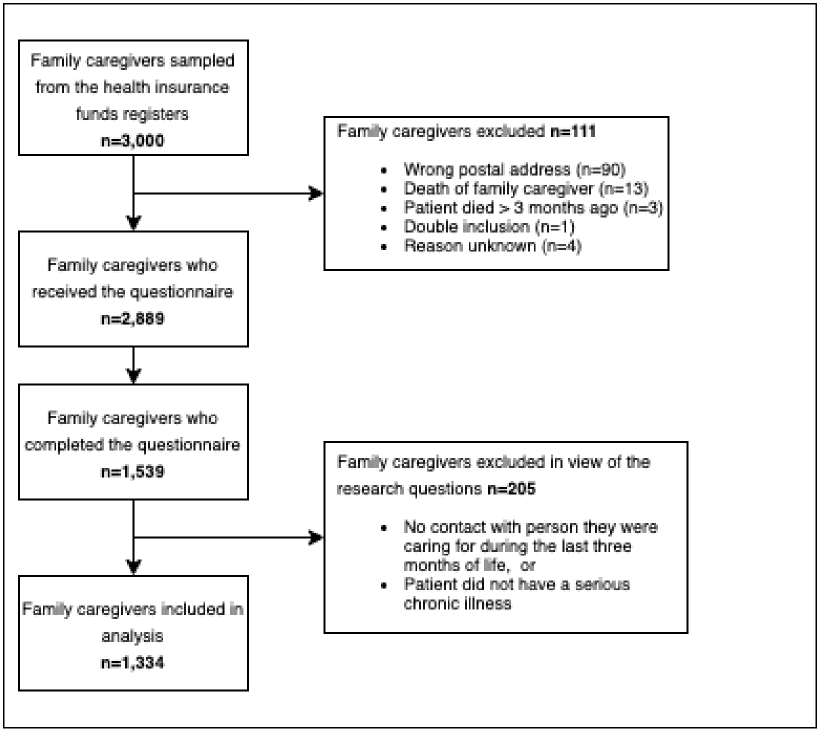

Table 1: Characteristics of the sample (N=1.334)

Characteristics of bereaved family caregivers	**N *(%)***
Age in years	
18-55	238 *(18.2)*
56-65	488 *(37.3)*
66-75	305 *(23.3)*
76-85	202 *(15.4)*
>85	76 *(5.8)*
Mean *(SD)*	65.5 *(11.96)*
Sex	
Female	892 *(68.2)*
Male	416 *(31.8)*
Educational attainment	
Primary education	212 *(16.2)*
Secondary education	603 *(46.1)*
Bachelor's degree or equivalent	364 *(27.9)*
Master's degree (University)	90 *(6.9)*
None of the above	38 *(2.9)*
Relationship with the deceased person, family caregiver is …	
Daughter or son (in law)	687 (51.7)
Partner	457 *(34.4)*
Parent	67 *(5.0)*
Sibling	34 *(2.6)*
Other family member	55 *(4.1)*
Not family	29 *(2.2)*
Lived together with deceased person in the last three months	478 *(36.7)*
Has a physician, nursing, or healthcare degree	167 *(13.2)*
Employment status	
Retired	612 *(46.9)*
Full-time employed	271 *(20.8)*
Part-time employed	232 *(17.8)*
Homemaker	103 *(7.9)*
Other	58 *(4.4)*
Unemployed	30 *(2.3)*
PANAS score	Mean (*SD*)
Positive Affect	29.38 *(8.01)*
Negative Affect	21.67 (*7.90)*
Characteristics of deceased person	
Age in years	
18-55	89 *(6.7)*
56-65	181 *(13.9)*
66-75	204 *(15.7)*
76-85	318 *(24.4)*
>85	510 *(39.2)*
Mean *(SD)*	78.34 *(13.79)*

Serious illness*	
Cancer	424 *(31.8)*
Dementia	410 *(30.7)*
Other	315 *(23.6)*
Heart failure	262 *(19.6)*
Respiratory disease	227 *(17.0)*
Diabetes	195 *(14.6)*
Renal or liver disease (not cancer)	171 *(12.8)*
Stroke (or the consequences thereof)	146 *(10.9)*
Disease of the nervous system other than dementia	95 *(7.1)*
Capable of making decisions about their care in the last 3 months of life	
Yes	529 *(40.2)*
No	430 (*32.7)*
Sometimes / partly	357 *(27.1)*
Specialised palliative care received	
No	762 (60.3)
Yes	464 (36.7)
I don’t know	38 (3.0)

Missing values bereaved family caregivers: Age in years: n=25 (1.9%); Sex: n=26 (1.9%); Education: n=27 (2.0%); Relationship with the deceased: n=5 (0.4%); Region: n=25 (1.9%); Living together with deceased loved one in the last three months: n=30 (2.2%); Diploma of doctor. nurse or healthcare formal: n=65 (4.9%); Employment status: n=28 (2.1%)
Missing values deceased person: Age in years: n=32 (2.4%); Capable of making decisions about his/her care in the last 3 months: n= 18 (1.3%); Specialised palliative care received: n=70 (5.2%)
*Percentages do not add up to 100% as multiple answers were possible.

Family caregivers’ emotional wellbeing post-bereavement

The scores for the Positive and Negative Affect Schedule are shown in Table 2. The positive affect (PA) and negative affect (NA) sub-scales demonstrated very high internal consistency (Cronbach’s Alpha of 0.898 and 0.847, respectively). The mean value of the PA sub-scale increasing from 10 (very slightly or not at all) to 50 (extremely) was 29.38 with a standard deviation of 8.01. This mean value for PA is lower compared to the mean in a normative sample (31.31)[31]. At item level, the item ‘Feeling interested’ had the highest mean value of 3.48 (SD=1.122); ‘enthusiastic’ had the lowest mean value of 2.45 and the highest variation (SD=1.149). The mean value of the NA sub-scale going from 10 (very slightly or not at all) to 50 (extremely) was 21.7 with a standard deviation of 7.9. This mean value for NA is higher compared to the mean in a normative sample (16.0)[31]. ’Distressed’ had the highest mean value of 3.33 and the highest variation (SD=1.29). ‘Ashamed’ had the lowest mean value of 1.36 and the lowest variation (SD=0.805).

Table 2: Emotional wellbeing of family caregivers after bereavement (PANAS)

	Scores (%)					Descriptive values		Internal consistency
	Very slightly or not at all (1)	A little (2)	Moderately (3)	Quite a bit (4)	Extremely (5)	Mean score	SD	Cronbach's Alpha
Positive Affect*						29.38	*8.01*	*.898*
Interested	5.4	12.4	33.3	27	21.9	3.48	*1.12*	
Excited	20.8	22.4	37.2	16.6	3.1	2.59	*1.08*	
Strong	10.2	15.1	38.9	27.2	8.6	3.09	*1.08*	
Enthusiastic	28.6	19	35.4	12.9	4	2.45	*1.15*	
Proud	11.4	19.6	39.7	21.2	8.1	2.95	*1.09*	
Alert	5.7	12.7	37.4	30.1	14.2	3.34	*1.05*	
Inspired	24.6	21.8	37.1	12.5	4	2.49	*1.11*	
Determined	10.7	16.4	41.5	22.2	9.1	3.03	*1.09*	
Attentive	5.7	14.9	39.8	28.3	11.2	3.25	*1.02*	
Active	14.5	19.5	41.3	18.2	6.5	2.83	*1.09*	
Negative Affect*						21.67	*7.90*	*.847*
Distressed	8.6	22.6	19.8	25.2	23.8	3.33	*1.29*	
Upset	27.9	27.8	19.9	15.8	8.6	2.49	*1.28*	
Guilty	64.9	17.4	8.3	5.5	3.8	1.66	*1.09*	
Scared	54.5	22.1	11.6	7	4.9	1.86	*1.17*	
Hostile	80.1	9.2	6.1	3.2	1.5	1.37	*.85*	
Irritable	32	29.1	19.7	14.2	5.1	2.31	*1.20*	
Ashamed	79.5	9.5	8	1.7	1.3	1.36	*.81*	
Nervous	18.1	29.7	21.8	20.9	9.5	2.74	*1.24*	
Jittery	23.8	25.8	21.6	19.4	9.4	2.65	*1.29*	
Afraid	52.9	21.5	11.8	7.3	6.6	1.93	*1.23*	

*The minimum score for Positive and Negative Affect is 10. The maximum score for Positive and Negative Affect is 50.

Family caregivers' evaluation of pre-bereavement collaboration with healthcare professionals

Based on the exploration of the scree plot of the factor analysis of the collaboration items, we identified one clear dimension that described the collaboration of family caregivers with healthcare professionals (Appendix A11). A further exploration of Cronbach's Alpha resulted in the removal of the first item of the collaboration items ('*I was given sufficient freedom to help determine how the care for my loved one was organized and carried out*').

The majority of family caregivers evaluated the pre-bereavement collaboration items with healthcare professionals positively (Table 3); 79% felt attuned with healthcare providers about the care for their loved one; 76% felt that their healthcare professionals were always available when they wanted to call on them; 79% stated that they received sufficient information about the condition of their loved one; 74% thought that the information was provided in an appropriate manner; and 78% indicated that, in general, healthcare professionals communicated well with them.

About one out of four family caregivers reported that they weren't given enough freedom to co-determine how care for their loved one was organized and carried out. Additionally, 18% of family caregivers stated that they had not received sufficient information about available healthcare professionals and services they could turn to for support.

The association between family caregivers' evaluation of pre-bereavement collaboration with healthcare professionals and family caregivers' emotional wellbeing post-bereavement

Family caregivers' evaluation of collaboration with healthcare professionals was positively correlated with PA (r=.13 p<.001) and negatively correlated with NA (r=-.13, p<.001) (Table A12 in Appendix). A multivariable multivariate analysis showed a statistically significant association of emotional wellbeing post-bereavement with collaboration, as well as with the degree of surprise about the patient's death, relationship with patient, patient's decisional capacity, collaboration and patient staying at home (Table A13 and A14 in Appendix). A sensitivity analysis without mean imputation confirmed these results (i.e., same significant associations, Appendix A15).

The MANCOVA results (Table 4) showed that, when taking into account these confounding factors, the association between the evaluation of pre-bereavement collaboration with healthcare professionals on the one hand and positive and negative affect post-bereavement on the other hand remained significant (both p<.001), with a higher evaluated pre-bereavement collaboration being associated with a higher positive affect [F(1,825) = 20.549, p<.001] and a lower negative affect [F(1,825) = 18.229, p<.001] post-bereavement. For both PA and NA, effect sizes were small (η^2 = .024 and .022, respectively).

Table 3: Family caregivers' evaluation of collaboration with healthcare professionals (%)

		Answer options			
		(totally) disagree	neutral	(totally) agree	Not applicable
a)	I was given sufficient freedom to help determine how the care for my loved one was organized and carried out	24.6	13	52.7	9.6
b)	I think that I was well attuned to the healthcare professionals in the care for my loved one	6.5	11	78.6	3.9
c)	Healthcare professionals were always available when I wanted to call on them	11.1	9.1	76.3	3.5
d)	Healthcare professionals showed me sufficiently that I was allowed to ask them questions when I had them	14.3	12.9	65.9	6.9
e)	I have been given enough information about the available healthcare professionals and services that I could turn to for help	18.4	13.2	61.9	6.5
f)	I have received sufficient information about my loved one's condition	11.9	7.3	78.6	2.1
g)	Information was generally provided to me in an appropriate manner (e.g. clearly, on time, taking into account my feelings) by healthcare professionals	10.6	12	74.1	3.3
h)	In general, I found that healthcare professionals communicated well with me	7.2	11.9	78.3	2.6
i)	The healthcare professionals had enough expertise to support me appropriately as the end of my loved one's life approached	13.8	12.2	66.2	7.8

Missing values: a) 9.0%, b) 6.9%, c) 6.8%, d) 8.8%, e) 8.5%, f) 5.8%, g) 7.9%, h) 5.8%, i) 9.1%

Table 4: The predictors of emotional wellbeing post-bereavement

Test of between-subjects effects

Source	Dependent variable	df	F	Sig.	Partial Eta Squared (η^2)
Corrected Model	Positive Affect	34	3.773	<.001	.135
	Negative Affect	34	3.119	<.001	.114
Intercept	Positive Affect	1	664.058	<.001	.446
	Negative Affect	1	266.158	<.001	.244
Collaboration	Positive Affect	1	20.549	<.001	.024
	Negative Affect	1	18.229	<.001	.022
Degree of surprise about death of patient	Positive Affect	1	4.865	.028	.006
	Negative Affect	1	3.694	.055	.004
Relationship with patient	Positive Affect	5	3.009	.011	.018
	Negative Affect	5	2.947	.012	.018
Capability of patient of making own decisions	Positive Affect	2	1.711	.181	.004
	Negative Affect	2	1.62	.199	.004
Patient staying at home	Positive Affect	4	1.768	.133	.008
	Negative Affect	4	4.635	.001	.022
Error	Positive Affect	825			
	Negative Affect	825			
Total	Positive Affect	860			
	Negative Affect	860			
Corrected Total	Positive Affect	859			
	Negative Affect	859			

MANCOVA assumptions were evaluated; Box's M=43.427 indicates that the homogeneity of covariance matrices is assumed [F(30,1155.390)=.87, p=.663].
Levene's test shows that the variances for both PA [F(799,60)=.776, p=.926] and NA [F(799,60)=1.322, p=.087] are homogeneous.
The contrast results of the significant predictors can be found in Appendix A14.

Discussion and conclusion

Discussion

This study investigated the association between pre-bereavement collaboration with healthcare professionals and the emotional wellbeing of family caregivers of people with a serious illness after bereavement.

We found that bereaved family caregivers experience lower emotional wellbeing in the two to six months post-bereavement, compared to a reference average population. This corroborates previous research, in which bereaved family caregivers report high rates of anxiety and depressive symptoms[35]. This finding is not surprising, as caring for a person with a serious illness and losing that loved one are recognized as very emotional and distressing events that can occur during an individual's life[2]. The reduced emotional wellbeing post-bereavement highlights the importance of post-loss support for family caregivers. However, even though bereavement care is an integral component of palliative care[36], in reality it is not always applied[37].

While our findings show that most family caregivers evaluated the pre-bereavement collaboration with healthcare professionals positively, previous qualitative research shows that even though family caregivers are generally satisfied with the collaboration, they also indicate that there are many missed opportunities for collaboration and that there is still room for improvement to recognize family caregivers as both clients in need of care support and as collaborating members of the care team [34]. Relatives sometimes feel uninformed and 'left in the dark'[38,39]. Vermorgen[34] suggests five important attention points for effective collaboration in palliative and end-of-life care: respecting the family caregiver both as someone with care needs and as a member of the care team; the continuous availability and accessibility of healthcare professionals; the sharing of information and communication on (for example) family caregivers' issues; the coordination of care between all parties; and contextual factors (e.g., family caregivers' vocational experience in healthcare).

Our study adds to the literature by suggesting a positive association between effective collaboration at the end of life between healthcare professionals and family caregivers and the bereavement process of family caregivers. While further prospective longitudinal studies and mixed methods studies are perhaps warranted to confirm and better understand the mechanism for this association, we can speculate on plausible mediators. Family caregivers' evaluation of collaboration with healthcare professionals pre-bereavement was positively correlated with positive affect and negatively correlated with negative affect post-bereavement. This corroborates previous research, which found that, when collaboration is integrated in end-of-life care, relatives report higher satisfaction with the quality of care the patient received[40]. A better perceived quality of care at the end of life is, in its turn, associated with a better bereavement response[41]. Family caregivers who are well informed about the patient's health status cope better with grief[18]. This association is possibly mediated by higher self-efficacy, reduced uncertainty, mutual communication, and understanding.

Our study has several strengths. First, we focused on the collaboration with the family caregiver as a member of the care team, whereas most studies mainly focus on family caregivers as providers of care or as people in need of care themselves. Second, we used a unique sampling frame by combining registers of health insurers. This method has distinct advantages compared to most other studies that suffer from selection bias, as they often recruit family caregivers through professional services (like palliative care), which means that they have already found their way to a professional support service. Thus, our study sample represents the targeted population of family caregivers more accurately. Third, the survey was available both on paper and online to minimize technical barriers, which resulted in a high response rate (55.0%) compared to other studies with a similar population[42–44].

Our study also has several limitations. First, the cross-sectional design of the study allowed us to explore the association between pre-bereavement collaboration with healthcare professionals and emotional wellbeing post-bereavement of family caregivers, but this design is not suitable for making causal inferences. Therefore, additional research using other designs is necessary to examine the possible causal mechanism of this association. Second, the sample was based on registered family caregivers, so we did not include people who provided family care without being registered as such by one of the health insurers. This likely introduces some remaining selection bias with those who do not regard themselves as a family caregiver. Nevertheless, we believe this selection bias is minimal. Third, the retrospective approach of the questionnaire can introduce recall bias, possibly altering the assessment of the support received to some extent. However, the time between questionnaire completion and the family caregiving period was maximum nine months. Additionally, the death of a loved one is an example of a highly emotional, infrequent life event, which is more easily recalled than a neutral recurring event[45]. Fourth, the emotional wellbeing of family caregivers was measured at one point in time in the months after bereavement. More frequent assessments of emotional wellbeing using longitudinal design could provide more in-depth insights into the evolution of the emotional states of bereaved family caregivers over time. Finally, collaboration in end-of-life care is a relatively new topic that has not been widely studied. Consequently, pre-bereavement collaboration between healthcare professionals and family caregivers was measured with self-developed items, as there were no validated questionnaires at hand. However, the self-developed items were based on a preceding qualitative study[34] and existing instruments[32,33].

Conclusion

Family caregivers' evaluation of pre-bereavement collaboration with healthcare professionals was positively associated with PA and negatively associated with NA post-bereavement, also when controlling for confounding effects of socio-demographic and clinical characteristics of the bereaved family caregiver and the deceased person. On average, bereaved family caregivers scored lower on positive affect (PA) and higher on negative affect (NA) compared to a normative sample. In general, family caregivers evaluated the pre-bereavement collaboration with healthcare professionals positively.

This population-based survey of bereaved family caregivers of people with serious illness provides provisional evidence that good collaboration between family caregivers and healthcare professionals can lead to better emotional wellbeing post-bereavement. Future research could provide confirmation for this association, further explore how this collaboration can be enhanced, and shed light on the mechanisms of how collaboration positively affects emotional wellbeing of family caregivers post-bereavement.

Practice implications

The association between pre-bereavement collaboration with healthcare professionals and bereavement further underlines the importance of high quality collaboration between healthcare professionals and family caregivers, which is in keeping with the standards of palliative care, which stress that the needs of family caregivers should be taken into consideration. It was already known that pre-bereavement collaboration has an impact on the quality of care[41], but this study suggests that it can also have an impact on family caregiver health post-bereavement. Our findings suggest the pertinence of attention from healthcare professionals to effective collaboration. Previous research has found that attention points for improved family caregiver/health professional collaboration concern respecting the family caregiver as both someone with care needs and as a member of the care team and providing tailored information to family caregivers specifically[34]. Formally developing guidelines based on these insights to improve effective collaboration could positively impact the emotional wellbeing of family caregivers post-bereavement.

Declarations

Authorship

J.C., A.D.V., L.D., P.H. and C.V. designed the study. O.M., S.D., A.D.V., J.C., L.L., L.D. and P.H. contributed to the interpretation of the results. O.M. wrote the manuscript, and all authors critically revised the manuscript and approved the final version.

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Conflicts of interest

The authors declare that there is no conflict of interest.

Data sharing

The datasets are not publicly available to safeguard the privacy of the participants but are available from the corresponding author on reasonable request.

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PART II
The development of the DIAdIC study

Chapter IV

Effectiveness of a nurse-delivered (FOCUS+) and a web-based (iFOCUS) psychoeducational intervention for people with advanced cancer and their family caregivers (DIAdIC): study protocol for an international randomized controlled trial

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Abstract

Background: Worldwide, millions of people with advanced cancer and their family caregivers are experiencing physical and psychological distress. Psychosocial support and education can reduce distress and prevent avoidable healthcare resource use. To date, we lack knowledge from large-scale studies on which interventions generate positive outcomes for people with cancer and their informal caregivers' quality of life. This protocol describes the DIAdIC study that will evaluate the effectiveness of two psychosocial and educational interventions aimed at improving patient-family caregiver dyads' emotional functioning and self-efficacy.

Methods: We will conduct an international multicenter three-arm randomized controlled trial in Belgium, Denmark, Ireland, Italy, The Netherlands, and the United Kingdom. In each country, 156 dyads (936 in total) of people with advanced cancer and their family caregiver will be randomized to one of the study arms: 1) a nurse-led face-to-face intervention (FOCUS+), 2) a web-based intervention (iFOCUS) or 3) a control group (care as usual). The two interventions offer tailored psychoeducational support for patient-family caregiver dyads. The nurse-led face-to-face intervention consists of two home visits and one online video session and the web-based intervention is completed independently by the patient-family caregiver dyad in four online sessions. The interventions are based on the FOCUS intervention, developed in the USA, that addresses five core components: family involvement, optimistic outlook, coping effectiveness, uncertainty reduction, and symptom management. The FOCUS intervention will be adapted to the European context. The primary outcomes are emotional functioning and self-efficacy of the patient and the family caregiver, respectively. The secondary outcomes are quality of life, benefits of illness, coping, dyadic communication, and ways of giving support of the patient and family caregiver.

Discussion: DIAdIC aims to develop cost-effective interventions that integrate principles of early palliative care into standard care. The cross-country setup in six European countries allows for comparison of effectiveness of the interventions in different healthcare systems across Europe. By focusing on empowerment of the person with cancer and their family caregiver, the results of this RCT can contribute to the search for cost-effective novel interventions that can relieve constraints on professional healthcare.

Trial registration: Registration on ClinicalTrials.gov on 12/11/2020, identifier NCT04626349.

Background

Background and rationale

Each year, 3.7 million people in Europe are diagnosed with cancer, accounting for 1.9 million deaths[1]. The symptoms and burden of cancer patients range from anxiety and depression to pain and fatigue[2]. Something that is often overlooked is that the effects of cancer extend from patients to their family caregivers. A family caregiver is an unpaid, informal provider of care who has a personal connection to the patient (a friend, partner, ex-partner, sibling, parent, child, or other blood or non-blood relative) and provides one or more physical, social, practical, and emotional tasks[3]. The caregiving role they take on can result in severe physical, psychological, and emotional health problems (co-suffering) and an overall decline in quality of life (QoL), which has major public healthcare and health resource implications[4]. Taking into account an expected rise in the number of people with cancer, a significant increase in the ageing population, governments' efforts to limit the healthcare spending, and shortages of professional health caregivers, it is likely that the future need for adequate care in the population will increase dramatically and cannot be borne entirely by formal healthcare. At the same time, the population of unpaid caregivers is also becoming older and frailer, increasing the need to support their efforts.

Despite the serious problems that cancer creates for patients and their family caregivers, there are only a few interventions that target both patient and family caregiver to self-manage the effects of the advanced phase of the illness[5–7]. Literature shows that dyadic interventions, i.e. targeting the patient and family caregiver together, are more likely to result in better outcomes for both parties and are more cost-effective than single target interventions[8]. Interventions focusing on the QOL of both the patient and the family caregiver (i.e. the dyad) may promote their wellbeing, lessen their burden, and reduce the economic toll of advanced cancer care. By focusing on the empowerment of the dyad, pressure on professional care providers may also be reduced.

Currently, we lack the evidence to recommend which psychosocial and educational interventions, provided to both patients and their family caregivers will generate the most favourable outcomes for both. To select the most promising dyadic interventions to examine, the DIAdIC research consortium has assessed existing interventions that support patients with advanced cancer and their family caregivers, with a potential fit for Europe and that are relevant to the health objectives of the European Commission as outlined in the white paper "Together for Health: A Strategic Approach for the EU 2008-2013". The FOCUS intervention developed in the USA by Northouse et al[5] was identified as among the most effective and potentially relevant. The face-to-face FOCUS program was developed as a nurse-delivered face-to-face intervention offering information and support to both patients and family caregivers. Three randomized controlled trials (RCTs) in the USA demonstrated improved QoL and wellbeing of both patients and caregivers[5,7,9]. The dyads also reported significantly less negative appraisal of illness and caregiving, less uncertainty and hopelessness, improved communication within dyads, and improved caregiver self-efficacy compared to control dyads. To make the FOCUS program available to more people, the core component (increasing family involvement) of the face-to-face program was later translated into a tailored, web-based format[6]. For the web-based FOCUS intervention, significant effects were found in a pre-post study on dyads' QoL, emotional distress, perceived benefits of illness/caregiving, and caregivers' self-efficacy. The option of delivering a psychoeducational intervention via a computer program fits well in the era of telemedicine. The importance of providing support remotely is currently highlighted during the COVID-19 pandemic.

The existing FOCUS interventions from the USA have been substantially tailored, updated, and adapted by the DIAdIC research consortium to meet the needs of patients with advanced cancer and their family caregivers in six European countries. The core components of the face-to-face program have been translated into a web-based format. These adaptations and updates have led to the development of two new interventions: 1) the face-to-face FOCUS+ intervention and 2) the iFOCUS web intervention. The adaptation process will be reported elsewhere.

The **effectiveness, cost-effectiveness, and mechanisms of action** of both interventions will be investigated in a large-scale international randomized controlled trial (RCT). The current manuscript aims to present the research protocol of this RCT study. The **Standard Protocol Items: Recommendations for Interventional Trials** (SPIRIT) statement was applied to describe all relevant aspects of the trial.

Objectives

The overall aim of this project is to **evaluate the effectiveness, cost-effectiveness, and mechanisms of action of two psychoeducational interventions** (a face-to-face nurse-led intervention called FOCUS+ and a web-based intervention called iFOCUS) aimed at improving the emotional functioning and self-efficacy of patients with advanced cancer and their family caregiver. Both interventions are compared to care as usual.

Project objectives

(1) To compare 1) the face-to-face FOCUS+ intervention and 2) the iFOCUS web-based intervention to 3) care as usual in terms of their:

- Effect on the emotional functioning and self-efficacy (primary outcomes), appraisal of illness, uncertainty, hopelessness, coping, dyad communication, QoL, and healthcare resource use of patients with advanced cancer and their family caregivers

- Cost-effectiveness, taking into account the use of the formal health system, unpaid care burden, and QoL
- Effects on vulnerable subgroups (particularly women and those of lower socioeconomic status)
- Effectiveness in different healthcare systems

(2) To evaluate the implementation process of the interventions in terms of the acceptability, feasibility, usefulness as perceived by patients, family caregivers, and healthcare staff in each country, and their mechanisms of action.

Trial design

This study is an international multicenter parallel-group three-arm superiority trial comparing 1) the FOCUS+ face-to-face intervention (intervention 1) and 2) the iFOCUS web-based intervention (intervention 2) to 3) standard care (control group). We use a parallel-group design meaning that each group receives either intervention 1, intervention 2, or standard care as usual. As the risk of contamination is limited, an individual RCT rather than a cluster RCT is feasible and more appropriate.

Randomization will be performed per a computer randomization schedule with a **1:1:1 allocation ratio** to one of the two intervention arms or the standard care arm (control group).

Methods: Participants, interventions, and outcomes

Study setting

Both interventions (FOCUS+ and iFOCUS) will be administered in the homes of the patient-caregiver dyads (or in the location of the dyad's preference).

The interventions will be conducted in six countries (Belgium, Denmark, Ireland, Italy, the Netherlands, and the United Kingdom). The selection of countries is based on a number of considerations: (1) feasibility and capacity to conduct a large-scale complex trial in the targeted population, (2) a variation in healthcare and welfare system typologies (Bismarck, Beveridge, Social-Democrat systems[10]), (3) regional variation across Europe (Northern, Western, Southern) and (4) a relatively advanced level of palliative care development and integration within oncology care.

Eligibility criteria

Participants

The study population will consist of patients with advanced solid organ cancer (except brain cancer) and their primary family caregiver (as determined by the patient). The inclusion and exclusion criteria for both the patient and the family caregiver are described in Table 1. Patients with brain cancer are excluded as they may experience difficulty completing the intervention and questionnaires due to cognitive issues. Patients with a prognosis of fewer than 3 months are also excluded as they may be too vulnerable, and the interventions are tested over 3 months.

Table 1: Inclusion and exclusion criteria for patients and family caregivers

Inclusion criteria	***Screened by***	**Exclusion criteria**	***Screened by***
Patient			
Diagnosis of cancer: solid organ (lung, colorectal, breast, prostate, and other)	Treating clinician or RA*	Brain cancer, non-solid cancers	Treating clinician or RA
No longer receives curative treatment (only life-prolonging or palliative treatments)	Treating clinician or RA	Prognosis of fewer than 3 months	Treating clinician or RA
Treating clinician would not be surprised if the patient died within 2 years[19]	Treating clinician or RA	Has no family caregivers	RA

Written informed consent	RA	< 18 years old	RA
Lives within feasible distance for intervention nurses to travel	RA	Unable to participate in available languages	RA
Family caregiver			
Written informed consent	RA	Unable to physically or mentally participate	RA
Primary family caregiver as determined by patient	RA	Cancer diagnosis in the last 12 months	RA
Lives within feasible distance for intervention nurses to travel	RA	<18 years old	RA
		Unable to participate in available language	RA
Dyad			
Patient and/or family caregivers have access to and are familiar with the use of the internet	RA		
RA* = research assistant, either from the study team or in situ			

Previous studies of FOCUS interventions in the USA have found the interventions to be feasible and effective in a variety of solid cancer types as the interventions are tailored to the specific cancer type and symptoms patients experience[4,8].

Study centers

In each country, patients with advanced cancer and their primary family caregiver will be recruited and enrolled via participating hospitals. Inclusion criteria for hospitals participating in this study are that they 1) treat patients with advanced cancer and 2) deliver oncology care. The first selection of hospitals and departments within these hospitals (e.g. oncology, pneumology) is informed by the number of individual patients seen per year meeting the eligibility criteria, to ensure that we will be able to include sufficient patients to meet the requirements for statistical power.

Nurses performing the FOCUS+ face-to-face intervention

Two to four nurses per country will be hired on the project to conduct the FOCUS+ face-to-face intervention. They will be able to communicate in the language appropriate for their country and must be sufficiently proficient in English to be able to participate in the study training which will be delivered in English. They will have a professional nursing qualification as recognized in each participating country. The nurses will have significant clinical experience with people with advanced cancer and/or palliative care. An overview of the qualification criteria for intervention nurses is provided in Table 2.

Table 2: Nurse entry-level skills

- Communicate in a language appropriate to their country
- Sufficient proficiency in English to be able to participate in the training
- A professional nursing qualification recognized in each participating country
- Experience in advanced cancer care or palliative care
- Excellent communication skills
- Perceptive listening and questioning skills
- Ability to cope with emotionally demanding situations
- Willingness to work flexibly
- Desirable criteria: a post-graduate qualification in nursing

Interventions and control

This study comprises two interventions: the FOCUS+ face-to-face intervention and the iFOCUS web-based intervention. Both interventions are delivered in addition to usual care. Both interventions are psychoeducational interventions focusing on teaching dyads optimal ways to jointly manage the implications of advanced cancer and responding to their priority concerns.

The theoretical framework behind the interventions is the transactional model of stress and coping of Lazarus and Folkman[11]. In this model, stress is produced by an individual's response to stressors in their environment and the response of an individual to these stressors. In the context of advanced cancer, a series of personal, social, and illness-related factors (antecedents) influence how patients and caregivers appraise the illness and cope with the demands associated with it. Previous studies have shown that these antecedents are significant predictors of psychosocial outcomes in cancer patients and their family caregivers[12].

The interventions are designed to be tailored to the specific needs and wishes of the patient-caregiver dyads. The tailoring is based on the information from the baseline measures and the responses in the intervention sessions. Both interventions aim to enhance dyads' emotional functioning and their self-efficacy.

The FOCUS+ and iFOCUS interventions have different modes of administration (face-to-face vs. web-based) but have the same core content by addressing five core components: (1) supporting family involvement, communication, and mutual support, (2) supporting outlook and meaning, (3) increasing coping effectiveness, (4) reducing uncertainty and (5) teaching symptom management and giving them the confidence to handle specific tasks and problems.

These five core components stem from the original FOCUS intervention[5] developed in the USA and have been translated and adapted to the current European context (Table 3).

Face-to-face intervention (FOCUS+)

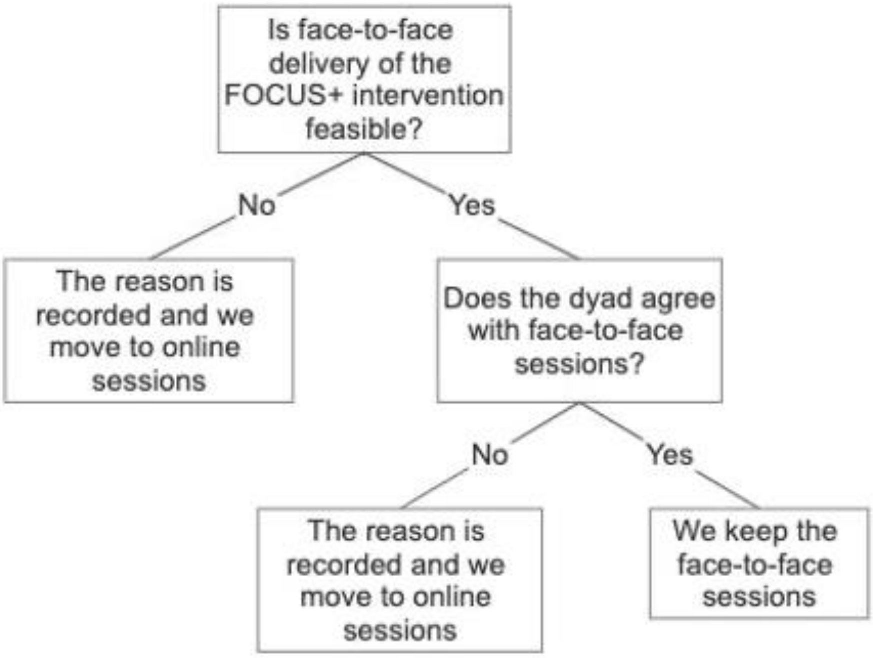
The face-to-face FOCUS+ intervention is a home-based intervention consisting of two 90-minute home visits and one 30-minute online video session, conducted by a trained intervention nurse over 12 weeks, focusing on the five core components. An overview of the participant timeline can be found in Figure 2. In case of tightened measures to contain the COVID-19 pandemic, the delivery of the FOCUS+ sessions via a GDPR-approved online platform (e.g. MS Teams, Zoom,..) will be allowed, if necessary. The decision-making process is visualized in Figure 1 and will be recorded for each dyad in each country.

Table 3: Five conceptual core components of the FOCUS+ and iFOCUS interventions

Core concept	Goals
Supporting family involvement, communication, and mutual communication (F)	- Discuss and support communication - Encourage mutual support and teamwork in a planned program of care - Identify family strengths - Help children in the family as needed
Supporting outlook and meaning (O)	- Help dyads share fears and concerns - Discuss positive and negative feelings of dyads - Educate dyads about different kind of feelings and attitudes - Encourage dyads to set realistic short-term goals
Increasing coping effectiveness (C)	- Help dyads deal with overwhelming stress - Discuss and support active coping strategies by dyads - Assist caregivers to manage the demands of illness
Reducing uncertainty (U)	- Educate dyads about disease and treatments as needed - Teach dyads how they can obtain additional information - Help dyads learn ways to live with uncertainty
Teaching symptom management and giving the confidence to handle specific tasks and problems (S)	- Assess symptoms in patients and family caregiver - Teach self-care strategies to manage symptoms (e.g. ways to manage reactions and side effects associated with the illness, treatments, and adjustment) - Help dyads identify relevant resources in the community (community services and support)

The nurses will receive extensive online training (including both synchronous and asynchronous training modules) and additional continuous follow-up training to provide them with the knowledge and skills required to successfully implement the intervention. The specific learning outcomes of the training are: (1) Understand the overall aims and objectives of the intervention, (2) Demonstrate understanding of the principles of FOCUS+ and the need to support both the patient and carer together, (3) Prepare for, conduct and complete the intervention, including the delivery of the intervention through online sessions with the dyads if needed and (4) Demonstrate how to use the intervention manual and other identified materials specific to the nurses' country. The training will be interactive. This means that the participating nurses will have the opportunity to share their experience and insights and considerable time will be spent reviewing the developed nurse intervention manual and discussing the intervention fidelity. Nurses will also be asked to review and analyze case studies, engage in reflection and discussion regarding training content, and will be invited to discuss potential barriers and facilitators to implementing the intervention in their home countries. The synchronic online training sessions will be video recorded to give participating nurses the opportunity to review the material as needed and to facilitate the training of new nurses who may join the study over time.

Figure 1: Decision-making process in method of delivery of FOCUS+ intervention in light of possible COVID-19 developments



The intervention is comprehensively manualized with a checklist-format and there is a protocol to guide the delivery of the intervention for each home visit and online video session, including strategies to respond to relevant issues with the patient and their family caregiver.

Adherence to, and fidelity of, the intervention is monitored by the use of the fidelity checklist. As part of the face-to-face intervention, it is proposed that all intervention sessions are audio-recorded to allow assessment of fidelity for a stratified random selection (20%) of dyads. A stratified random sample will be used to ensure that objective fidelity checks are performed across the timeline of the study, allowing for the maintenance of fidelity to be assessed. As such, it is proposed that the 15-month timeframe for intervention delivery be divided into five three-month blocks, with 20% of completed sessions with dyads assessed in each block. For reflexive fidelity, intervention nurses will be asked to self-assess fidelity based on the recordings of the first of each of the three FOCUS+ sessions they complete. These fidelity checks will be conducted in the early phases of delivery (block 1), to allow for intervention nurses to adapt their practice if needed to ensure that appropriate levels of fidelity are met. These reflexive checks will also be conducted by a member of the research team, allowing for a discussion between the intervention nurses and the researchers on the implementation of the intervention. Following these early reflexive fidelity checks, nurses will receive reports of fidelity findings every three months to support ongoing reflection on the consistency of intervention delivery.

A printed FOCUS+ guide will be handed out to the dyads providing practical information, concrete tips, and advice for persons with advanced cancer and their family caregiver. In addition, more detailed national cancer-related information via brochures, leaflets, and websites will be made available to the dyad, based on their needs. Both the FOCUS+ guide and the additional brochures and information leaflets serve as additional supporting resources for reference between or after the sessions.

By taking into account the dyad's comments and questions during the sessions, the content of the sessions is always tailored to the specific needs of the dyads. The nurse can spend more time on components that can be of particular use to the dyad, or some content areas can be discussed minimally if the dyad does not require assistance in a particular area.

Web-based intervention (iFOCUS)

The web-based iFOCUS intervention is a self-managed intervention that is completed autonomously by the patient-caregiver dyads together in their home (or a location of their preference). It encompasses four sessions spread over 12 weeks, focusing on the same five core components as the face-to-face intervention. The sessions are completed simultaneously by the patient and the family caregiver, sitting side by side at a computer or tablet. Access to the sessions will be provided via a link sent by email. All sessions of the iFOCUS intervention are available in the official language of the participating countries.

Similar to FOCUS+, except fully automated by a web-program, dyads are asked to assess their strengths, problems, and needs, and based on these assessments tailored educational content is presented to the dyad. The FOCUS+ guide from the face-to-face intervention will be replaced by an online personal workbook. It contains the results of the interactive exercises that are provided to the dyads during the web-sessions, supplemented with related information from the FOCUS+ guide and links to other cancer information brochures, leaflets, and websites. A helpdesk is available (via email or telephone) for dyads doing the web-sessions to resolve any technical difficulties in each country.

Routine data from the web-platform will be accessed by a member of the research team to allow for fidelity assessment. Mirroring the FOCUS+ fidelity checklist, this will assess both completion of key iFOCUS elements and the time spent by dyads on each of the five (F O C U S) components.

The content of the iFOCUS intervention will also be tailored to their demographics (age, sex, and the relationship of the dyad) and information provided during the web-based sessions. The tailoring is done to enhance the relevance of the intervention content.

Control group (standard care as usual)

Patients in the control group will receive standard care as usual, as determined by the healthcare system in the participating countries. The dose and frequency of usual care will be deemed appropriate by the medical practitioner in charge of their treatment.

Criteria for discontinuing or modifying allocated interventions

When a patient or family caregiver dies during the study period, a bereavement protocol will be in place. The national trial manager will be notified about the death of a participant by either the intervention nurse (for the FOCUS+ intervention) or the data collector (for the FOCUS+ and iFOCUS intervention) who should be informed about this when trying to make an appointment with the dyad. The bereaved participant from the iFOCUS intervention will be able to inform the national trial manager about the passing of their relative via e-mail. For the FOCUS+ intervention, the bereaved participant will receive a phone call from the intervention nurse outlining condolences and the options for where they can access support (relevant to each country) if required and what the implications are for the study. For the iFOCUS intervention, the bereaved participant will receive a similar phone call from a research assistant appointed within each research team, that has relevant qualifications and/or significant clinical experience (e.g. a psychologist). If the bereaved person seems very distressed, the nurse or research assistant can offer to call the person a second time (e.g., one week later) to determine whether the person has made contact with a source of support (e.g., family, clergy, physician, bereavement group). Bereaved persons will not be asked or expected to complete follow-up study questionnaires but will be offered the option to continue to fill out an abbreviated package of follow-up questionnaires that are relevant to the remaining partner (e.g. emotional functioning and QoL scale). Any other reason for discontinuing the interventions is described in the informed consent (dyads can withdraw from the study at any moment) or under the section of adverse events (such as psychological distress).

Strategies to improve adherence to the intervention protocols

Strategies include:

- Nurses delivering the intervention will receive extensive training and additional continuous follow-up training to provide them with the knowledge and skills required to successfully implement the intervention.
- The FOCUS+ intervention is comprehensively manualized. Nurses will be trained in the use of an intervention manual to deliver the FOCUS+ intervention.
- Adherence and fidelity monitoring: nurses delivering the FOCUS+ intervention will be required to self-assess fidelity based on the recordings of the initial delivery of the three FOCUS+ sessions with dyads with whom they have carried out the intervention. These fidelity checks will be conducted in the early phases of delivery, to allow for intervention nurses to reflect on the initial experience of delivery. Following this early

phase, intervention nurses will be provided with routine reports on overall fidelity checks to allow them to adapt their practice if needed to ensure appropriate levels of fidelity are met throughout delivery.

- It is proposed that 20% of dyads are assessed for objective fidelity using the intervention fidelity checklist by a member of the research team, with the dyad's full intervention participation (that is all sessions of the intervention) assessed as one check.
- Discussing fidelity of FOCUS+: planned and unplanned adaptations in the interventions during the training of the nurses, the regular community of practice sessions with trainers and nurses, and the monthly follow-up sessions between the trainers and nurses (virtual meetings during the study period).
- A number of aspects of adherence are built into the iFOCUS web-module; e.g. during web-sessions dyads are asked to confirm that both of them are present and indicate where they are sitting at the computer.
- If dyads do not fully complete an iFOCUS web-session and exit the session before finishing, a reminder will be sent via email.
- Dyads who experience problems with onboarding for the web-sessions will receive help from the national trial manager with onboarding via a phone call.
- Routine monitoring will also include surveys of satisfaction with the interventions.

Relevant concomitant care and interventions that are permitted or prohibited during the trial

There are no restrictions regarding concomitant care during the trial outside of the three trial arms.

Outcomes

Study endpoints and assessments

This study uses both qualitative and quantitative data to measure the outcomes of the intervention. Data will be collected three times from patient-caregiver dyads; (1) baseline measure before randomization to the study arms (T_0) (2) first follow-up at 12 weeks (T_1) and (3) second follow-up at 24 weeks (T_2).

The primary endpoints are emotional functioning and self-efficacy of both the person with advanced cancer and the family caregiver at T_1. The secondary endpoints are QoL of the patient and caregiver, benefits of illness, coping, dyadic communication, ways of giving support at T_1. All listed primary and secondary outcomes are measured at T_2 and formal healthcare use and costs are measured at T_1 and T_2.

Validated questionnaires will be used to measure the primary and secondary endpoints. In addition, data on socio-demographic characteristics, care received and participant perspectives on the acceptability, feasibility, and usefulness of the intervention will be collected. An overview of the instruments, the underlying measured concepts, and their timing can be found in Table 4. The complete questionnaire for patients and family caregivers can be found in Appendix A3 and A4.

Table 4: Instruments, underlying concepts, and timing

Concept	**Measured by**†	**Timing***		
		T_0 (Before randomization)	T_1 (T_0 + 12 weeks)	T_2 (T_0 + 24 weeks)
Outcome measures used for the primary endpoints				
Emotional Functioning	EORTC[20–22] 10 emotional functioning items described by Jabbarian et al[21]. For **patients** (10 items): For **caregivers** (10 items):	✓	✓	✓
Self-efficacy	The Lewis´ Cancer self-efficacy scale[23] (validated by Northouse[5]) For **patients** (17 items) For **caregivers** (17 items)	✓	✓	✓
Outcome measures used for the secondary endpoints				
Quality of life (also covers additional secondary outcomes such as hopelessness, anxiety, depression, etc.)	For **patients** (23 items): - EORTC QLQ-C15-PAL[24] plus two social functioning items (#26, 27) + one item about overall health (#29) from EORTC QLQ-C30[25] - Social wellbeing scale from FACT-G[26] For **caregivers** (35 items):	✓	✓	✓

	- The Caregiver Quality of Life Index-Cancer (CQOLC)[27]			
Benefits of illness	Benefits of illness scale[28] For **patients** (5 items) For **caregivers** (5 items)	✓	✓	✓
Coping	A shortened version of Brief Cope[29] (#1-3,5-10,13-16,19-21,23-26) For **patients** (20 items) For **caregivers** (20 items)	✓	✓	✓
Dyad communication	The five items ’Active engagement scale’ from the ´Ways of giving support questionnaire´[30]. Three scales (10 items) from the ‘Dyadic Coping Inventory’[31]: ‘Stress communication by oneself’, ‘Stress communication by partner’ and ‘Evaluation of dyadic coping’. For **patients** (15 items) For **caregivers** (15 items)	✓	✓	✓
Health economic measures	EQ5D5L[32] and CSRI[33] For **patients** (23 items) For **caregivers** (14 items)	✓	✓	✓
Background characteristics				
Socio demographics, illness-related factors, social factors	A mix of socio-demographic items from different studies (self-constructed): - Sex, age, relationship status, living situation, having children, educational level, employment status, total monthly net income, financial difficulties related	✓		

	to physical condition or medical treatment, private medical insurance, religion, member of a minority ethnic group, dyad's relationship For **patients** (14 items) For **caregivers** (15 items)			
Other aspects				
Items about computer skills	Three FOCUS items about computer skills (self-constructed) For **patients** (2 items) For **caregivers** (2 items)	✓		
Process evaluation	FOCUS items asking about **experience** and **satisfaction** with the intervention. (self-constructed) For **patients** (12 items) For **caregivers** (12 items)		✓	
Process evaluation	**Experiences with the intervention**: (self-constructed) - Interviews with patients and family caregivers - Interviews with nurses delivering the intervention		✓	
	Fidelity: FOCUS+ (self-constructed) Session characteristics (e.g. length, timing), random sample intervention checklists, random sample audio-taped intervention sessions		✓	
	Fidelity: iFOCUS (self-constructed)		✓	
	Data from web-based program (e.g. number of sessions logged	✓		

	into, time taken to complete session)			
	Routine data on recruitment (self-constructed) (e.g. potential participants, initial engagement, eligible participants, enrolment)	✓		

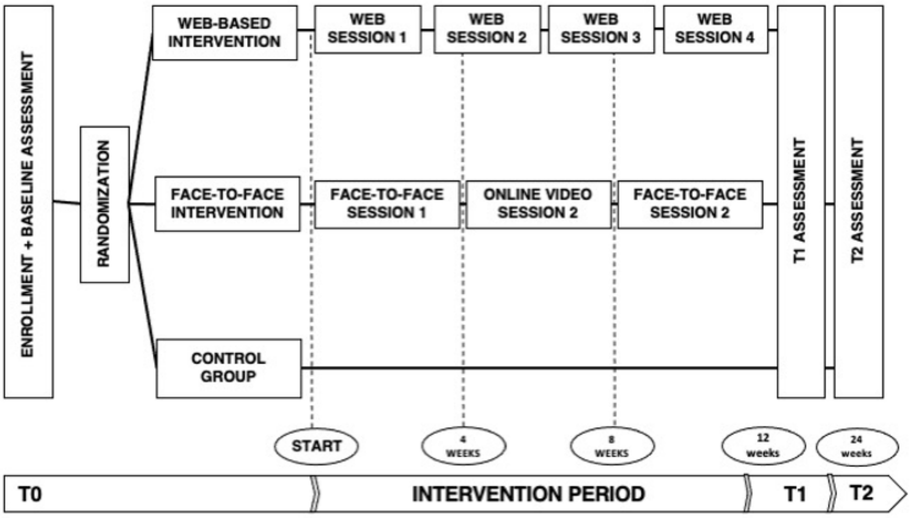
*For T_1, questionnaires can be filled in between T_0 + 12 weeks minimum and T_0 + 16 weeks maximum. For T_2, questionnaires can be filled in between T_0 + 24 weeks minimum and T_0 + 28 weeks maximum.

†All measures were validated in each of the participating countries

Participant timeline

The face-to-face FOCUS+ intervention is a home-based intervention consisting of two 90-minute home visits and one 30-minute online video session, conducted by a trained intervention nurse who visits the dyads at home over 12 weeks, with four weeks between each session. The web-based iFOCUS intervention is a self-managed intervention that is completed autonomously by the patient-caregiver dyads at home. The iFOCUS intervention encompasses four sessions for the dyads (with three weeks between each session) over 12 weeks. Data will be collected three times from patient-caregiver dyads: 1) baseline measure (T_0) after which the dyad will immediately be randomized to one of the study arms, 2) first follow-up at 12 weeks after the baseline (T_1), and 3) second follow-up at 24 weeks after baseline (T_2). Figure 2 provides a flowchart of the participant timeline and the data collection.

Figure 2: Participant timeline



Sample size calculation

We consider the demonstration of an intervention effect (for each of both interventions) on at least one of the primary endpoints for either the patient or the caregiver as a success. A pre-determined strict fixed sequence (FS) procedure defines the prospectively hierarchical ordering of the endpoints, for this study the hierarchical order is emotional functioning (1) and self-efficacy (2). Testing of null hypotheses proceeds according to their hierarchical order, that is, H(1)0 is tested first at a significance level of 5%, and if H(1)0 is rejected then H(2)0 is tested at the same significance level, otherwise H(2)0 is not tested at all. The strict FS approach has the highest power for testing the first hypothesis (outcome: emotional functioning) compared to the other methods, as it does not save any portion of alpha for testing later hypotheses[10]. The reference mean value for emotional functioning from EORTC for all cancer patients, stage III-IV is 71.5 (SD: 23.8)[13]. Alpha is set at 0.0125 instead of 0.05 to account for multiplicity (2 comparisons with control group * 2 participant groups [patients and caregivers]). We set 1-beta (i.e. statistical power) at 0.9. The expected difference between the control group and the intervention arms in the primary outcomes is 0.375 SD at T1 (12 weeks).

With these parameters n= 203 is needed in each arm across all countries (i.e. 609 in total). Anticipating a 65% retention rate at T1, which is more conservative than found in previous studies in the USA on the FOCUS interventions[5–7] due to the advanced cancer population included in this study, 938 dyads must be enrolled across the 6 countries (313 per group). This means that 156 dyads (i.e. 52 in each of the 3 arms) need to be enrolled in each country. Based on previous studies in the US[5–7] we expect an enrolment rate of 55% of those dyads referred to the study, meaning that about 282 dyads will need to be screened and identified in each country. The feasibility of recruitment has been evaluated based on previous research and discussions with clinicians in eligible hospitals.

Recruitment

Staff in each department in the participating hospitals will screen for patients meeting the eligibility criteria. After eligible patients are identified, the study is orally presented to the patient-caregiver dyad and they are invited to participate in the study by a research assistant. This research assistant will explain the study and refer the patient and their family caregiver to the contact person of the research team. A data collector will make an appointment with the dyad at home (or preferred location of the dyad) to obtain informed consent.

The recruitment period will last a total of 12 months. Screening will continue until the target population is achieved. Based on conservative estimations of the number of eligible dyads that could be enrolled, obtaining the numbers required by the power calculations is realistic.

Assignment of interventions

Allocation

Randomization will be performed per a computer randomization schedule with a 1:1:1 allocation ratio to one of the two intervention arms or the standard care arm (control group) using simple randomization. Participants will be randomized using the Mersenne Twister Random Number Generator, which is an online, central randomization service[14]. Each dyad will be randomized to one of the three study arms. Recruitments for the study within a country will continue until at least 52 dyads were randomized.

Allocation concealment will be ensured, as the randomization service will not release the randomization code until the patient has been recruited into the trial, which takes place after all baseline measurements have been completed.

All dyads who fulfil the inclusion criteria, who give consent for participation, and complete the baseline measurements (obtained by the data collector) will be randomized. Randomization will be immediately requested after completion of the baseline questionnaires from the online service Mersenne Twister Random Number Generator by the data collector, who is then able to inform the dyads of their allocation to one of the study arms. Randomization will thus be conducted without any influence of the principal investigators, raters, or clinicians. Research staff responsible for the data analyses of the trial will not be allowed to receive any information about the group allocation.

Blinding

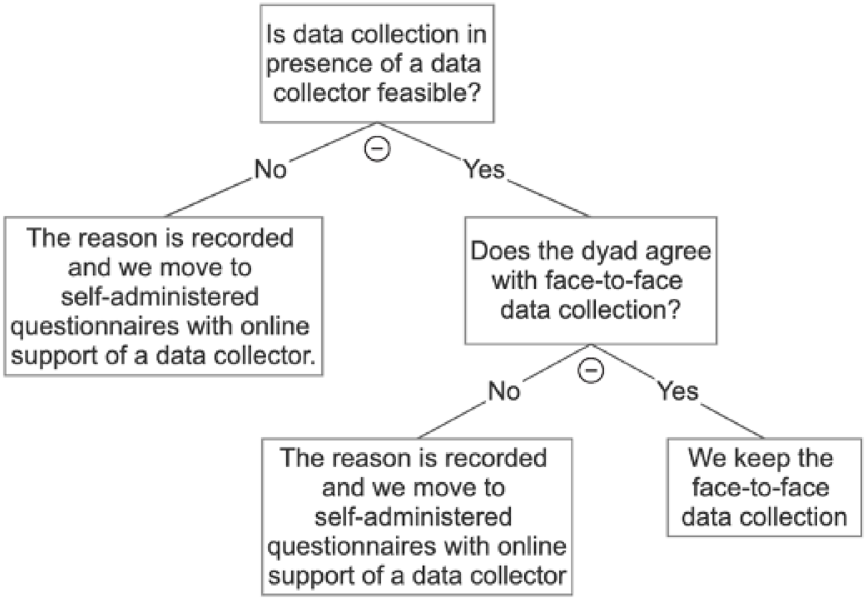
Due to the nature of the intervention neither the patient-caregiver dyads nor the intervention nurses (for the face-to-face FOCUS+ intervention) can be blinded to allocation. Those conducting the data analyses will remain blind as to what trial arm dyads were randomized to until the end of the last data-collection point.

Data collection, management, and analysis

Data collection methods

The outcomes and outcome measures are described in Table 4. Quantitative data will be collected via computer-assisted self-interview in the presence of a data collector that can assist dyads with the completion of the questionnaires at T_0 and T_1. In case of tightened measures to contain the COVID-19 pandemic, data collection at T_0 and T_1 via a GDPR-approved online platform (e.g. MS Teams, Zoom,..) will be allowed, if necessary. The decision-making process is visualized in Figure 3 and will be recorded for each dyad in each country. At T_2, questionnaires will be self-administered online (without the presence and support of a data collector), with a telephone follow-up in case of nonresponse. The questionnaires were pilot tested among a small number of dyads before the start of the study to identify problems and limitations concerning respondent comprehension and acceptability.

Figure 3: Decision-making process for data collection procedure in light of possible COVID-19 developments



To address the aim regarding the evaluation of the process of implementation both quantitative data and qualitative data will be collected throughout and after the interventions in each country and used for the evaluation:

(1) Detailed documentation of the recruitment process allows us to obtain information about the way patients and family caregivers were recruited and their reasons for participating or not.

(2) To measure the extent to which the intervention is implemented as intended (fidelity and consistency across the countries), the nurses delivering the intervention will be required to audio record intervention sessions, allowing members of the research team to complete a structured intervention checklist on a random sample of recordings every three months to record any deviations from the program. Adherence to the intervention is monitored by the use of these checklists.

(3) Repeated interviews with nurses who delivered the face-to-face FOCUS+ intervention in each country (n= 6 in total) and research staff supporting the delivery of the Web intervention (n= 6 in total) are also planned. These interviews will provide information on perceived barriers and facilitators to the delivery of the intervention and their experience or observations on the elements of the interventions that may represent mechanisms/agents of change. If necessary, in light of the COVID-19 pandemic, these interviews will take place online.

(4) A selection of 10 dyads who received either of the interventions is interviewed in every country to explore their perception of the intervention, their experience of the impact of the program, the core elements of the program that were central to their experience, and any recommendations for the further development of the intervention. The interviews will be

conducted with a minimum of 10 dyads in each country, to include four dyads who complete either intervention and two dyads who did not complete either intervention. This information will allow consideration of the mechanism of impact or agents of change. All interviews will be audio-recorded and transcribed verbatim in the local language.

To reduce loss to follow-up and improve retention, **retention gifts** with the logo of the study on them will be provided after the completion of each data collection. These gifts are a coffee mug at T_0, a magnetic notepad at T_1, and plant seeds at T_2. With these gifts, we intend to encourage participants to complete the data collections.

Data management

The data collected through the questionnaires will be coded and stored in a safe data environment. Data cleaning will be carried out following a data cleaning protocol already developed and used by the coordinating partner Vrije Universiteit Brussel.

The consortium certifies that all research activities will adhere most strictly to all applicable legal, ethical, and safety provisions of the individual states and the EU. Participants will conform to relevant EU legislation including (1) The Charter of Fundamental Rights of the EU, December 2009 and (2) EU Regulation 2016/679 on the protection of natural persons concerning the processing of personal data and on the free movement of such data (GDPR).

The overall trial manager (Vrije Universiteit Brussel) will take the overall responsibility for data management throughout the DIAdIC project. Ultimately responsibilities for data management will be transferred to consortium partners to allow a collaborative and efficient collection of research findings throughout the time of the project.

Statistical methods/Data analysis

Quantitative analysis

Four main analyses will take place.

(1) **Primary hypotheses testing**

a. Testing the null hypothesis of the first primary endpoint: emotional functioning.

The **effectiveness of the FOCUS+ face-to-face intervention and the iFOCUS web-based intervention will be compared with the standard care** (control group) for each participant population (patients/caregivers) separately. In total, 4 comparisons are performed for one outcome variable (alpha=0.0125). The hypotheses related to the first primary outcome (emotional functioning) will be tested using a mixed model (per participant population) with the T1 measurement value for emotional functioning as the outcome variable, recruitment center as random effect and randomization group, and the baseline measure of emotional functioning (T0) as predictor variables. We will perform analyses on both 'intention-to-treat' and per-protocol principles. The primary principle is intention-to-treat. After completion of the baseline measurement (T0), dyads will be randomized to one of the trial arms. All randomized dyads will be included in the mixed model. Multiple imputations will be applied. Predictors for the imputation model will include the baseline measurement, randomization group, age, and other variables (e.g. severity of the illness). The secondary principle is the per-protocol analysis that functions as a sensitivity analysis. The per-protocol population will be defined as dyads who have completed all sessions of the FOCUS+ or iFOCUS intervention (except for dyads in the control group) and T1 measurement. By including the baseline measurement as a predictor variable (ANCOVA), preexisting differences will be controlled for, enhancing the sensitivity of the analyses. To interpret the magnitude of the effects for the different outcomes, we will estimate effect sizes (Cohen’s d).

b. *Testing the null hypothesis of the second primary endpoint: self-efficacy (the Lewis´ Cancer self-efficacy scale from FOCUS)*

As per the fixed sequence (FS) procedure, the null hypotheses of the second primary endpoint (self-efficacy) will only be tested if a significant result is found for the first primary endpoint (emotional functioning). The same strategy is then followed for the analyses as for the first primary endpoint, with an alpha level of 0.0125.

(2) **Secondary hypotheses testing**

All identified secondary endpoints (Quality of Life [including separate items of hopelessness, anxiety, depression], benefits of illness, coping, dyad communication, all at T1) will be evaluated by testing the FOCUS+ and iFOCUS against care as usual (control group) for each participant population (patients/caregivers) separately. In total, 4 comparisons are performed for each outcome variable. For each secondary outcome variable, a mixed model is applied with the T1 measurement value as the outcome variable, recruitment center as random effect, and randomization group and baseline measurement of the variable (T0) as predictor variables. We will perform analyses on both 'intention-to-treat' and per-protocol principles, applying the same principles as described above.

By including the baseline measurement as a predictor variable (ANCOVA), preexisting differences will be controlled, enhancing the sensitivity of the analyses. To interpret the magnitude of the effects for the different outcomes, we will estimate effect sizes (Cohen’s d). All statistical tests will be two-sided and considered significant if $p < 0.0125$.

All primary outcomes and secondary outcomes as listed above will also be analysed at T2 (6 months) to evaluate longer-term effects, using the same analysis procedures.

The cost-effectiveness of the interventions will be determined by analyzing patterns and costs of healthcare utilization and effects on quality of life. Costs will be estimated by combining the reported frequency of health care use by participants with country-specific unit costs for each service domain. Quality of life will be measured by combining EQ5D5L with country-specific preference weights. We will evaluate the robustness and consistency of results in population-specific outcome measures EORTC, FACT-G and CQOLC. Data will also be collected on the types and amounts of informal care provided to patients in each arm of the study, to investigate if the amount or patterns of informal care change as a result of the intervention. The outputs will be mean costs of care for patients in each arm of the study, cost per year of life gained (if survival is affected significantly by the intervention and the costs in the intervention groups overall are higher), and (if appropriate) the additional costs of achieving a better quality of life outcomes (including estimates of cost per quality-adjusted life-year gained).

(3) **Exploratory hypotheses testing**

For all exploratory endpoints, two-sided statistical tests will be considered significant if $p < 0.05$.

a. For the outcomes that are measured identically for the patient and the caregiver, we will assess the effect on the dyad as a whole (i.e. both patient and family caregiver). For the outcome instruments that led to comparable estimated differences between FOCUS+ and standard care and iFOCUS and standard care, the effect will be assessed on the dyad as a whole by adding an extra level (dyad) to the linear regression model.
b. For each of the primary and secondary endpoints, subgroup analyses will be performed using formal interaction tests to explore the extent to which the outcomes of the trial differ by country, gender, and socioeconomic status. Interaction terms between respectively country, gender, and socioeconomic status on the one hand and the trial arms on the other hand will be added to the analysis models. For the country variation multilevel mixed model analyses will also be performed to additionally account for potential clustering by country (i.e. participants nested within a country). Outcomes will be analysed with country as random factor.

(4) **Other analyses**

a. Background reports describing care as usual for people with advanced cancer will facilitate the understanding of the results of the between-country comparisons.

b. Process evaluation of the implementation of the interventions will be analyzed following the MRC framework for evaluating complex interventions[15], integrating normalization process theory (NPT)[16] and the RE-AIM framework[17]. Data analysis for the process evaluation will include a) standard statistical descriptions of the quantitative data from the intervention checklist and routine monitoring to describe adherence to the implementation. This analysis will determine cut-off points for good intervention adherence and, hence, inform the per-protocol analyses; b) analyses of the qualitative data (semi-structured interviews with patients and their family caregiver and post-intervention interviews with the nurses who delivered the face-to-face FOCUS+

intervention) will be performed (see below - Qualitative analysis).

Qualitative analysis

With the transcription of interviews into the local language, the analysis process will involve a collaborative process (Richards & Hemphill, 2017)[12] involving researchers from each partner site collecting data. The general process will be guided by the **thematic analysis framework** proposed by Braun and Clarke (2006)[13], with quality ensured with criteria for trustworthiness reported by Nowell et al. (2017)[14] and applied procedures for auditing the analysis process. Thematic analysis allows for both **inductive and deductive analysis** and can be implemented with a range of computer-based software to support the management of the analysis process (e.g., NVIVO, MAXQDA).

Deductive analysis will be informed by semantic information sought from the interview (i.e., were participants satisfied, were particular elements of the programmes described as positive or negative) and themes evident in previous evaluations of the Focus Intervention. This will involve developing themes in advance of the analysis process and assessing the presence or absence of these themes across the data. Inductive analysis will be structured using the objectives of the process evaluation to target key topics, with more latent or interpretative themes isolating more experiential findings from the data. Qualitative analysis will be conducted at two levels, an initial assessment of themes in each data source (stakeholders, staff, researchers, patients and carers, different language groups) followed by a higher-level analysis of superordinate themes of convergence and divergence evident across groups. Additional strategies for managing the potential impact of multilingual analysis are recommended by Richards and Hemphill (2017)[12], including peer debriefing during the process of coding and the development of candidate themes, triangulation across researchers and language sources. Analysis will be informed by an open discussion of conceptual issues in the data, as highlighted in Larkin, Dierckx de Casterlé, and Schotsmans (2007)[15], to explore variations in interpretation and identify shared meaning relevant to the focus of the process evaluation.

Data monitoring

Data monitoring

An Ethical and Data Monitoring Board will monitor the intervention and data collection and any adverse events will be reported to the Board. This Board consists of an Ethics Evaluator and the independent trial monitors. The Ethical and Data Monitoring Board will review the accumulating data periodically and determine if the trial should be modified or discontinued. The monitoring visits will be conducted by national independent trial monitors.

Harms

The FOCUS+ and iFOCUS interventions are non-invasive psycho-educational interventions focused on the provision of information; they are not intended to be a therapeutic or cognitive behavioral treatment. Based on previous research with similar FOCUS interventions in the USA, it is unlikely that there will be any adverse effects. However, a protocol will be in place for trial managers, data collectors, and intervention nurses involved in delivering the intervention on how to handle unanticipated adverse events should they occur.

Auditing

Auditing will be independent of investigators and the sponsor. The first Monitoring Visit following initiation of each site will take place approximately 6 weeks after the inclusion of the first dyad, which allows that the first dyads are enrolled in the study and have completed already some parts of the face-to-face FOCUS+ intervention or web-based iFOCUS intervention to be monitored. Subsequent monitoring visits will be conducted in weeks 22, 38, 54 and 70 of the trial. A close-out monitoring visit will be planned in week 73. The interval for Monitoring Visits may be longer or shorter than stated above, depending on enrolment rate, site compliance, or quality issues.

Ethics and dissemination

Research ethics approval

The protocol is already approved by Commissie Medische Ethiek UZ Gent, Belgium, 22/10/2020; Ethisch Comité AZ Maria Middelares, Belgium, 16/11/2020; St. Vincent’s University Hospital Research Ethics Committee, Ireland, 04/12/2020; Comitato Etico dell'Area Vasta Emilia Nord (AVEN), Italy, 13/04/2021; NHS/HSC Research Ethics Committee, United Kingdom, 05/03/2021; Medisch Ethische Toetsings Commissie Erasmus Medisch Centrum Rotterdam, the Netherlands, 15/01/2021. The Denmark Scientific Ethical Committee system (protocol no. 19043825) determined that the protocol did not require further formal approval on 22/08/2019; this decision was confirmed after the submission of the final protocol.

Protocol amendments

Any modifications to the protocol which may impact the conduct of the study, the potential benefit of participants, or may affect patient safety, including changes of study objectives, study design, patient population, sample sizes, study procedures, or significant administrative aspects will require a formal amendment to the protocol. Such amendment will be agreed upon by the DIAdIC consortium partners and approved by the Ethics Committee before implementation.

Consent

The data collector will obtain informed consent from dyads willing to participate. Patients and caregivers will be given ample time to consider participation and they will be assured that they are free to withdraw from participating in the study without any effect on their care. Participants will be made aware that consent is fluid and that they have the right to withdraw their consent at any time throughout the study without any negative impact on their healthcare or management. Written consent will be obtained without any coercion of study participants. The research team will provide all participants with full disclosure about the nature and goal of the study. Participants will be given the opportunity to ask questions before they decide if they want to participate.

Confidentiality

All project partners will take all required steps to guarantee compliance with the provisions of the EU Regulation 2016/679 on the protection of natural persons concerning the processing of personal data and on the free movement of such data (GDPR) as well as the related legislation of the Member States of the project partners.

Declaration of interests

There are no financial and other competing interests for principal investigators for the overall trial and each study site.

Access to data

All data collected will be stored on a dedicated server in France which has accredited medical data hosts. Data access is strictly limited to those who require access to perform the study. The people who have access will be appointed by the data protection officer of the coordinating partner (VUB).

Ancillary and post-trial care

Dyads in the trial are referred to specific existing services or community resources based on the problems or needs identified during the intervention sessions (ancillary care) or after the trial (post-trial care).

Dissemination policy

The DIAdIC project will use an extensive dissemination and exploitation strategy and apply a broad range of communication activities to inform the scientific community about the project results and their implications. There are six dissemination objectives; (1) at least 6 Ph.D. dissertations, (2) publication in open access, green and gold international journals, (3) publication in national topic-specific journals, (4) communication to and interaction with all scientific stakeholders through active contributions at international conferences, (5) events and workshops organized at the premises of the DIAdIC partners and (6) an end-of-project conference.

Discussion

This project aims to study the effect of two psycho-educational interventions on emotional functioning and self-efficacy of patients with advanced cancer and their informal caregivers. DIAdIC is a large-scale study conducted across different countries and provides knowledge about intervention dosage and different modes of administration. Psychosocial support and education for people with advanced cancer and their family caregivers can substantially reduce their distress, improve their QoL, and prevent avoidable health resource use[4,8]. Often, family caregivers have a double role: as a provider of care to the person with cancer, but also as a person in need of support for themselves[18]. Both interventions focus on the empowerment of non-professionals (the family caregiver and the patient with advanced cancer) by improving their mutual communication, assisting them to identify positive aspects related to their situation, and increasing their self-efficacy.

Few studies have systematically assessed the cost-effectiveness of large scale psychosocial and psychoeducational interventions. As the cost-effectiveness of the interventions will be determined by analyzing patterns and costs of healthcare utilization and effects on QoL, the results of this RCT can thus contribute to the search for cost-effective novel interventions that can relieve constraints on professional healthcare.

The cross-country setup in six European countries allows for a comparison of the effectiveness of the interventions in different healthcare systems and regimes across Europe. The DIAdIC interventions are complex interventions where contextual factors such as country-specific healthcare systems and dyad characteristics influence the mechanisms of action of the interventions. Therefore, a thorough process evaluation following the normalization process theory and the RE-AIM framework is embedded in the study. This analysis will determine cut-off points for good intervention adherence and, hence, inform the per-protocol analyses.

We anticipate some limitations and challenges in the DIAdIC trial. First, the inclusion of participants might be difficult for several reasons. As the target population includes patients with advanced cancer with a limited life expectancy of maximum two years and their family caregivers, eligible patient-caregiver dyads might be reluctant to enroll in a time-consuming trial. They might feel too tired or want to spend the time they have left doing different things. Additionally, a dyad can only participate in the trial when both the family caregiver and the patient agree to participate. Hence, we need consent from two people to include one participating entity or dyad in the study, which can cause the enrolment rate to be lower than other studies. Second, to address all the different outcomes of the DIAdIC trial, data will be collected three times from patient-caregiver dyads through long self-administered questionnaires, which may cause a considerable burden and can lead to high nonresponse. To limit the risk of nonresponse, the data collector is present at T_0 and T_1. For T_2 the data collector will do a telephone follow-up in case of nonresponse. Third, the complexity of the study and the many aspects of tailoring and context does not allow for unambiguous identification of the active component of the interventions. This challenge is anticipated by conducting a thorough process evaluation to determine the mechanisms of action of the interventions. Fourth, as a consequence of the COVID-19 pandemic, the mode of delivery of the FOCUS+ intervention can differ between dyads, i.e. either face-to-face or via an online video platform. By recording the mode of delivery of the FOCUS+ intervention for each dyad in each country, within-group variations in effectiveness can be monitored.

Abbreviations

DIAdIC: Diadic Interventions for people with Advanced and their Informal Caregiver; QoL: Quality of Life; RCT: Randomized Controlled Trial; SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials; GDPR: General Data Protection Regulation

Declarations

Consent for publication

Not applicable

Availability of data and materials

Sharing of datasets will be defined on a case-by-case basis. Based on the type of dataset, it will be decided which datasets can be made public, shared or have to be kept confidential. However, we will publicly share certain research data under 'open access' on the project repository, as mandated by the EU:

- Public-use files: Datasets not containing personal data, and the content of the web-based tool or any other tools that will be developed in the project, will be made publicly available and will be published online (e.g. in an open access repository such as https://zenodo.org/). After removing direct and indirect identifiers, data can also be shared directly via the DIAdIC website to allow an easy access for any researcher or civilian who is interested.
- Restricted-use data files: files containing confidential information and/or direct and indirect identifiers that cannot be shared publicly. These files will be under 'restricted access' on the repository. Datasets containing personal data will be made available upon request by mail and upon signing a data user agreement, to prevent further dissemination of personal data beyond the researchers that get approval for re-use.

Research data from DIAdIC will be supplied to an online data repository as soon as publishable and within the duration of the project.

Competing interests

The authors declare that they have no competing interests.

Funding

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Authors' contributions

AdV, JC, LN, PH, AvdH, RH, KeB, LD, MC, MG, CN, PL, SG and SDL designed the study. OM, AdV, SD and JC drafted the manuscript with input from all authors. OM, AdV, SD, LD, VVG, LL, MG, LL, CMA, LS, HP, ATJ, SG, PJL, CJ, MC, PD, MC, SDL, MG, ET, AvdH, EW, JR, MvdW, KB, GP, JR, DS, KeB, RH, CN, PM, CC, LN, PH and JC have substantively revised the manuscript, approved the submitted version and have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of the work are appropriately investigated, resolved, and the resolution documented in the literature.

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PART III
Results from the DIAdIC study

Chapter V

Sexual satisfaction and its predictors in patients with advanced cancer and their family caregivers in six European countries: Baseline data from the DIAdIC study

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Abstract

Objective: To identify predictors of sexual satisfaction in patients with advanced cancer and their family caregivers.

Methods: Cross-sectional study using baseline survey data from a randomized controlled trial in six European countries. Patients with advanced cancer and their family caregiver completed measures on sexual satisfaction (one item from Functional Assessment of Cancer Therapy - General questionnaire for patients and Caregiver Quality of Life Index-Cancer scale for family caregivers) and health-related characteristics. Multivariable linear regressions were performed for all predictors (identified based on literature) with sexual satisfaction as dependent variable.

Results: The sample comprised 431 patient-family caregiver dyads. Patients with prostate or gynecological cancer reported lower sexual satisfaction (respectively B=-.267 95%CI: -1.674, -.594 and B=-.196, 95%CI -2.103, -.452). Higher emotional (B=.278, 95%CI .024, .057) physical (B=.305, 95%CI .012, .025) and social functioning (B=.151, 95%CI .001, .013), global health (B=.356, 95%CI .007, .013) and social wellbeing (B=.161, 95%CI .013, .082) among patients were associated with higher sexual satisfaction. Among family caregivers, sexual satisfaction was lower with increased age (B=-.142, 95%CI -.022, -.004). Higher emotional functioning (B= .027, 95%CI .011, .043) and quality of life (B=.165, 95%CI -.165, .716) were associated with higher sexual satisfaction in family caregivers.

Conclusions: The results underscore that sexual wellbeing of patients and family caregivers is related to health related factors in physical, emotional, and social domains. Patients and family caregivers could benefit from a dyadic approach to address sexual wellbeing.

Background

Sexuality is a multidimensional construct involving physical, psychological, interpersonal, and behavioral aspects and can significantly be afflicted by cancer and its treatment[1,2]. After breast cancer treatment for example, women can experience a negative body image[3] and loss of femininity[4]. Breast cancer patients undergoing systemic treatment report poorer sexual functioning compared to women undergoing surgical treatment[5]. The reports of sexual problems in men with prostate cancer vary from erectile dysfunction[6] to orgasm related issues[7]. Patients with other types of cancer (e.g. gastrointestinal) can also experience sexual dysfunction[8,9].

However, while cancer treatment commonly affects sexual functioning, it does not necessarily impact sexual satisfaction. A focus group study concluded that while many participants experienced a decline in sexual function, they also expressed being satisfied with their sex lives[10]. It thus might be important to distinguish sexual satisfaction and sexual functioning when considering the implications of cancer.

It is widely recognized that the consequences of cancer and its treatment are not limited to the patient, but also affect their partner[11]. In a qualitative study, patients dealing with breast cancer and their partners reported difficulties in resuming sexual activity[12]. Additionally, partners of patients with cancer typically struggle with combining their role as sexual partner and as caregiver[13].

Sexual satisfaction is one aspect of sexual health that is determined by multiple factors. A study with couples coping with metastatic breast cancer showed that depressive symptoms afflict sexual satisfaction[14]. Additionally, a study with prostate cancer patients found that erectile function, relationship closeness and anxiety were strong predictors for sexual satisfaction[15]. Further studying predictors for sexual satisfaction can lead to improved wellbeing.

Most studies mainly focus on specific patient populations of a specific gender with cancers affecting sexual organs (e.g. women with breast cancer or men with prostate cancer), while sexuality in patients with other cancers remains understudied[16]. As patients with advanced cancer often face different symptoms compared to those with early-stage cancer[17,18], this patient and caregiver population requires specific attention in research. Additionally, sexuality in the advanced cancer population is also understudied, as it is often wrongly dismissed as an unimportant topic[1].

This study explored the predictors of sexual satisfaction in patients with advanced cancer and their family caregivers recruited for the DIAdIC trial[19].

Methods

Study design and setting

The study applied a cross-sectional design using baseline data of the DIAdIC study[19], a randomized controlled trial comparing the effectiveness of two psychoeducational interventions (experimental groups) to usual care (control group). Both interventions are aimed at improving emotional functioning and self-efficacy of patients with advanced cancer and their family caregivers.

Participants and recruitment

The DIAdIC study[19] included patients with advanced cancer and their family caregiver in six European countries (Belgium, Denmark, Ireland, Italy, The Netherlands and United Kingdom). Eligible patients were over 18 years old and been diagnosed with an advanced solid tumor. Exclusions were made for patients with a life expectancy under 3 months, brain cancer, or language barriers (see Appendix A16 for a complete overview of inclusion criteria). The family caregivers participating in the trial could have any relation to the patient, e.g. partner, sibling, child, or friend. Staff from the participating hospital departments screened patients and presented the study to patient-caregiver dyads. See Appendix A17 for an overview of the recruiting hospitals.

Data collection

Before randomization, participants completed a baseline measurement (T0) either on paper or online. After completion of an intervention (experimental groups) or after 12 weeks (control group) the same questionnaire was administered (T0 + 3 months), and then once again at 24 weeks (T0 + 6 months). Only baseline data is reported here. Data was collected from February 2021 to September 2023.

Measures

We used a wide range of measurements in the DIAdIC trial[19], but only the ones relevant to address the aims of this study are described below. Potential predictors of sexual satisfaction were identified based on existing literature[20,21].

Sexual satisfaction (outcome of interest)

We measured sexual satisfaction with 1 item from the Functional Assessment of Cancer Therapy - General questionnaire[22] (patients) and 1 item from the Caregiver Quality of Life Index-Cancer scale[23] (family caregivers). The question read as follows: ‘I am satisfied with my sex life’ ranging from 0 (not at all) to 4 (very much). Patients had the option to indicate ‘prefer not to answer’.

Demographic and clinical information

We collected demographic information about patients and family caregivers' age, gender, individual relationship status, relationship to each other, having children and educational level. Additionally, we included information on the patient's cancer type and treatment.

Active engagement

We measured active engagement through 5 items of the Ways of Giving Support scale[24], using a five-point Likert format that ranged from 1 (never) to 5 (very often), both for patient and family caregiver.

Quality of life

For patients, quality of life was measured with the EORTC QLQ-C15-PAL[25], including subscales on emotional, physical, and social functioning and global health from EORTC QLQ-C30[26] and the social wellbeing scale from Fact-G[22]. For the caregiver, we used the CQOLC[23].

Coping

Both for patient and family caregiver, we measured coping using 20 items from the Brief Cope[27], ranging from 1 (I haven't been doing this at all) to 4 (I've been doing this a lot).

Dyadic coping

Additionally, we used 10 items from the Dyadic Coping Inventory[28], ranging from 1 (very rarely) to 5 (very often), both for patient and family caregiver.

Statistical methods

Descriptive statistics were performed for demographic variables and variable sexual satisfaction. Directed acyclic graphs were constructed to identify confounding variables for each predictor. Multivariable linear regressions were performed for all predictors with sexual satisfaction as dependent variable for patients and family caregivers separately, while controlling for the identified confounders. Statistical analysis was performed using SPSS. We applied the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement[29] to report the results of this study.

Ethical considerations

The DIAdIC study was approved by Commissie Medische Ethiek UZ Gent, Belgium, 22/10/2020; AZ Maria Middelares, Belgium, 16/11/2020; AZ Sint-Lucas, Belgium, 28/12/2021; AZ Damiaan, Belgium, 26/08/2022; St. Vincent's University Hospital Research Ethics Committee, Ireland, 04/12/2020; Comitato Etico dell'Area Vasta Emilia Nord (AVEN), Italy, 13/04/2021; NHS/HSC Research Ethics Committee, United Kingdom, 05/03/2021; Medisch Ethische Toetsings Commissie Erasmus Medisch Centrum Rotterdam, the Netherlands, 15/01/2021. The Denmark Scientific Ethical Committee system (protocol no. 19043825) determined that the protocol did not require formal approval on 22/08/2019 which was confirmed after submission of the protocol. Amendments can be consulted with each ethical committee.

Participants in the study provided written informed consent after receiving both oral and written information about the study.

Results

Demographic characteristics of patients and family caregivers

The sample consisted of 431 patients and 431 family caregivers who participated in the DIAdIC trial[19] in six European countries; Belgium (34.1%), Italy (29.2%), Denmark (24.8%), the Netherlands (2.6%), Ireland (2.8%) and UK (6.5%) (Table 1).

Patients

The mean age of patients was 63. Slightly more than half of patients were female (54.8%). Three out of four patients (75.6%) were partners to the family caregiver. The most frequently reported cancer diagnoses were gastrointestinal and breast cancer (respectively 28.8% and 25.5%). The most frequently reported oncological treatment type at the time of enrolment was chemotherapy (70.8%).

Family caregivers

Family caregivers had a mean age of 58. Three out of five family caregivers (59.2%) were female.

Table 1: Characteristics of obtained sample

	Patients (N = 431)	Family caregivers (N = 431)
Characteristic		
Age in years		
18-55	109 (25.3)	162 (37.6)
56-75	286 (66.4)	242 (56.1)
>76	36 (8.4)	27 (6.3)
Mean (SD)	62.61 (10.103)	58.12 (13.730)
Gender		
Male	195 (45.2%)	176 (40.8%)
Female	236 (54.8%)	255 (59.2%)
Educational attainment		
Primary Education	13 (3.1%)	8 (1.9%)
Secondary Education	239 (56.4%)	253 (59.1%)
Higher Education	172 (40.5%)	167 (39%)
Trial location		
Belgium	147 (34.1%)	147 (34.1%)
Italy	126 (29.2%)	126 (29.2%)
Denmark	107 (24.8%)	107 (24.8%)
The Netherlands	11 (2.6%)	11 (2.6%)
Ireland	12 (2.8%)	12 (2.8%)
UK	28 (6.5%)	28 (6.5%)
Relation to family caregiver		
Spouse/Partner	326 (75.6%)	NA
Other	103 (24.0%)	NA
Cancer Type[a]		
Gastrointestinal	124 (28.8%)	NA
Breast	110 (25.5%)	NA
Lung	47 (10.9%)	NA
Prostate	33 (7.7%)	NA
Gynecological	27 (6.3%)	NA
Kidney	21 (4.9%)	NA
Other	69 (16.0%)	NA
Days since diagnosis		
Mean (SD)	1292.86 (1,858.51)	NA
Having children		
Yes	367 (85.5%)	330 (78.8)
No	62 (14.5%)	87 (20.2)
Treatment type[b]		
Chemotherapy	305 (70.8)	NA
Radiotherapy	17 (3.9)	NA
Antihormonal therapy	44 (10.2)	NA
Immunotherapy	91 (21.1)	NA
Surgery	19 (4.4)	NA

Table 1: Characteristics of obtained sample

	Patients (N = 431)	Family caregivers (N = 431)
Characteristic		
Targeted therapy	21 (4.9)	NA
Other	32 (7.4)	NA
No treatment	12 (2.8)	NA

NA = not applicable

Missing values patient: Age n=0 , Gender n=0, Educational attainment n=7 (1.6%)[c], Recruitment country n=0, Relation to family caregiver n=2 (.5%), Cancer type n=0, Days since diagnosis n=0, Having children n=2 (.5%), Treatment type n=0

Missing values family caregiver: Age n=0, Gender n=0; Educational attainment n=3 (.7%)[b], Recruitment country n=0, Having children n=14 (3.2%)

[a] Gastro-intestinal cancers included: esophageal, intestinal, liver, pancreatic, rectal and stomach cancer. Gynecological cancers included: cervical and ovarian cancer. Other cancers included: Bladder, head and neck, malignant cancer of other and ill-defined sites and melanoma.

[b] Percentages don’t add up to 100% as multiple answers were possible

[c] Response category ‘prefer not to answer’ was chosen and interpreted as missing

Sexual satisfaction in patients and family caregivers

One out of three patients (34.3%) preferred not to answer the question about sexual satisfaction, with varying rates observed in different countries: Belgium 38.4%, Italy 36.3%, and Denmark 22.4% (other countries are not listed as there are not enough respondents to draw meaningful conclusions). The 'prefer-not-to-answer' option was not offered to family caregivers but the latter had more missing values to the sexual satisfaction question compared to patients (respectively 8.6% and 1.2%). Of those who answered (omitting 'prefer not to answer' responses in patients), 42% of patients and 33% of caregivers indicated to be not at all satisfied with their sex life (mean score of respectively 1.21, SD=1.21 vs 1.43, SD=1.21) (Table 2).

Table 2: Sexual satisfaction in obtained sample

	Patients (N=431)	Family caregivers (N=431)
	%	%
Sexual satisfaction		
Not at all	27.5	32.5
A little bit	9.4	19.8
Somewhat	18.3	27.4
Quite a lot	8.0	12.7
A lot	2.3	7.6
Prefer not to answer	34.3*	N/A
Mean (SD)	1.21 (1.21)	1.43 (1.21)

Missings: Patient n=5 (1.2%), Family caregiver n=37 (8.6%)

*Belgium: 38.4%, Italy: 36.3%, Denmark: 22.4%. Other countries are not listed as there are not enough participants to draw conclusions.

Predictors of sexual satisfaction in patients and family caregivers

Patients

Confounders for each predictor as identified through directed acyclic graphs (see Appendix A18 and A19) are listed in Table 3. Patients with prostate and gynecological cancer reported lower sexual satisfaction compared to patients with gastrointestinal cancer (respectively B=-.267, 95% confidence interval [CI] -1.674, -.594, p<.001 and B=-.196, CI -2,103, -.452, p=.003). When adjusted for confounders, higher sexual satisfaction in patients was associated with higher emotional (B=.278 CI .024, .057, p<.001), physical (B=.305, CI .012, .025, p<.001) and social functioning (B=.151, CI .001, .013, p=.032), global health (B=.356, CI .007, .013, p<.001) and social wellbeing (B=.161, .013, .082, p=.008). Gender, age, relation to family caregiver, individual relationship status, having children, treatment, coping, active engagement and dyadic coping did not significantly predict sexual satisfaction.

Family caregivers

In family caregivers, sexual satisfaction was lower as age increased (B= -.142, CI -.022, -.004, p=.005). Family caregivers who were not the patient’s partner reported higher levels of sexual satisfaction compared to family caregivers who were the patient’s partner (B= .257, CI .481, 1.056, p<.001). Family caregivers of patients with gynecological or prostate cancer reported lower levels of sexual satisfaction compared to family caregivers of patients with gastrointestinal cancer but only if the family caregiver was partner to the patient (respectively B=-1.310, CI -2.179, -.442, p=.003 and B=-1.088, CI -1.652, -.523, p<.001, results not in table). Family caregivers with higher emotional functioning reported higher sexual satisfaction (B=.177, CI .011, .043, p=.001). Higher quality of life was associated with higher sexual satisfaction (B=.165, CI -.165, .716, p=.002). Family caregivers of patients, whose physical functioning was higher, reported higher sexual satisfaction. (B=.110, CI .001, .013, p=.032). Gender, individual relationship status, having children, treatment, coping, active engagement, and dyadic coping did not significantly predict sexual satisfaction.

Table 3: Predictors of sexual satisfaction in patients with advanced cancer and their family caregiver in the DIAdIC trial

	Patients				***Family caregivers***			
	Unstandardized B	Standardized B	95% CI	P-value	Unstandardized B	Standardized B	95% CI	P-value
Gender (no confounders)								
Female	Reference				Reference			
Male	-.010	-.004	-.296, .276	0.944	.196	.129	-.059, .450	.131
Age (no confounders)	-0.005	-.042	-.019, .009	.484	-.013	-.142	-.022, -.004	.005
Relation to family caregiver/patient (no confounders)								
Partner	Reference				Reference			
Not partner	.078	.025	-.286, .442	.673	.768	.257	.481, 1.056	<.001
Individual relationship status (No confounders)								
Married or in a relationship	Reference				Reference			
Separated/divorced/widowed	-.282	-.059	-.850, .287	.330	-.071	-.010	-.802, .660	.848
Single/not in a relationship	.104	.017	-.601,.810	.771	.442	.087	-.064, .948	.087
Having children (Confounder: Age)								
Yes	Reference				Reference			
No	-.174	-.049	-595, .246	.414	.027	.009	-.317, .371	.876
Cancer type of patient (Confounders: Gender, age)								
Gastrointestinal	Reference				Reference			
Breast	-.260	-.094	-.728, .208	.276	.012	.004	-.357, .380	.949
Lung	.134	.240	-.339, .607	.578	.208	.053	-.225, .640	.346
Prostate	-1.134	-.267	-1.674, -.594	<.001	.093	.018	-.454, .639	.739
Gynaecological	-1.278	-.196	-2.103, -.452	.003	.078	.014	-.497, .653	.790
Kidney	-.256	-.046	-.925, .414	.453	.203	.035	-.397, .803	.506
Other	-.261	-.082	-.686, .165	.229	-.221	-.061	-.622, .180	.278
Treatment of patient (Confounders: Age, cancer type)								
Chemotherapy	Reference				Reference			
Radiotherapy	-.005	-.001	-.711, .702	.990	.339	.053	-.308, .986	.304
Anti-hormonal	-.114	-.030	-.620, .392	.658	.304	.077	-.177, .784	.215
Immunotherapy	.146	.051	-.236, .528	.453	.205	.065	-.153, .564	.261
Surgery	-.143	-.025	-.831, .545	.682	-.180	-.031	-.791, .431	.563

Targeted therapy	.092	.018	-.519, .702	.767	.134	.023	-.444, .711	.650
Other	-.427	-.101	-.953, .099	.111	-.070	-.009	-.576, .437	.787
None	.182	.023	-.718, 1.081	.691	.015	.002	-.765, .794	.971
Emotional functioning (Confounders: Gender, Age, Cancer type, Treatment, Having children, Social wellbeing, Active engagement)	.040	.278	.024, .057	<.001	.027	.177	.011, .043	.001
Physical functioning of patient (Confounders: Gender, Age, Cancer type, Treatment)	.018	.305	.012, .025	<.001	.007	.110	.001, .013	.032
Social functioning (Confounders: Gender, Age, Cancer type, Treatment, Physical functioning)	.007	.151	.001, .013	.032	NA	NA	NA	NA
Global health[p]/Quality of life[c] (Confounders: Gender, Age, Cancer type, Treatment, Physical functioning[p])	.010	.356	.007, .013	<.001	.009	.165	-.165, .716	.002
Social wellbeing (Confounders: Gender, Age, Cancer type, Treatment, Having children)	.048	.161	.013, .082	.008	NA	NA	NA	NA
Coping (Confounders: Gender, Age, Cancer type, Treatment, Active engagement, Emotional functioning, Social wellbeing[p])	.115	.064	-.100, .329	.295	-.009	-.004	-.233, .215	.937
Active engagement (Confounders: Gender, Age, Cancer type, Treatment, Relation to family caregiver/patient)	.155	.090	-.058, .368	.154	.178	.082	-.041, .397	.110
Dyadic communication (Confounders: Gender, Age, Cancer type, Treatment, Relation to family caregiver/patient)	.067	.038	-.145, .280	.533	.094	.045	-.116, .304	.378

Discussion

Main findings

We examined predictors of sexual satisfaction among patients with advanced cancer and their family caregivers. A diagnosis of prostate or gynecological cancer was associated with lower sexual satisfaction, both for patients and caregivers. Higher emotional functioning, physical functioning (and in patients also social functioning, global health, and social wellbeing) was associated with higher sexual satisfaction of both. Sexual satisfaction of family caregivers was lower with increasing age and in those who were partner to the patient. Among family caregivers, higher levels of emotional functioning and quality of life were associated with higher sexual satisfaction. We also found a frequent use of the "prefer-not-to-answer" option on the sexual satisfaction question among patients.

Interpretation

The finding that gynecological and prostate cancer serve as a predictor for lower sexual satisfaction in both patients and partner family caregivers strengthens previous research. Women with gynecological cancer often experience sexual dissatisfaction in intimate relationships[30], resulting in physiological difficulties, psychological distress and relationship problems[31]. Similarly, for men with prostate cancer, erectile dysfunction is a common side effect of treatment, affecting sexual intimacy, causing changes in their sexual satisfaction[32]. The finding that physical functioning, social functioning, emotional functioning, and global health of patients are associated with higher sexual satisfaction, is in line with previous research. A cross-sectional study with prostate cancer patients found that physical and psychosocial variables (depression, anxiety, relationship closeness) were predictive of sexual satisfaction[15]. This highlights the interconnectedness of various aspects of health and wellbeing in patients with advanced cancer.

Of the ones who responded to the question, about two in five patients (42%) and one in three family caregivers (32.5%) indicated that they were ‘not at all satisfied’ with their sex life. In another survey study using the FACT-G[22], between 5.3% and 12.2% of cancer patients of all stages reported to be not at all satisfied with their sex life[33], which is much lower compared to our sample. This points to the impact on sexual satisfaction of the advanced stage of cancer on the patient and on being a family caregiver. To our knowledge, no research is available on reference values for sexual satisfaction in a similar population (patients with advanced cancer and their family caregiver) using the same instrument as employed in our study. In a study with prostate cancer patients and their partners, utilizing the Index of Sexual Satisfaction[34], patients averaged a score of 56.91, while their partners scored 54.94 out of a possible 100[15]. Our findings thus suggest that patients and family caregivers in our study also exhibit low scores for sexual satisfaction (mean of respectively 1.21 and 1.43 on a 0 to 4 Likert scale).

There thus is a need for interventions addressing sexual health needs of both patients and family caregivers. Even though most interventions focus on individual sexual health, a review by Li and colleagues showed that for dyadic couple-based interventions on sexuality, improvements for both parties involved are found; patients mostly reported improved physical health and partners improved sexual relationships[35]. The pilot intervention by Canada and colleagues is an example of an intervention stimulating sexual communication based on sex therapy principles to enhance sexual wellbeing in cancer patients and their sexual partners[36].

Clinical implications

The study's findings suggest the importance of several strategies in clinical practice to adequately address sexual health. A first implication is the usefulness for healthcare professionals to incorporate the impact of cancer on sexuality into routine care plans, especially for gynecological and prostate cancer patients. This can positively impact the relational dynamics between patients and their partners, as well as enhance overall quality of life. A second implication is the need for tailored approaches. Certain cancer types, such as prostate and gynecological cancers, are associated with lower sexual satisfaction. While all those with cancer may face issues, those with cancer affecting sexual organs face unique challenges. A third implication is the need for a dyadic approach. Both patients and family caregivers report low sexual satisfaction, which can be predicted by health parameters in both parties. Li and colleagues recommend that psychoeducation, skills training, and therapeutic counseling are the most effective combination for interventions focused on sexuality[37]. Additionally, healthcare professionals should introduce support to cope with sexual problems, as assessment might be difficult considering that patients and family caregivers might be hesitant to openly disclose their sexual problems. A fourth implication is the importance of prioritizing emotional resilience and coping strategies, as we observed a significant relationship between emotional functioning and sexual satisfaction in both patients and family caregivers. Integrating education and support in these areas into care provided to both patients and family caregivers can contribute to their overall experience and adjustment to the challenges posed by advanced cancer and vice versa, integrating emotional support for patients and family caregivers can contribute to higher sexual satisfaction.

Study strengths and limitations

This study was part of a large international randomized controlled trial, which included many measures in the baseline survey. This allowed us to map many possible predictors for sexual satisfaction in patients and family caregivers. Additionally, we were able to obtain a large sample size (n = 431).

However, certain limitations of the study must be acknowledged. Our study is cross-sectional and correlational and thus only allows to explore predictors of sexual satisfaction but not to provide conclusive evidence about causal attribution. However, we tried to minimize bias due to confounding by carefully designing directed acyclic graphs to guide the deconfounding strategy for the relationship between each of the predictors and sexual satisfaction. Selection bias is another risk. The population of our study consists of patients and family caregivers enrolled for a psychoeducational trial[19] and are therefore not representative for the entire population of patients with advanced cancer and their family caregivers. However, our aim was not to make population estimates but to explore associations for which theoretical generalizability suffices[38]. Next, differences in the measurement validated for patients and family caregivers in the survey also introduced measurement bias issues. A 'prefer not to answer' option when asking about sexual satisfaction was only available for patients and not for family caregivers. When given the option, approximately one in three patients chose the 'prefer not to answer option' for the sexual satisfaction item, while missing values for the same item in family caregivers were not nearly as high. By giving the option of 'prefer not to answer', you give respondents 'an escape route' which many respondents used, which underlines the sensitivity of the topic of sexual satisfaction. Another limitation of our study is the fact that we only measured sexual satisfaction in one single item, so we cannot presume that the construct was adequately measured. Incorporating additional sexual health variables (e.g., function or activity frequency) could enhance our understanding of sexual health in the study population.

A particular strength of the study lies in its consideration of the sexual satisfaction of family caregivers who are not the patient's partner, and therefore expanding the perspective beyond the focus on the patient's sexual partner[39–41]. Further research on the impact of non-partner caregiving on sexual satisfaction can enrich our findings. Another strength is its inclusion of patients with different types of advanced cancer, which allows for comparisons in sexual satisfaction across various cancer types.

Conclusions

The results underscore that sexual satisfaction of patients and family caregivers is related to health factors in physical, emotional, and social domains. Patients and family caregivers could benefit from a dyadic approach to address sexual satisfaction. Openness about sexual health concerns by healthcare professionals and patients and family caregivers can contribute to a more effective approach to address the sexual health needs of patients and family caregivers.

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Conflict of Interest Statement

There is no conflict of interest.

Author contributions

OM, AdV, JC, SD and LD designed the study. OM drafted the manuscript with input from all authors. All authors have substantively revised the manuscript and approved the final version before submission.

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Data availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Chapter VI

The DIADIC advanced cancer psychoeducational intervention RCT: impact on emotional function and self-efficacy

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Abstract

Background: Dyadic psychoeducational interventions demonstrate benefits in oncology by concurrently addressing challenges for patients and family caregivers. This trial compares the effects of two psychoeducational interventions for patients with advanced cancer and their family caregivers.

Methods: In this international multicenter individual parallel-group superiority randomized controlled trial, patients were eligible if diagnosed with advanced solid cancer, along with their primary family caregiver. Dyads were randomly assigned (1:1:1) to a web-based intervention (iFOCUS), a face-to-face intervention (FOCUS+), or standard care. The two primary endpoints were emotional functioning assessed by 10-item short form based on the European Organization for Research and Treatment of Cancer (EORTC) item bank, and self-efficacy assessed by Cancer Self-efficacy Scale (CASE) at 12 weeks (T1).

Findings: Between February 2021 and August 2023, 431 dyads were randomized (without blinding) to iFOCUS (148), FOCUS+ (140) or standard care (143). iFOCUS did not yield significant improvements compared to control group at T1 for patients or family caregivers in emotional functioning (-·27; 95% CI -2·11 to ·76 and ·30; 95% CI -1·41 to 2·00) or self-efficacy (·49; 95% CI -6·21 to 7·19 and 3·66; 95% CI -3·36 to 10·61), respectively. FOCUS+ did not yield statistically significant improvements at T1 for patients or family caregivers in emotional functioning (·12; 95% CI -1·65 to 1·89 and ·17; 95% CI 1·45 to 1·79), but significantly improved self-efficacy compared to control group among patients (9·02; 95% CI 2·45 to 15·58), but not family caregivers (3·88; 95% CI -2·84 to 10·61) at T1. No significant T2 improvements were found.

Interpretation: The improvement in patient self-efficacy from FOCUS+, might be assumed to positively impact family caregivers in other areas as well. The web-based version of the intervention seems less promising.

Funding: The European Union’s Horizon 2020 research and innovation programme. Registration on clinicaltrial.gov (NCT04626349). The trial is now closed.

Introduction

Background

The consequences of advanced cancer seriously impact the quality of life of patients. But also family caregivers report it to be a physically and psychologically demanding illness.[1,2] The impact of advanced cancer on patients and family caregivers is also interrelated; the self-efficacy in coping with the illness and the wellbeing of the patient affect that of the family caregiver and vice versa.[3] Individual theoretical models on coping and stress (e.g., model by Lazarus and Folkman)[4] have therefore been adapted to include an interdependent and relational context of stress and coping.[5]

Empirical evidence suggests that dyadic interventions (targeting patients and family caregivers as the unit of care) have the capacity to concurrently address symptoms and challenges affecting patients, caregivers, and the dynamics of their interdependency.[6,7] Additionally, dyadic interventions have been shown to not only result in better outcomes for both patients and family caregivers, they have also proven to be more cost-effective, compared to single target interventions.[8]

Psychoeducational dyadic interventions have also increased the quality of mutual communication and support.[9,10] For example, the FOCUS program developed in the United States has demonstrated effectiveness in several randomized control trials.[11–13] The FOCUS program is a face-to-face intervention delivered by a trained nurse providing psychoeducation to both patients and family caregivers. In dyads affected by advanced cancer it led to a small but significant improvement in dyads' coping, self-efficacy and social quality of life (QoL) and in caregivers' emotional QoL.[11] Earlier RCTs of FOCUS in dyads affected by breast cancer showed reduction in negative illness appraisal and hopelessness in patients and decrease in negative caregiving appraisal in family caregivers.[12] In prostate cancer, patients experienced a significant reduction in illness uncertainty and increased communication about their illness with caregiver; caregivers reported significantly better mental and overall QoL, less negative appraisal, lower hopelessness, reduced uncertainty, higher self-efficacy, improved communication, and less symptom distress.[13] A phase 2 feasibility study also demonstrated promising results of a web-based version of the FOCUS program on dyads' emotional distress, QoL, and family caregivers' self-efficacy.[14]

Despite the reported benefits of FOCUS, it is yet to be adapted and tested in European healthcare systems. As part of European Union's Horizon 2020 research and innovation programme, the original FOCUS program was adapted for use in dyads coping with advanced cancer in six European countries. This adaptation process, comprehensively described elsewhere, modified the original FOCUS program into the face-to-face FOCUS+ program to ensure cultural relevance to the six participating European countries.[15]

Additionally, a web-based adaptation of the entire program was developed, the iFOCUS intervention. The rationale for this web-based version was the current challenges, including staff time and other resources required for in-person interventions. Furthermore, there is some evidence on the effectiveness of web-based interventions as compared to human-facilitated psychoeducation interventions.[16,17]

Objective

The overall aim of this study is to evaluate the effectiveness of two psychoeducational interventions (a face-to-face nurse-led intervention called FOCUS+ and a web-based intervention called iFOCUS), aimed at improving the emotional functioning and self-efficacy (primary outcomes) of patients with advanced cancer and their family caregiver at 12 (T1) and 24 (T2) weeks. Both interventions are compared with care as usual.

Methods

Trial design

We conducted an international multi-center parallel-group three-arm superiority trial comparing 1) the FOCUS+ face-to-face intervention (intervention 1) and 2) the iFOCUS web-based intervention (intervention 2) to 3) standard care (control group). Dyads were randomly assigned to one of the three groups in a 1:1:1 allocation ratio. Details on the trial procedures are fully described in the research protocol.[18] However, we have included key information here to assist in contextualizing our results. We applied the Consolidated Standards of Reporting Trials (CONSORT) statement to report on all relevant aspects of the trial.[19]

Participants

For this study, individuals diagnosed with advanced solid organ cancer (excluding brain cancer) with an estimated life expectancy of two years were recruited along with their primary family caregiver, as determined by the patient. A detailed overview of the inclusion and exclusion criteria for both patients and family caregivers can be found in Box 1. Exclusion of patients with brain cancer was based on the potential challenges they might encounter in completing the intervention and questionnaires due to cognitive issues. Additionally, individuals with a prognosis of less than three months were excluded due to their vulnerability, as the interventions took place over a three-month period. In August 2022, following recurrent input from all recruitment centers, it was decided to remove the inclusion criterion “the treating physician not being surprised if death were to take place within two years or less”, as it was judged to create an unnecessary barrier for recruitment of the population of interest.

Setting

The trial took place in Belgium (Flanders), the Netherlands, Italy, Denmark, Ireland, and the United Kingdom. The interventions (FOCUS+ and iFOCUS) were administered in the homes of the patient-caregiver dyads or at another location preferred by the dyad.

Participants were recruited from participating hospitals and their respective departments (e.g., oncology or pneumology) in each country (see Appendix A20 for overview of recruiting hospitals and departments).

Box 2: Inclusion and exclusion criteria for patients and family caregivers

Inclusion criteria	*Screened by*	Exclusion criteria	*Screened by*
Patient			
Diagnosis of cancer: solid organ (lung, colorectal, breast, prostate, and other)	Treating clinician or RA*	Brain cancer, non-solid cancers	Treating clinician or RA
No longer receives curative treatment (only life-prolonging or palliative treatments)	Treating clinician or RA	Prognosis of fewer than 3 months	Treating clinician or RA
Written informed consent	RA	Has no family caregivers	RA
Lives within feasible distance for intervention nurses to travel	RA	< 18 years old	RA
		Unable to participate in available languages	RA
Family caregiver			
Written informed consent	RA	Unable to physically or mentally participate	RA
Primary family caregiver as determined by the patient	RA	Cancer diagnosis in the last 12 months	RA
Lives within feasible distance for intervention nurses to travel	RA	<18 years old	RA
		Unable to participate in available languages	RA
Dyad			
Patient and/or family caregivers have access to and are familiar with the use of the internet	RA		
RA* = research assistant, either from the study team or in situ			

Interventions

Both FOCUS+ and iFOCUS interventions were administered in addition to usual care and focused on psychoeducation, aimed at teaching dyads optimal strategies for jointly managing the implications of advanced cancer and addressing their prioritized concerns. The interventions were tailored to meet the specific needs and preferences of the patient-caregiver dyads based on the information shared during the intervention sessions. While the FOCUS+ and iFOCUS interventions differed in their modes of delivery (face-to-face vs. web-based), they shared the same core content, addressing five essential core components: (1) supporting family involvement, communication, and mutual support, (2) fostering outlook and meaning, (3) enhancing coping effectiveness, (4) reducing uncertainty, and (5) teaching symptom management while instilling confidence to handle specific tasks. The interventions are intended to be completed by both members of a dyad together, to increase communication and support between patient and family caregiver. Both interventions are based on dyadic stress and coping frameworks that state that personal, social, and illness-related factors influence how patients and family caregivers appraise the illness and cope with the demands associated with it together.[5]

A completed TIDieR checklist[20] of both interventions can be found in Appendix A21.

Face-to-face intervention (FOCUS+)

The face-to-face FOCUS+ intervention was a home-based program comprising two 90-minute home visits, and one 30-minute online video session, facilitated by a trained intervention nurse over a 12-week period, with a focus on the five core components (Box 2). A total of 16 nurses recruited to the project underwent an extensive online training to equip them with the necessary knowledge and skills for effective intervention implementation, including a regular follow-up in both a national (within each country) and an international community of practice where cases and experiences were exchanged and strategies to improve adherence to the intervention protocol were discussed. The national community of practice was facilitated by the national FOCUS+ lead (who also followed the training), the international community of practice was facilitated by the team that developed the original FOCUS intervention in the USA. Dyads were also provided with a printed FOCUS+ guide, which offered practical information and tailored tips for individuals coping with advanced cancer and their family caregivers. This guide served as an additional resource for reference during and after the sessions. To ensure relevance, the content of the sessions was tailored to the dyads' specific needs, which allowed nurses to allocate more time to topics perceived to be particularly beneficial for the dyad or to minimize discussion on certain content areas if the dyad did not require assistance in those specific areas. More details on the development and content of the FOCUS+ intervention is reported elsewhere.[15]

Web-based intervention (iFOCUS)

The iFOCUS web-based intervention was a self-managed program designed for autonomous completion by patient-caregiver dyads at home or in another preferred location. Spanning four sessions spread evenly over a period of 12 weeks, it entailed the same five core components addressed in the face-to-face intervention (Box 2). Dyads engaged in the sessions simultaneously, seated together in front of a computer or tablet, with access provided through an emailed link. In each session, dyads were prompted to assess their strengths, problems, and needs, and tailored educational content was then presented based on these evaluations. The content of the iFOCUS intervention was further tailored to demographic factors (age, sex, and the dyad's relationship) and information gathered during web-based sessions, to enhance the intervention's relevance. Further information regarding the development of the iFOCUS intervention is reported elsewhere.[21]

Control group (standard care as usual)

Similarly to patients in the intervention arms, dyads in the control group were administered standard care in accordance with the healthcare system protocols of the participating countries. The medical practitioner overseeing their treatment assessed and determined their care.

Box 2: Five core components of the FOCUS+ and iFOCUS interventions

Core concept	Goals
Supporting family involvement, communication, and mutual communication (F)	- Discuss and support communication - Encourage mutual support and teamwork - Identify family strengths - Help children in the family as needed
Supporting outlook and meaning (O)	- Help dyads share fears and concerns - Discuss positive and negative feelings of dyads - Educate dyads about different kind of feelings and attitudes - Encourage dyads to set realistic short-term goals
Increasing coping effectiveness (C)	- Help dyads deal with overwhelming stress - Discuss and support active coping strategies by dyads - Assist caregivers to manage the demands of illness
Reducing uncertainty (U)	- Educate dyads about disease and treatments as needed - Teach dyads how they can obtain additional information - Help dyads learn ways to live with uncertainty
Teaching symptom management and giving the confidence to handle specific tasks and problems (S)	- Assess symptoms in patients and family caregiver - Teach self-care strategies to manage symptoms (e.g. ways to manage reactions and side effects associated with the illness, treatments, and adjustment) - Help dyads identify relevant resources in the community (community services and support)

Data collection procedures and outcomes

All outcome measures were collected from patient-caregiver dyads at three time points: T0 (baseline measurement before randomization), T1 (first follow-up, 12 weeks after baseline) and T2 (second follow-up, 24 weeks after baseline). Participants had the option to complete the self-reporting questionnaire online or on paper, with aid from a data collector for questionnaire completion via telephone or in person depending on preference.

Two primary endpoints were defined: 1) emotional functioning and 2) self-efficacy of both the person with advanced cancer and the family caregiver at first follow-up at 12 weeks (T1). Emotional functioning (EF) was measured using a 10-item short form (EF10) based on the European Organization for Research and Treatment of Cancer (EORTC) EF item bank.[22] Self-efficacy was measured with 17 items from the Lewis Cancer self-efficacy scale[23], validated by Northouse.[11] The scale assessed the confidence patients and family caregivers had to manage cancer. A higher score on both scales indicated a higher emotional functioning or self-efficacy. Several secondary endpoints were defined (see protocol[18]), including QoL, benefits of illness, coping, dyadic communication, ways of giving support and formal healthcare use and costs at T1 and T2, as well as including the two primary outcome variables measured at T2 (only the primary outcomes are reported in this manuscript).

Socio-demographic and clinical characteristics (such as diagnosis, time of diagnosis, treatment type) of patients and family caregivers were collected during enrolment or at baseline through a questionnaire.

Sample size

To detect a 0·375 SD difference between the control group and the intervention arms at T1 (12 weeks) in the primary outcomes with alpha set at 0·0125 (to correct for multiplicity) and power at 90% (see detail in study protocol[18]), we anticipated that 203 dyads were needed in each arm across all countries (i.e. 609 in total). Anticipating a 65% retention rate at T1, 939 dyads needed to be enrolled across the 6 countries (313 per group).

Randomization

Randomization was performed with a computer randomization schedule (Mersenne Twister Random Number Generator[24]) with a 1:1:1 allocation ratio to one of the two intervention arms or the standard care arm. The computer randomization schedule used a block randomization that was concealed to the research team. The responsible trial managers in each country communicated the study arm allocation to the dyads by phone or email. Allocation concealment was safeguarded, as the randomization to one of the study arms only occurred after baseline measurement was completed by patient and family caregiver. Given the nature of the intervention, it was not feasible to implement blinding for the patients, family caregivers or intervention nurses involved in the face-to-face FOCUS+ intervention.

Statistical methods

We performed 'intention-to-treat' (ITT) as primary analysis and per-protocol (PP) as a sensitivity analysis. For the ITT analysis performed multiple imputations (n=50) for missing data using the Fully Conditional Specification (FCS) method. Based on relevant literature and discussions within the author team, the predictors in the imputation model for emotional functioning were baseline emotional functioning, days since diagnosis, study arm, recruitment site, sex, age, and cancer type. The predictors in the imputation model for self-efficacy were baseline self-efficacy, days since diagnosis, study arm, recruitment site, sex, age, cancer type, and education level. We examined the percentages of loss to follow-up at the T1 measurement for our primary outcomes. Loss to follow-up was defined as incomplete items pertaining to emotional functioning and self-efficacy for participants randomized in the trial.

The ITT population consisted of all dyads randomized to one of the intervention groups. The PP population at T1 consisted of the ITT population minus those in the intervention groups who did not complete all FOCUS+ or iFOCUS sessions and T1 measurements. Similarly, the PP population at T2 consisted of the ITT population minus those in the intervention groups who did not complete all FOCUS+ or iFOCUS sessions and T2 measurements. No imputations were performed in the PP analysis.

Linear mixed-model analyses were conducted with the primary endpoints emotional functioning and self-efficacy as the dependent variables, study arm as the fixed effect, and baseline measurements of emotional functioning and self-efficacy as covariates. We specified an intercept random effect with recruitment site as the subject variable. Data imputation was performed using R software and the ITT and PP analyses were performed by 2 authors independently using R software and IBM SPSS version 28 software to guarantee reliability of the results.

Registration, protocol, and funding

The trial is registered on ClinicalTrials.gov, identifier NCT04626349. The protocol of the DIAdIC trial was published in 2021.[18] The DIAdIC project received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 825722.

Results

Baseline characteristics

We enrolled 431 dyads into the DIAdIC study. Dyads were randomized to the iFOCUS intervention (n=148), FOCUS+ intervention (n=140) or the control group (n=143). Figure 1 shows the participant flowchart with a progression of participants throughout the study.

Recruitment to the trial took place between February 2021 and August 2023. An overview of the enrolment results in each country and the demographic baseline and clinical characteristics of participating patients and family caregivers is shown in Table 1.

Intervention compliance in the iFOCUS intervention group was 52% and 76·4% in the FOCUS+ intervention group. Questionnaire compliance was 78·4% for patients and 78·7% for family caregivers at 12 weeks (T1) and 65% for patients and 64·5% for family caregivers at 24 weeks (T2). The loss-to-follow up tables can be found in Appendix A22.

Primary endpoints

Intention to treat (ITT) analysis

The mean scores at baseline for emotional functioning and self-efficacy can be found in Appendix A23.

iFOCUS vs control

Patients

Emotional functioning scores (EF10[22]), did not differ significantly between the iFOCUS intervention group and control group at T1 in patients (baseline-adjusted mean difference, -·27; 95% CI, -2·11 to 1·57; P = ·774) (Table 2). We also did not find a significant difference for self-efficacy (CASE[23]), between patients in the iFOCUS intervention group and control group at T1 (baseline-adjusted mean difference, ·49; 95% CI, -6·21 to 7·19; P = ·887). No significant improvements were observed at T2, with negligible effect sizes (Cohen’s d) for patients in the iFOCUS intervention at both T1 and T2.

Family caregivers

Emotional functioning did not differ significantly between the iFOCUS intervention group and control group at T1 in family caregivers (baseline-adjusted mean difference, ·30; 95% CI, -1·41 to 2·00; P = ·732). For self-efficacy, we did not find a significant difference between the iFOCUS intervention group and control group at T1 in family caregivers (baseline-adjusted mean difference, 3·66; 95% CI, -3·36 to 10·68; P = ·306). No significant improvements were observed at T2, with negligible effect sizes (Cohen’s d) for family caregivers in the iFOCUS intervention at both T1 and T2.

Figure 1: Participant flowchart

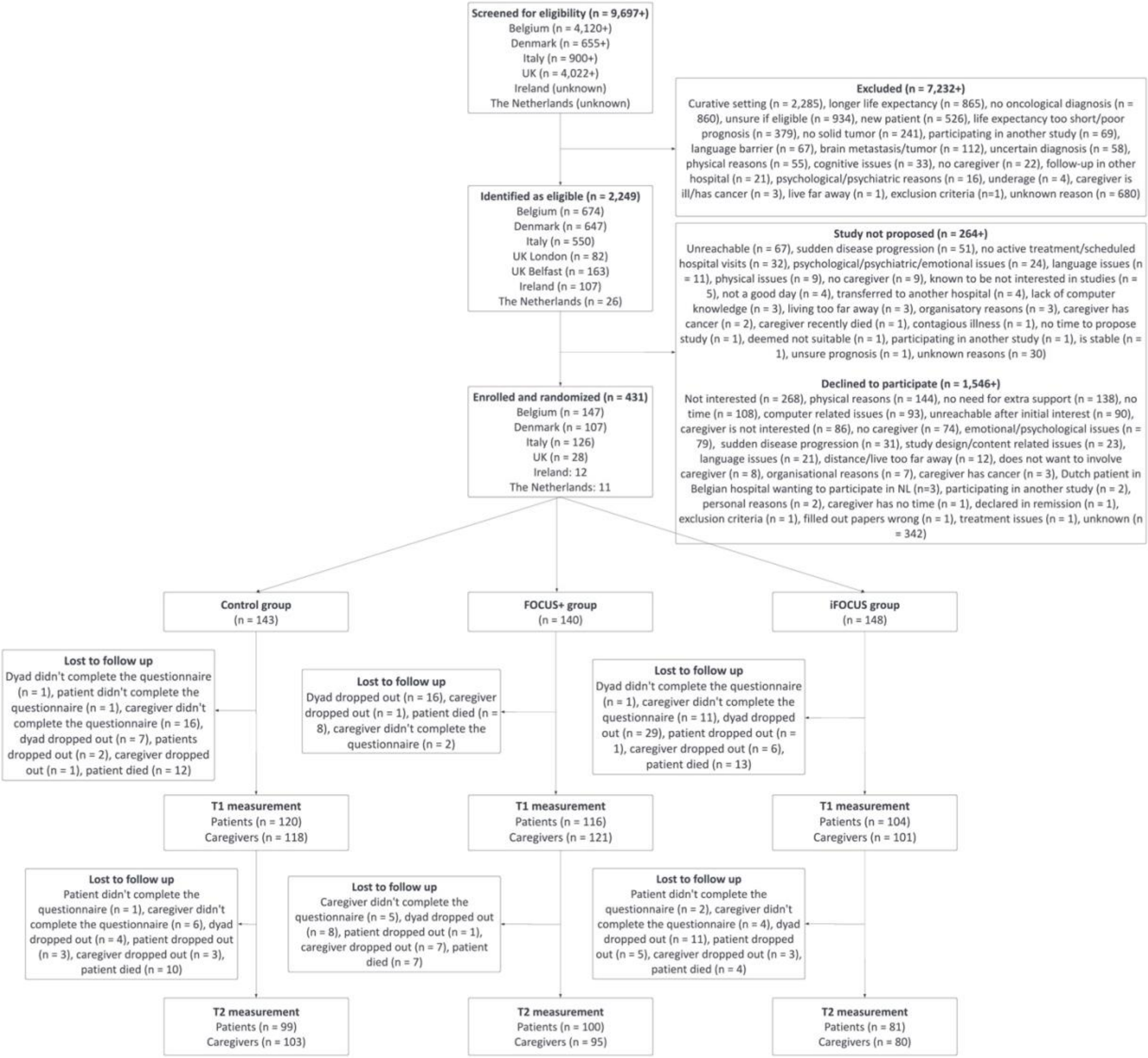

Table 1: baseline characteristics

	Patient				Family caregiver			
Characteristics	**Overall** N = 431	**iFOCUS** N = 148	**FOCUS+** N = 140	**Control Group** N = 143	**Overall**, N = 431	**iFOCUS**, N = 148	**FOCUS+**, N = 140	**Control Group**, N = 143
Recruitment Country								
Belgium	147 (34·1)	46 (31·1)	50 (35·7)	51 (35·7)	147 (34·1)	46 (31·1)	50 (35·7)	51 (35·7)
Italy	126 (29·2)	52 (35·1)	37 (26·4)	37 (25·9)	126 (29·2)	52 (35·1)	37 (26·4)	37 (25·9)
Denmark	107 (24·8)	35 (23·6)	35 (25·0)	37 (25·9)	107 (24·8)	35 (23·6)	35 (25·0)	37 (25·9)
The Netherlands	11 (2·6)	5 (3·4)	5 (3·6)	1 (0·7)	11 (2·6)	5 (3·4)	5 (3·6)	1 (0·7)
Ireland	12 (2·8)	3 (2·0)	5 (3·6)	4 (2·8)	12 (2·8)	3 (2·0)	5 (3·6)	4 (2·8)
UK	28 (6·5)	7 (4·8)	8 (5·7)	13 (9·1)	28 (6·5)	7 (4·8)	8 (5·7)	13 (9·1)
Age in years								
18-55	109 (25·3)	45 (30·4)	30 (21·4)	34 (23·8)	162 (37·6)	63 (42·6)	43 (30·7)	56 (39·2)
56-75	286 (66·4)	93 (62·8)	96 (68·6)	97 (67·8)	242 (56·1)	75 (50·7)	86 (61·4)	81 (56·6)
>76	36 (8·4)	10 (6·8)	14 (10·0)	12 (8·4)	27 (6·3)	10 (6·8)	11 (7·9)	6 (4·2)
Sex								
Male	195 (45·2)	71 (48·0)	62 (44·3)	62 (43·4)	176 (40·8)	49 (33·1)	64 (45·7)	63 (44·1)
Female	236 (54·8)	77 (52·0)	78 (55·7)	81 (56·6)	255 (59·2)	99 (66·9)	76 (54·3)	80 (55·9)
Educational attainment								
Primary Education	13 (3·1)	3 (2·0)	7 (5·1)	3 (2·1)	8 (1·9)	3 (2·0)	3 (2·1)	2 (1·4)
Secondary Education	239 (56·4)	86 (58·5)	77 (56·2)	76 (54·3)	253 (58·7)	84 (56·8)	86 (61·4)	83 (58·0)
Higher Education	172 (40·6)	58 (39·5)	53 (38·7)	61 (43·6)	167 (38·7)	59 (39·9)	50 (35·7)	58 (40·6)
Unknown	7 (1·6)	1 (0·7)	3 (2·1)	3 (2·1)	3 (0·7)	2 (1·4)	1 (0·7)	0
Relationship with family caregiver								
Spouse/Partner	326 (76·0)	107 (72·8)	109 (78·4)	110 (76·9)	N/A	N/A	N/A	N/A
Other	103 (24·0)	40 (27·2)	30 (21·6)	33 (23·1)	N/A	N/A	N/A	N/A
Unknown	2 (0·5)	1 (0·7)	1 (0·7)	0	N/A	N/A	N/A	N/A
Cancer Type								

Table 1: baseline characteristics

Characteristics	Patient				Family caregiver			
	Overall N = 431	**iFOCUS** N = 148	**FOCUS+** N = 140	**Control Group** N = 143	**Overall**, N = 431	**iFOCUS**, N = 148	**FOCUS+**, N = 140	**Control Group**, N = 143
Gastrointestinal	124 (28·8)	41 (27·7)	36 (25·7)	47 (32·9)	N/A	N/A	N/A	N/A
Breast	110 (25·5)	34 (23·0)	37 (26·4)	39 (27·3)	N/A	N/A	N/A	N/A
Lung	47 (10·9)	15 (10·1)	17 (12·1)	15 (10·5)	N/A	N/A	N/A	N/A
Prostate	33 (7·7)	15 (10·1)	12 (8·6)	6 (4·2)	N/A	N/A	N/A	N/A
Gynecological	27 (6·3)	9 (6·1)	10 (7·1)	8 (5·6)	N/A	N/A	N/A	N/A
Kidney	21 (4·9)	6 (4·1)	8 (5·7)	7 (4·9)	N/A	N/A	N/A	N/A
Other	69 (16·0)	28 (18·9)	20 (14·3)	21 (14·7)	N/A	N/A	N/A	N/A
Days since diagnosis								
Mean (SD)	1292·86 (1858·51)	1308·03 (1841·30)	1324·52 (1767·11)	1246·17 (1972·20)	N/A	N/A	N/A	N/A
Relationship status								
Single/Not in a relationship	27 (6·3)	16 (10·8)	7 (5·0)	4 (2·8)	30 (7·0)	16 (10·8)	4 (2·9)	10 (7·0)
Married/in a relationship	360 (83·5)	119 (80·4)	115 (82·1)	126 (88·1)	382 (88·6)	127 (85·8)	127 (90·7)	128 (89·5)
Separated/Divorced/Widowed	41 (9·5)	12 (8·1)	17 (12·1)	12 (8·4)	15 (3·5)	5 (3·4)	7 (5·0)	3 (2·1)
Prefer not to answer	3 (0·7)	1 (0·7)	1 (0·7)	1 (0·7)	4 (0·9)	0	2 (1·4)	2 (1·4)
Treatment type (multiple answers possible)								
Chemotherapy	305 (70·8)	103 (69·6)	102 (72·9)	100 (69·9)	N/A	N/A	N/A	N/A
Radiotherapy	17 (3·9)	1 (0·7)	10 (7·1)	6 (4·2)	N/A	N/A	N/A	N/A
Antihormonal therapy	44 (10·2)	17 (11·5)	15 (10·7)	12 (8·4)	N/A	N/A	N/A	N/A
Immunotherapy	91 (21·1)	30 (20·3)	29 (20·7)	32 (22·4)	N/A	N/A	N/A	N/A
Surgery	19 (4·4)	5 (3·4)	7 (5·0)	7 (4·9)	N/A	N/A	N/A	N/A
Targeted therapy	21 (4·9)	4 (2·7)	8 (5·7)	9 (6·3)	N/A	N/A	N/A	N/A
Other	32 (7·4)	14 (9·5)	9 (6·4)	9 (6·3)	N/A	N/A	N/A	N/A
None	12 (2·8)	6 (4·1)	2 (1·4)	4 (2·8)	N/A	N/A	N/A	N/A

Table 1: baseline characteristics

Characteristics	Patient				Family caregiver			
	Overall N = 431	**iFOCUS** N = 148	**FOCUS+** N = 140	**Control Group** N = 143	**Overall**, N = 431	**iFOCUS**, N = 148	**FOCUS+**, N = 140	**Control Group**, N = 143
Children (multiple answer possible)								
Under the age of 18	49 (11·4)	18 (12·2)	17 (12·2)	14 (9·9)	70 (16·2)	28 (18·9)	18 (12·9)	24 (16·8)
Over the age of 18	334 (77·9)	110 (74·3)	109 (78·4)	115 (81·0)	288 (66·8)	89 (60·1)	104 (74·3)	95 (66·4)
No Children	62 (14·5)	25 (16·9)	18 (12·9)	19 (13·4)	87 (20·2)	35 (23·6)	22 (15·7)	30 (21·0)
Living situation (multiple answer possible)								
With spouse/partner	348 (90·7)	115 (77·7)	114 (81·4)	119 (83·2)	368 (85·4)	119 (80·4)	126 (90·0)	123 (86·0)
With children < 18	49 (11·4)	20 (13·5)	16 (11·4)	13 (9·1)	61 (14·2)	27 (18·2)	15 (10·7)	19 (13·3)
With children > 18	75 (17·4)	24 (16·2)	25 (17·9)	26 (18·2)	52 (12·1)	16 (10·8)	20 (14·3)	16 (11·2)
With other person	2 (0·5)	1 (0·7)	0	1 (0·7)	7 (1·6)	1 (0·7)	0	6 (4·2)
Alone	48 (11·1)	19 (12·8)	15 (10·7)	14 (9·8)	22 (5·1)	9 (6·1)	7 (5·0)	6 (4·2)
Financial difficulties								
Not at all	265 (61·5)	96 (64·9)	78 (55·7)	91 (63·6)	296 (68·7)	110 (74·3)	92 (65·7)	94 (65·7)
A little	92 (21·3)	27 (18·2)	30 (21·4)	35 (24·5)	87 (20·2)	22 (14·9)	32 (22·9)	33 (23·1)
Quite a bit	38 (8·8)	10 (6·8)	20 (14·3)	8 (5·6)	27 (6·3)	11 (7·4)	8 (5·7)	8 (5·6)
Very Much	26 (6·0)	12 (8·1)	7 (5·0)	7 (4·9)	7 (1·6)	1 (0·7)	4 (2·9)	2 (1·4)
Prefer not to answer	10 (2·3)	3 (2·0)	5 (3·6)	2 (1·4)	13 (3·0)	4 (2·7)	3 (2·1)	6 (4·2)
Living together with person with whom you participate in the study with								
Yes	349 (81·5)	115 (78·7)	113 (80·7)	121 (84·6)	349 (81·5)	115 (78·7)	113 (80·7)	121 (84·6)
No	79 (18·5)	31 (20·9)	26 (18·7)	22 (15·4)	79 (18·5)	31 (20·9)	26 (18·7)	22 (15·4)
Unknown	3 (0·7)	2 (1·4)	1 (0·7)	0	3 (0·7)	2 (1·4)	1 (0·7)	0

FOCUS+ vs control

Patients

No significant difference was found between patients in the FOCUS+ intervention group and control group at T1 for emotional functioning (baseline-adjusted mean difference, ·12; 95% CI, -1·65 to 1·89; P = ·897). A statistically significant difference was found between patients in the FOCUS+ intervention group and control group at T1 for self-efficacy (baseline-adjusted mean difference, 9·02; 95% CI, 2·45 to 15·58; P = ·007). No significant differences were found at T2 for patients in the FOCUS+ intervention. A small effect size was found for patients in FOCUS+ at T1 for self-efficacy (Cohen's d = ·36; 95% CI, ·13 to ·60). Other effect sizes were negligible.

Family caregivers

No significant difference was found between the FOCUS+ intervention group and control group at T1 for emotional functioning in family caregivers (baseline-adjusted mean difference, ·17; 95% CI, -1·45 to 1·79; P = ·834). Similarly, no significant difference was found between the FOCUS+ intervention group and control group at T1 in self-efficacy for family caregivers (baseline-adjusted mean difference, 3·88; 95% CI, -2·84 to 10·61; P = ·258). No significant differences were found at T2. Negligible effect sizes were found for all family caregiver outcomes in all comparisons.

Table 2: Primary endpoints effect (intention-to-treat principle)

		Mean difference (95% CI)				**Effect size (Cohen's d) (95% CI)**				**p-value**			
		T1		***T2***		***T1***		***T2***		***T1***		***T2***	
		iFOCUS vs control group	***FOCUS+ vs control group***	***iFOCUS vs control group***	***FOCUS+ vs control group***	***iFOCUS vs control group***	***FOCUS+ vs control group***	***iFOCUS vs control group***	***FOCUS+ vs control group***	***iFOCUS vs control group***	***FOCUS+ vs control group***	***iFOCUS vs control group***	***FOCUS+ vs control group***
Emotional functioning	Patient	-·27 (-2·11 to 1·57)	·12 (-1·65 to 1·89)	1·68 (-·20 to 3·56)	·00 (-1·87 to 1·86)	-·05 (-·28 to ·18)	·02 (-·21 to ·25)	·19 (-·03 to ·43)	·00 (-·23 to ·23)	·774	·897	·080	·997
	Family caregiver	·30 (-1·41 to 2·00)	·17 (-1·45 to 1·79)	·89 (-1·25 to 3·02)	-·66 (-2·67 to 1·34)	·04 (-·19 to ·27)	·02 (-·21 to ·26)	·10 (-·13 to ·33)	-·08 (-·31 to ·16)	·732	·834	·414	·516
Self-efficacy	Patient	·49 (-6·21 to 7·19)	9·02 (2·45 to 15·58)	1·68 (-6·11 to 9·48)	1·44 (-5·83 to 8·72)	·02 (-·21 to ·25)	·36 (·13 to ·60)	·05 (-·18 to ·28)	·04 (-·19 to ·28)	·887	·007	·671	·697
	Family caregiver	3·66 (-3·36 to 10·68)	3·88 (-2·84 to 10·61)	3·11 (-4·95 to 11·16)	3·55 (-4·02 to 11·11)	·14 (-·09 to ·37)	·14 (-·09 to ·38)	·09 (-·14 to ·32)	·11 (-·13 to ·34)	·306	·258	·448	·357

Per-protocol (PP) analysis

The per-protocol analysis functioned as a sensitivity analysis. The mean scores at baseline, mean differences, effect sizes and p-values are presented in Appendix A24 and A25.

iFOCUS vs control

Patients

Similar results as in the ITT analysis were found for patients for iFOCUS, across all time points, with non-significant p-values (P > ·0125). A medium effect size was found for emotional functioning for patients in the iFOCUS intervention group at T2 (d = ·44; 95% CI, ·13 to ·76), while other effect sizes were negligible.

Family caregivers

Similar results as in the ITT analysis were found for family caregivers for iFOCUS, across all time points, with non-significant p-values (P > ·0125). Small effect sizes were found for self-efficacy at T1 for iFOCUS (d = ·34; 95% CI, ·04 to ·64) and T2 (d = .25; 95% CI, -·07 to ·57) and emotional functioning for family caregivers in iFOCUS at T2 (d = ·35; 95% CI, ·03 to ·66).

FOCUS+ vs control

Patients

For patients, we found a significant difference in self-efficacy between the FOCUS+ intervention group and control group at T1 (baseline-adjusted mean difference, 9·13; 95% CI, 1·18 to 17·08; P = ·006) with a small effect size (d = ·47; 95% CI, ·21 to ·74), which did not persist at T2. No other significant effects were found.

Family caregivers

Similar results as in the ITT analysis were found for family caregivers for FOCUS+, across all time points, with non-significant p-values (P > ·0125). We did find a small effect sizes for self-efficacy for family caregivers in FOCUS+ at T1 (d = ·24; 95% CI, -·03 to ·50) and T2 (d = ·22; 95% CI, -·08 to ·51).

Conditional power analysis

To account for our study being underpowered due to recruiting 431 dyads instead of the planned 938 dyads, a conditional power analysis was performed to assess probability to find significant results if the trial had continued to include participants as originally intended. Two scenarios were investigated for the remaining theoretical recruitment; 1) the effect size with which the original sample size calculation was done and 2) currently observed effect size. The conditional power analysis showed that, had the originally planned sample size been reached, there was a 10% to 63% likelihood of significant impact from the iFOCUS intervention on family caregiver self-efficacy, and an 11% to 67% likelihood from the FOCUS+ intervention on the same outcome.

Discussion

Main findings
Our randomized controlled trial across six European countries evaluated the effect of two dyadic psychoeducational interventions for patients with advanced cancer and their family caregiver on the a priori determined primary endpoints. In this trial, the FOCUS+ intervention significantly improved patients' self-efficacy at 12 weeks (T1) compared with the control group. This improvement was not sustained at 24 weeks (T2) and was not found in family caregivers. Across all other comparisons, no significant improvements were observed. The consistency between the intention-to-treat (the primary analysis) and the per-protocol analysis (a sensitivity analysis) in terms of statistical significance suggests the robustness of our findings.

Limitations
We implemented our randomized controlled trial across six European countries and included a heterogeneous group of patients with advanced cancer and their family caregivers in terms of cancer diagnoses and the relationship between the patient and family caregiver (partners, siblings, parents, adult children, friends, or other). This design enhances the external validity of the findings.

However, the implementation of the trial faced several methodological difficulties that might have impacted internal validity of the study. A first issue relates to sample size. Enrollment to the study was lower than anticipated and because time and resources of the project had run out due to limited funding, enrollment was terminated before the target numbers were reached. This resulted in our study being under powered, hence decreasing the probability of finding statistically significant differences. Major reasons for slower than anticipated recruitment were the COVID-19 pandemic and its consequences (hospital staff being overwhelmed and patients more hesitant to join a study).[25]

A second issue relates to the relatively low participation rate to the study, which makes it possible that selection bias might have occurred, given the participants' awareness of the psychosocial nature of the study. A third issue relates to conduct. We collected data using a range of validated instruments where a data collector was often present for support with questionnaire completion. However, this method of data collection could have introduced placebo effects from the possible dyadic reflection and communication resulting from them. While data collector assistance was solely intended for aiding questionnaire completion, it often naturally resulted in conversations about coping with the illness and this may have inadvertently resulted in a supportive effect for participants in such interactions, which might have contaminated the care-as-usual group. Another limitation is the relatively low program adherence with only 52% of dyads completing all sessions of iFOCUS as intended and a more commonly found 76·4% in those of FOCUS+.

Interpretation

The FOCUS+ intervention significantly improved self-efficacy in patients at 12 weeks. Given the mutual burden in dyads, this improvement in patients may have also positively impacted family caregivers across various domains. One study found a significant association between patient self-efficacy and family caregiver adjustment, indicating that low self-efficacy in patients was associated with higher burden and psychological distress in the family caregiver.[26] Examining the impact on secondary outcomes for patients and family caregivers could provide additional support for this assertion.

The interventions evaluated in this trial were based on the FOCUS program[27], which has shown effectiveness in multiple randomized controlled trials.[11–13] Our study partially corroborates previous findings from trials conducted by Northouse; however, notable differences in outcomes were observed. Our study found a significant improvement for self-efficacy in patients in the FOCUS+ intervention arm at 12 weeks but this effect was not observed at 24 weeks. The trial by Northouse with advanced cancer patients and their spouses also found a significant improvement in dyads self-efficacy at 3 months, but this effect also did not sustain at 6 months.[11] However, that same trial also found an improvement for family caregivers, which our study did not. The trial by Northouse with prostate cancer patients and their spouses only found an improvement for self-efficacy for spouses (not patients) which did sustain at 12 months.[13]

There are several possible reasons as to why we were not able to demonstrate positive findings of any of our programs for family caregivers, for the outcome measure of emotional functioning, and for the iFOCUS program. First, our trial had insufficient power. However, a conditional power analysis indicated that if the trial had proceeded as initially intended, there is a 10% to 63% chance of significant impact from the iFOCUS intervention on family caregiver self-efficacy, and an 11% to 67% chance from the FOCUS+ intervention on the same outcome. Second, the issue of the so-called replication crisis should be considered. Research that replicated 100 experimental studies, demonstrated that where 97% of the original study findings yielded statistically significant results only 36% of the replicated studies achieved statistical significance.[28] Third, perhaps the effects of the FOCUS intervention were larger in the studies in USA than in our European replication study because the health care and cultural contexts were different and effects are difficult to compare. Our study also was conducted in different circumstances than the original study. The original FOCUS interventions were developed in the US, so even though thorough cultural adaptations and translations of the original FOCUS interventions were carried out[15], the adapted content of the interventions might still not fully meet the needs of the patients and family caregivers in Europe. Care-as-usual in Europe during the study period possibly already involved more psychoeducation and support for patients and family caregivers compared to the US in the years of the studies conducted by Northouse (between 1996 and 2009), potentially limiting the additional contribution of the intervention. Finally, our study was conducted during the COVID-19 pandemic, which posed additional challenges for the cancer population. These circumstances may have influenced the study outcomes.

Our study developed a full translation of the FOCUS intervention to a web-based program and was the first to formally evaluate it in a RCT. Our trial did not yield statistically significant improvements of iFOCUS on primary outcomes. This lack of effect could be attributed to many factors. First, reports in literature on participants' experiences with web-based support are inconsistent, with perceptions ranging from impracticality due to illness to convenience and time-saving benefits[29]. A review on other web-based psychoeducational interventions for cancer patients revealed varied findings, with some showing effectiveness in reducing fatigue and depression but lacking evidence on distress and QoL[30]. Second, we observed lower intervention adherence in the iFOCUS intervention arm which suggests that participants may be less inclined to engage with the online format of the intervention, potentially due to the absence of face-to-face interaction. Introducing some form of face-to-face support or follow-up by a nurse could potentially stimulate engagement. Third, one of the core aspects of both programs was the engagement in dyadic communication and mutual understanding of diverse needs and strengths. It can be questioned whether stimulus from a computer can achieve this to the same extent, and a thorough process evaluation will be able to describe whether the mechanisms of action were triggered less by a computer than by a human-facilitated interaction. This evaluation could also further enhance the iFOCUS program, possibly by including a human interaction component or by technological enhancement of the tailoring.

The lack of impact on emotional functioning of either of the interventions prompts further reflection. Possibly emotional functioning may not have been the most sensitive measure to capture the impact of our interventions and we may have had incorrect assumptions on the mechanisms of action from the interventions. Process evaluation data will be able to shed more light on this.

The current study shows promising results that can inform guidelines for implementation in clinical practice. The effectiveness of the FOCUS+ intervention underscores that healthcare professionals should consider its incorporation in oncology settings.

Conclusion

This randomized controlled trial across six European countries evaluated a nurse-delivered face-to-face psychoeducational intervention (FOCUS+) for patients with advanced cancer and their caregiver and a standalone web-delivered intervention (iFOCUS). The FOCUS+ intervention showed a positive effect for self-efficacy in patients at 12 weeks, which potentially benefited the family caregiver in other domains. The lack of improvements in our primary endpoints from the web-based iFOCUS intervention suggest that expectations about the promise of eHealth for psychoeducation may need to be tempered, or that it can benefit from design enhancements.

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Chapter VII
General discussion and conclusions

Introduction

In the final chapter of this dissertation, I present a summary of the main findings of each study and discuss the strengths and limitations of each of the methods used. Furthermore, I compare our findings to other studies in cancer care and family caregiving. Lastly, I also outline several recommendations for research, policy, and practice.

Summary of main findings

In **Part I**, we outlined the results of a population-based cross-sectional survey among bereaved family caregivers of people with serious illness who cared for an individual who had died between 2 and 6 months before the sample was drawn. The family caregivers were identified through three sickness funds in Flanders, Belgium. In total, 1,539 completed the questionnaire, resulting in a response rate of 55%.

In **Chapter II** we discussed how family caregivers are supported in their caregiving tasks by their healthcare professionals. The results showed that family caregivers commonly facilitated safe mobility inside or outside the house (85%), talked about emotions (73%), promoted social interaction (73%), assisted with administration (71%), provided physical comfort (72%) and managed symptoms (65%). Less than half (47%) talked about end-of-life preferences or made home adjustments for safety and comfort (39%). The majority of respondents (72-93%) had wanted to perform those caregiving tasks themselves. Most family caregivers received support from one or more healthcare professionals for family caregiving tasks, ranging from 71% for promoting social interaction to 95% for managing symptoms. Home care nurses and GPs most frequently supported family caregivers in their caregiving tasks in the last three months of life. Palliative care nurses or doctors most frequently provided support for talking about end-of-life preferences (37%). The type of support mostly involved providing information. The majority of family caregivers indicated they had received sufficient support from healthcare professionals for all caregiving tasks, ranging from 78% for promoting social interaction to 89% for facilitating safe mobility. The use of specialised palliative care services was associated with receiving more support across physical ($p = .001$), psychosocial ($p < .001$), and practical ($p < .001$) tasks.

The association between pre-bereavement collaboration between family caregivers and healthcare professionals and the emotional wellbeing of family caregivers post-bereavement was examined in **Chapter III**. As measured by the Positive and Negative Affect Schedule (PANAS)[1], family caregivers scored lower on positive affect (PA) and higher on negative affect (NA) compared to a normative sample. Most family caregivers evaluated the pre-bereavement collaboration with healthcare professionals positively. About one out of four family caregivers reported that they weren’t given enough freedom to co-determine how care for their loved one was organized and carried out. Additionally, 18% of family caregivers stated that they had not received sufficient information about available healthcare professionals and services they could turn to for support. Family caregivers' evaluation of collaboration with healthcare professionals was positively correlated with PA (r = .13, p < .001) and negatively correlated with NA (r = -.13, p < .001), this effect persisted when controlling for confounding effects of socio-demographic and clinical characteristics of the bereaved family caregiver and the deceased person.

Having described the nature of support from healthcare professionals for family caregivers in **Part I**, we then shifted our focus to the two concrete interventions of the DIAdIC study that support patients and family caregivers together by first presenting the study protocol of the DIAdIC study in **Part II** (**Chapter IV**). The two interventions offer tailored psychoeducational support for patient-family caregiver dyads. The nurse-led face-to-face intervention (FOCUS+) consisted of two home visits and one online video session, and the web-based intervention (iFOCUS) was completed independently by the patient-family caregiver dyad in four online sessions. The interventions were based on the FOCUS intervention, developed in the USA, both of which addressed the same five core components: family involvement, optimistic outlook, coping effectiveness, uncertainty reduction, and symptom management. The FOCUS interventions were adapted to fit the needs of the European population.

To evaluate the interventions, we have set up an international multicenter parallel-group three-arm randomized controlled trial in Belgium, Denmark, Ireland, Italy, The Netherlands, and the United Kingdom. All patient-family caregiver dyads were randomized to one of the study arms: 1) the iFOCUS+ program, 2) the FOCUS+ program, or 3) a control group (care as usual). The primary outcomes were emotional functioning and self-efficacy of the patient and the family caregiver. The secondary outcomes were quality of life, benefits of illness, coping, dyadic communication, and ways of giving support of the patient and family caregiver. These endpoints were chosen as the DIAdIC interventions were designed to provide support in the five F O C U S domains (see above). These five areas are expected to have a direct effect on appraisal factors (appraisal of illness/caregiving, uncertainty,..) and coping resources (coping, self-efficacy, dyadic communication).

In **Part III**, we described the results that derived from the DIAdIC study. For the study described in **Chapter V**, we were interested in the predictors of sexual satisfaction in patients with advanced cancer and their family caregivers. Sexual satisfaction was low in patients and family caregivers; of those who answered (omitting 'prefer not to answer' responses in patients), 42% of patients and 33% of family caregivers indicated they were not at all satisfied with their sex life (mean score of respectively 1.21, SD = 1.21 vs 1.43, SD = 1.21). One out of three patients (34.3%) preferred not to answer the question about sexual satisfaction (this answer option was not given to family cargivers). Patients diagnosed with prostate or gynecological cancer reported lower sexual satisfaction (respectively B = -1.134, 95% CI -1.674, -.594 and B = -1.278, 95% CI -2.103, -.452, reference= gastrointestinal cancer). Higher levels of emotional functioning (B = .040, 95% CI .024, .057) physical functioning (B = .018, 95% CI .012, .025), social functioning (B = .007, 95% CI .001, .013), global health (B = .010, 95% CI .007, .013) and social wellbeing (B = .048, 95% CI .013, .082) among patients were associated with increased sexual satisfaction. Among family caregivers, sexual satisfaction was lower with increased age (B = -.014, 95% CI -.023, -.005) and in spousal relationships (B = .768, 95% CI .481, 1.056). Higher levels of emotional functioning (B = .026, 95% CI .011, .042) and quality of life (B = .815, 95% CI .546, 1.084) in family caregivers were associated with increased sexual satisfaction.

Next, **Chapter VI** described the results of the main analyses on the primary outcomes of the DIAdIC trial at the 12-week and 24-week mark. To restate, the DIAdIC trial aimed to evaluate the effectiveness of two interventions, iFOCUS and FOCUS+, on patient and family caregiver outcomes, focusing on emotional functioning and self-efficacy, compared to a control group. We defined the construct self-efficacy as individuals' confidence in their ability to manage cancer, for example, '*I am confident that I can handle the challenges from the cancer and its treatments*'. Results showed that neither intervention significantly improved emotional functioning in patients compared to the control group at either the 12-week mark (T1) (iFOCUS: p = .774, FOCUS+: p = .897) or 24-week mark (T2) (iFOCUS: p = .080, FOCUS+: p = .997). Likewise, self-efficacy levels <u>for patients</u> did not show significant improvement with the iFOCUS intervention at T1 (p = .887) or T2 (p = .671). We did find that the FOCUS+ intervention showed a significant improvement for patients on self-efficacy at T1 (p = .007), but this effect did not sustain at T2 (p = .697). Effect sizes across interventions and time points were generally minimal, although a small effect was noted for FOCUS+ at T1 for patient self-efficacy (d = .36). For <u>family caregivers</u>, neither intervention resulted in significant changes in emotional functioning compared to the control group at either assessment point (at T1; iFOCUS: p = .732, FOCUS+: p = .834 and at T2; iFOCUS: p = .414, FOCUS+: p = .516). Similarly, self-efficacy among family caregivers did not significantly differ between intervention and control groups at either T1 (iFOCUS: p = .306, FOCUS+: p = .258) or T2 (iFOCUS: p = .448, FOCUS+: p = .357). Effect sizes for family caregiver outcomes were consistently negligible across all comparisons.

Methodological considerations, strengths, and limitations

This dissertation presented multiple studies that used different methodologies, employing various study designs, based on different data sources. Two chapters were based on a population-based survey among bereaved family caregivers (**Chapters II** and **III**), one chapter entailed the study protocol for a randomized controlled trial (**Chapter IV**), and two chapters were based on the quantitative data collected as part of an international randomized controlled trial (**Chapters V** and **VI**). The individual strengths and limitations of each study are discussed in detail in this section.

*Cross-sectional survey of bereaved family caregivers on the collaboration between healthcare professionals and family caregivers of persons with a serious illness (**Chapters II** and **III**)*

This first study was a population-based cross-sectional survey of bereaved family caregivers of people with serious illness (N=3,000) who cared for a person who had died two to six months before the sample was drawn (November 2019). This data was used for two different sub-studies with different research aims.

This study used a unique sampling frame, using the databases of three of the largest health insurers in Flanders, Belgium. From the databases, 3,000 registered family caregivers of individuals who had a serious illness were randomly selected, which limited the risk of selection bias as most studies select family caregivers through the use of professional services. However, the recruitment of registered family caregivers in our sample might have still introduced some selection bias, excluding those providing family care who were not formally registered with one of the main health insurers. This potential limitation could have impacted our findings, for example in situations of sudden deaths with limited opportunity for family caregiving or the formal registration of caregiving. The self-administered survey format provided respondents with privacy and anonymity in completing the questionnaire, which minimized social desirability bias as there was no influence of an interviewer. However, despite these efforts to reduce bias, we encountered a notable number of missing responses throughout the questionnaire, which may have been influenced by the length of the questionnaire. The extensive format of the questionnaire might have caused participants to skip certain questions or disengage from the questionnaire as they completed the questionnaire independently without any form of assistance, possibly resulting in less qualitative answers. This could have been less likely if the questionnaire was with a data collector present to aid with questionnaire completion, which is not feasible. However, as missing data were random, it is unlikely that this limitation substantially affected our conclusions. Also, the retrospective nature of our questionnaire possibly introduced some recall bias, potentially influencing the assessment of received support. However, the relatively short time span between the support received and questionnaire completion (up to a maximum of nine months) mitigates this concern. Additionally, the death of a loved one is an example of a highly emotional, infrequent life event, which is more easily recalled than a neutral recurring event[2].

We also used the cross-sectional study design to explore the association between pre-bereavement collaboration and post-bereavement emotional wellbeing among family caregivers. Causal inferences were difficult to make due to the nature of the study design. While the mortality follow-back approach did involve querying different time periods (before and after the patient's death), seemingly meeting the temporality criterion for determining causality, we cannot rule out the possibility of post-hoc rationalization. It's possible that individuals have evaluated the support they received based on their current feelings, potentially biasing their retrospective assessments. Another complicating factor is residual confounding. For instance, certain individual characteristics of family caregivers might have influenced both their likelihood of seeking support at the time and the severity of their grief. These confounding variables could have impacted the true relationship between the support received and the outcomes observed. Additionally, assessing emotional wellbeing at a single point in the months following bereavement limited insight into its longitudinal evolution. More frequent assessments of emotional wellbeing over time by using a longitudinal design would have resulted in richer findings. Finally, this study explored a fairly novel topic: collaboration in healthcare with family caregivers at the end of life. This innovative focus not only addressed a gap in the literature but also offered the potential to enhance the quality of patient and family care. However, as a drawback, the novelty of the topic of collaboration in healthcare necessitated the development of new items for assessing pre-bereavement collaboration. These items were based on insights from prior qualitative research[3] and existing instruments[4,5]. Despite undergoing cognitive testing, these were not more extensively validated.

The DIAdIC study

Study on sexual satisfaction in patients and family caregivers of the DIAdIC trial

We used baseline data from the DIAdIC trial to study sexual satisfaction and its predictors in patients with advanced cancer and their family caregivers in six European countries. A major strength of this study is that it evaluated the baseline measurement of a large randomized controlled trial, which incorporates multiple validated measures. This allowed us to take many potential predictors for sexual satisfaction among both patients and family caregivers into consideration. Furthermore, by using the data obtained through a multisite international study, a large sample size was reached, comprising a total of 431 patients and 431 family caregivers. Another notable strength of this study is its investigation of sexual satisfaction of family caregivers who are not the patient's sexual partner (e.g. child, sibling, parent, friend), thereby broadening the perspective beyond the typical focus on the patient's sexual partner[6–8]. This approach acknowledges that taking on the role of a family caregiver, can impact one's sexual satisfaction, irrespective of their relationship with the person they are caring for. Additionally, the study included patients with diverse types of advanced cancer, resulting in meaningful comparisons in sexual satisfaction across a range of cancer types, as opposed to most studies that typically focus on patients with a specific cancer type (e.g. only patients with prostate or gynecological cancer). Additionally, we have information on multiple European countries that all have different care settings and cultural contexts.

Nevertheless, it is important to recognize certain limitations inherent to this study. The cross-sectional and correlational nature of our research, hindered our ability to draw strong causal conclusions, allowing only for the exploration of predictors of sexual satisfaction. To mitigate confounding, we drafted directed acyclic graphs to guide the deconfounding strategy for each predictor's relationship with sexual satisfaction. Additionally, external validity might have been an issue as our study population consisted of participants enrolled in a psychoeducational trial, making them non-representative of the broader population of patients with advanced cancer and their family caregivers. Despite this, our primary aim was not to extrapolate our findings to the entire population but rather to explore associations with theoretical generalizability. Furthermore, measurement bias was introduced by differences in the survey's validated measurements between patients and family caregivers. The absence of a 'prefer not to answer' option for family caregivers, which was available for patients (related to the design of the validated questionnaires), may have influenced response rates, with approximately one in three patients opting for this alternative for the sexual satisfaction item. This discrepancy emphasized the sensitive nature of the topic, potentially hindering comprehensive research on sexual satisfaction due to respondents' reluctance to disclose their concerns related to sexuality. Lastly, our study only measured one item on sexual satisfaction. The inclusion of additional sexual health variables, such as sexual function or frequency of sexual activity, could have contributed to a more comprehensive understanding of sexual health within our study population.

Effectiveness of a nurse-delivered (FOCUS+) and a web-based (iFOCUS) psychoeducational intervention for people with advanced cancer and their family caregiver (DIAdIC): a three-arm international randomized controlled trial

In the DIAdIC study, a randomized controlled trial across six European countries, several strengths and limitations should be acknowledged.

We aimed to ensure a diverse representation of patients with advanced cancer and their family caregivers. This diversity encompassed variations in cancer diagnoses and different types of relationships between patients and family caregivers, including partners, siblings, parents, adult children, friends, or other connections. This approach is unique compared to previous dyadic psychoeducational trials in cancer care, which often focused on a single center, a specific diagnosis group (e.g. only breast cancer or prostate cancer)[9–14], or a particular type of patient-caregiver relationship (often only spouses)[10,11,14–16]. Additionally, by including a broad spectrum of participants from multiple countries and centres, the external validity of our findings is enhanced, more accurately reflecting the real-world variability of patient-family caregiver dynamics in the context of advanced cancer. Furthermore, our trial employed validated instruments for the primary outcome measures[17,18], which added to the credibility of the study's conclusions. Also, the use of validated instruments provided a standardized method for collecting data, which facilitated possible replications of the study in the future.

In reflecting on the use of the MRC framework[19] within the context of the DIAdIC study, several considerations emerge. We emphasized the importance of process evaluation, recognizing the fundamental distinction between complex health interventions and pharmaceutical treatments. The complex healthcare interventions evaluated in the DIAdIC trial require methods that allowed us to evaluate their working mechanisms[20]. We thus thoroughly examined how the intervention was delivered, how it was received by participants, while considering the context. By conducting a comprehensive process evaluation alongside efficacy assessment, we gained insights beyond mere effectiveness. While the absence of a piloting phase may have implications for identifying potential flaws or inadequacies in the intervention, it is important to note that extensive evidence from previous research supported the effectiveness of the FOCUS interventions. This robust evidence base, derived from multiple randomized controlled trials conducted in diverse settings[13,16,21], provided confidence in the intervention's viability, which led to the decision to pursue a randomized controlled trial. Additionally, we conducted a comprehensive adaptation process for the interventions[22,23], adhering to a structured framework PIPFLA[24]. This process, aligning with MRC framework principles, entailed engaging multiple stakeholders, considering contextual factors, and integrating both emic (local perspectives of nurses, clinicians, patients, family caregivers) and etic (researchers) perspectives.

There are also some limitations to the DIAdIC trial. Recruitment proceeded at a slower pace than expected, primarily due to the impact of the COVID-19 pandemic. Hospital restrictions, overwhelmed healthcare staff, and patient reluctance to participate in studies involving human contact contributed to this delay. Consequently, these circumstances forced us to extend the recruitment period by 12 months. Despite this extension, we were still unable to attain the targeted sample size as outlined in the study protocol[25]. As a result, our study was underpowered. To account for this, we conducted a conditional power analysis that demonstrated that, had the trial progressed according to its original plan, there would have been a likelihood of 10% to 63% for significant impact from the iFOCUS intervention on family caregiver self-efficacy, and 11% to 67% from the FOCUS+ intervention on the same outcome. These findings suggest the potential for more significant results had the trial continued as planned.

Another limitation relates to the possibility of selection bias. Eligible participants were provided information about the psychosocial nature of the study, which could have attracted individuals who were more inclined to seek psychosocial support. However, the relatively low adherence to the intervention sessions, more problematic for iFOCUS (52%) than for FOCUS+ (76.4%) suggests that this potential bias might be less likely. This intervention adherence is low in contrast to a review of psychosocial interventions for advanced cancer patients, which found that all included studies focusing on dyads (patients and family caregivers) reported intervention adherence rates of at least 79%[26]. The discrepancy in adherence rates, particularly regarding the iFOCUS intervention, raises questions about potential barriers to engagement with the interventions. One plausible explanation for the low adherence rate to the iFOCUS intervention could be a lack of digital literacy skills and willingness to engage with digital tools among participants, limiting their ability to navigate and utilize the program effectively. This suggests a need for further investigation into the accessibility and usability of digital interventions, particularly for populations facing significant health challenges like advanced cancer.

Additionally, we have a low representation of the 75+ age population in our sample (only 8.4%), where research shows that most cancers reach their highest incidence rates from the age of 75[27]. Our hypothesis is that this is mainly due to our study's inclusion criterion 'familiarity with internet', which possibly served as a barrier to participation for older dyads. Additionally, this age group was more difficult to enroll into the study, considering they were often more physically impaired and frequently declined to participate. This disparity possibly has implications for the intervention's effectiveness, as it raises concerns about the generalizability of our findings to older individuals with advanced cancer who may not have internet access or proficiency. It suggests that the intervention may not effectively reach or engage this demographic, potentially limiting its impact on improving outcomes for older patients with advanced cancer.

Interpretation and discussion of the main findings of this dissertation

This dissertation has collected insights on available support and wellbeing for bereaved family caregivers of patients with serious illness, the development of the DIAdIC study, sexual satisfaction in patients with advanced cancer and their family caregivers, and the effectiveness of two psychoeducational interventions. Within this section, I will discuss the main findings of this dissertation, interpret the significance and relevance of these results, and make comparisons with findings from prior studies and current literature.

Supporting patients and family caregivers: a matter of diffusing the philosophies and approaches from palliative care

Palliative care represents a person-centered approach in healthcare, focusing its attention on both individuals facing serious illnesses and their family caregivers. Our study investigating the support provided to family caregivers in the last months of life of the patient they were caring for (**Chapter II**), indeed revealed that when palliative care services were involved more support was given to these family caregivers, across different forms of support. The explicit focus of palliative care on patients and caregivers as units of care also served as a foundational principle for the development of FOCUS+ and iFOCUS intervention within the DIAdIC trial.

Both interventions (as described in **Chapters IV** and **VI**) are using a palliative care philosophy and aim to extend comprehensive support to all family caregivers, irrespective of whether they are receiving support from specialized palliative care services. Two randomized controlled trials as conducted by Northouse[16,21] indicated that the FOCUS program fostered an increase in self-efficacy among patient-caregiver dyads. However, the DIAdIC trial showed that only the FOCUS+ program showed promising results in enhancing self-efficacy, but only for patients and the effects were only temporary.

It's important to note that the involvement of palliative care services appears to be relatively high in individuals diagnosed with cancer. A population-level study of DeSchreye et al found that 47.1% of persons dying from cancer in Belgium received support from specialized palliative home care teams or in palliative care units in hospital. A mortality followback survey study in Flanders by Vanbutsele et al. estimated the total proportion receiving any form of specialized palliative care at 73% for those dying from solid organ cancers[28]. In our survey with bereaved family caregivers of individuals with serious illnesses (not limited to cancer), the proportion where specialized pallative care services were reported to be involved was significantly lower, namely 36.7% (outlined in **Chapter II**). This corroborates ample research indicating lower palliative care involvement in serious illnesses other than cancer. Hence, it is plausible that implementing palliative care principles in other domains outside cancer care could yield more substantial benefits. Consequently, it is also conceivable that the interventions evaluated in the DIAdIC trial might have exhibited more pronounced effects would they be applied or implemented in non-cancer populations. This underscores the importance of broadening the reach of palliative care interventions to provide holistic support to all individuals facing serious illnesses and their family caregivers, irrespective of diagnosis.

Glorifying the support from healthcare professionals?

In the same population-based survey study among bereaved family caregivers, we found that the majority of family caregivers evaluated the support of healthcare professionals for their caregiving tasks that they received in the last three months before bereavement as sufficient (**Chapter II**). This finding requires further examination, as other studies have consistently found that family caregivers report needing more support from healthcare professionals, for example for practical tasks[29–32]. In our study, family caregivers were reflecting on their caregiving experiences retrospectively and, in doing so, possibly tended to positively assess (i.e. rationalize) the support they received during that period (post-hoc rationalization). This could further be explained by a sense of gratitude among family caregivers for the support they received during the caregiving period, which was used as a coping mechanism. After facing a negative experience or situation (such as losing a loved one), people often draw on their own psychological resources to return to a positive state[33]. They can rely on positive emotions (such as gratitude) to help them cope with negative emotions[34].

Additionally, the family caregivers of this survey study were invited to participate by their healthcare insurer. Despite a clear explanation in the study information letter on the anonymity of their responses, respondents might have still been hesitant to report unmet support needs out of fear that the healthcare professional they are referring to would read their response. Another possible explanation is a form of selection bias. People who decided to participate in the survey possibly were in fact very satisfied with the support they received and wanted to share this, while people who did not participate in the study possibly were less satisfied with the support they received and thus refused to take the time to fill out the survey.

Our contrasting finding underscores the complexity of investigating family caregivers' retrospective perceptions over time and emphasizes the need for a clear understanding of how retrospective evaluations of support before bereavement may differ from real-time assessments.

Lifting the taboo on sexuality in oncology

Another important finding in this dissertation is the taboo around sexuality among individuals coping with cancer. In **Chapter V** we described the results from the baseline data from the DIAdIC trial where we found that, when provided with the option, about one-third (34.3%) of patients opted for the 'prefer not to answer' option when responding to the sexual satisfaction item. In contrast, the incidence of missing values (8.6%) for the same item among family

caregivers was considerably lower (they were not offered the ‘prefer not to answer’ option). The inclusion of the 'prefer not to answer' option thus seemed to serve as an escape route for respondents, a route that many patients chose to take, emphasizing the sensitivity associated with the topic of sexual satisfaction.
Despite the sensitivity of the topic, there are many studies that show that sexuality is an important part of quality of life and wellbeing[35,36]. The WHO even defines sexuality as ‘a central aspect of being human’[37]. The majority of cancer patients also indicate that sexuality is still a priority to them[38].

However, further careful reflection on this finding is warranted. Introducing a ‘prefer not to answer’ option for the sexual satisfaction question may inadvertently signal our own sensitivity as researchers toward the topic of sexuality and thus could have unintentionally contributed to the perpetuation of the taboo surrounding sexuality in this population. Of course, the 'prefer not to answer' option for the item related to sexual satisfaction is inherent to the validated instrument (FACT-G)[39]. Therefore, it may be necessary to reconsider the instrument, as respondents always have the option to leave a question unanswered if they choose. Given this, it might be worth reassessing whether the 'prefer not to answer' option is essential for this specific item, with the potential benefit of encouraging more respondents to complete the item. To compensate for leaving out the ‘prefer not to answer option’ on item level, researchers could consider adding a short statement at the beginning of a questionnaire or survey, informing respondents that they can leave any item unanswered if they choose, and thereby avoiding unnecessary emphasis on specific items that might be considered sensitive.

Nevertheless, healthcare professionals also feel hesitant when discussing sexuality with patients. A survey study among healthcare professionals in oncology found that while 82% of healthcare providers recognize that addressing sexual health concerns is part of their responsibilities, only 17.4% regularly engage in discussions about sexual dysfunction problems[40]. Despite recognizing its importance, healthcare professionals report multiple reasons for not discussing sexuality such as limited knowledge and training, time constraints, and feeling too involved in the personal lives of patients[41,42]. There thus seems to be room for improvement in educating healthcare professionals in oncology settings on the topic of sexuality.

The researchers involved in the DIAdIC study regularly had interactions with the nurses who delivered the FOCUS+ intervention, further confirming this issue. It became evident that nurses exhibited certain hesitance when it came to bringing up the topic of sexuality with patients and family caregivers. They often used euphemisms like "intimacy" to avoid unsettling participants and expressed discomfort and embarrassment when addressing the subject, particularly when they speculated that the couple may no longer be sexually active.

Despite their training to discuss difficult topics with dyads, nurses also felt like they were crossing a boundary considering that they’ve only met with the dyad a few times before.

Depending on the dyad relationship (partners, siblings, friends,..), the DIAdIC interventions addressed the topic of sexuality and intimacy, both in the iFOCUS program and the FOCUS+ program (See Appendix A26 for the intervention manual). Dyads were asked about intimacy difficulties and their willingness to discuss this issue. The intervention nurses were trained to explain what intimacy is and that it did not necessarily have to refer to sexual intercourse. Dyads were also encouraged to openly discuss their feelings about changes in their intimacy towards each other and consider ways to problem-solve any issues they may have. The impact of the interventions in the DIAdIC study on the sexual satisfaction of patients and family caregivers, as well as their openness about the topic, will be examined in different publications, outside the scope of this dissertation. Investigating the impact of the interventions on openness about sexual satisfaction can demonstrate the possible benefits of interventions that help lift the taboo on sexuality.

Effectiveness of iFOCUS and FOCUS+ in the DIAdIC trial

The DIAdIC trial successfully demonstrated the positive effect of the face-to-face FOCUS+ intervention on patient self-efficacy at 12 weeks (**Chapter VI**). Self-efficacy in the context of the DIAdIC study refers to one’s ability to manage the symptoms and side effects associated with cancer and its treatment. This positive result from the DIAdIC study is supported by self-efficacy theories that state that interventions aimed at improving self-efficacy are more effective when delivered face-to-face (compared to other format such as web-based or telephone interventions)[43]. Self-efficacy is a construct that is known for fostering positive results in several other health outcomes (both intention and behavior)[44], which has proven its value in oncology. One study with lung cancer patients found that high self-efficacy was associated with less pain, fatigue, depression, symptoms of the cancer, and anxiety, as well as physical and functional quality of life[45]. Another study with cancer patients found a strong association between self-efficacy and mood and quality of life[46]. An intervention study with women with breast cancer undergoing chemotherapy found that increased self-efficacy was associated with a better quality of life and reduced symptom distress[47]. The observed positive impact of the FOCUS+ intervention on self-efficacy in patients suggests potential for similar beneficial effects on other outcomes assessed in the DIAdIC trial. Further examination of the trial's secondary outcome measures is necessary to substantiate this claim.

It is however surprising, that we did not find any impact of any of the interventions for family caregivers, especially since FOCUS+ and iFOCUS were dyadic interventions. Despite not finding a direct impact on emotional functioning or self-efficacy for the family caregiver, they might have still experienced benefits, albeit indirectly. As described above, increased self-efficacy in patients can lead to improved health outcomes. If the wellbeing of the patient thus improves due to the increased self-efficacy, the family caregiver might experience less burden or stress. One study found a significant association between patient self-efficacy and caregiver adjustment, indicating that low self-efficacy in patients was associated with higher burden and psychological distress in the family caregiver[45]. So indirectly, the family caregivers might have still benefitted from the FOCUS+ intervention, but this indirect effect may require more time to become apparent. As previously stated for patients, future research exploring secondary outcomes in family caregivers such as coping mechanisms, dyadic support, and quality of life, may also reveal significant effects for family caregivers.

The impact of the COVID-19 virus should also not be underestimated. During the pandemic, cancer services were often reduced in frequency due to limited resources and shifted priorities[48]. Policies concerning restrictions on family members being allowed to join patients for consultations were implemented in hospitals depending on local regulations and peaks in the pandemic which imposed additional challenges on the cancer population. The DIAdIC trial was conducted amid the pandemic, which may have resulted in physical consequences, but also in psychological issues in participants. A review of studies conducted during the COVID-19 pandemic found a prevalence of stress, anxiety, and depression among the general population of respectively 29.6%, 31.9%, and 33.7%[49]. A rerun of the DIAdIC trial without the context of a global pandemic, can thus possibly yield different results.

The web-based iFOCUS intervention of the DIAdIC trial did not demonstrate any statistically significant improvements on the primary outcomes. A systematic review of web-based psychoeducational interventions for cancer patients found that while the included interventions effectively decreased fatigue and depression, no evidence was found on their impact on distress and quality of life[50]. It is possible that the primary endpoints we selected for iFOCUS were not adequate. Another narrative review on supportive eHealth technology for patients and family caregivers also reported inconsistent experiences[51]. Among participants undergoing active cancer treatment, there was a perception that utilizing eHealth technology to report symptoms was either unnecessary or impractical due to feeling too unwell[52,53]. Other studies reported that the eHealth programs were too time-consuming[54,55]. However, other studies found more positive experiences, such as the ability to access the program at their own convenience[10,56,57] and saving time as they didn't have to travel to the hospital for support[58,59]. It thus seems that while support through web-based programs is often well-received, the delivery of support or care through online format does not suit every individual's needs or preferences. Because of the varied experiences and personal preferences of patients and family caregivers, the trial results may not have demonstrated consistent enough results that reflect significant improvements from the iFOCUS web-based program in the DIAdIC trial. Additionally, the ability to use the internet in the population of the DIAdIC study should be considered. A study based on a survey conducted in 2019 on computer usage among Europeans, showed that in the age groups of 45-54, 55-64, and 65-74, 32.48%, 35.32%, and 31.94% reported to have low digital skills, respectively, which reflects low familiarity with

ICT[60]. Although 'familiarity with the use of the internet' was an inclusion criterion for the study, significant differences in internet proficiency may still have existed in our population, potentially impacting participants' ability to effectively utilize the iFOCUS program. Furthermore, it should be acknowledged that the iFOCUS intervention evaluated in the DIAdIC trial represented a first version of the web-based program. The development of the intervention occurred within a relatively brief timeframe. There is potential for improvement in both the content and the design of the intervention, such as greater, in-depth tailoring or the incorporation of webinars. Additionally, it should be noted that while web-based interventions such as iFOCUS can be convenient and easily accessible, the lacking human factor might reduce its impact, especially when addressing psychosocial themes in an emotionally burdened population. Web-based psychoeducational interventions might struggle to effectively initiate and guide conversations within the dyad, due to the lack of empathy of a person present and the inability to pick up on non-verbal cues. Dyads coping with advanced cancer might thus have more complex needs that cannot be addressed entirely by a web-based intervention.

Another notable concern when comparing our findings with the results of previous trials conducted by Northouse is the difference in baseline scores for self-efficacy. Table 1 shows an overview of the baseline scores for self-efficacy (measured by the Lewis Cancer Self-efficacy Scale[18]) in the DIAdIC trial and the triage trial, which shows big differences between both studies[21]. The prostate cancer trial[61] and breast cancer trial[13] were not included in the table as either baseline scores were not reported or self-efficacy wasn't included as an outcome measure. It thus seems that there may be a significant difference between the population studied in the United States by Northouse and the population examined in our study across six European countries. Cultural differences between the populations might affect how they respond to questionnaires when reporting on self-evaluations of self-efficacy, as certain response categories of the questionnaire can have different connotations to them[62]. Furthermore, it's worth noting that the studies conducted by Northouse were conducted over 10 years ago, which could mean that societal attitudes and cultural norms have changed since then. These changes could potentially influence participants' responses due to the differences in the prevailing attitudes and circumstances of the respective time periods.

Table 1: Self-efficacy mean scores at baseline in the DIAdIC and Triage trial

		Mean score at baseline (T0)					
		DIAdIC trial			**Triage trial**		
		Control group	iFOCUS	FOCUS+	Control group	Brief FOCUS	Extensive FOCUS
Self-efficacy	Patient	119.67	118.25	122.66	136.24	131.43	131.92
	Family caregiver	118.30	113.24	114.68	134.99	133.87	130.73

Collaboration as an important contributor to post-bereavement wellbeing for family caregivers

In this dissertation, we found that family caregivers' evaluation of collaboration with healthcare professionals in the last three months pre-bereavement was associated with emotional wellbeing, the latter as measured by the Positive and Negative Affect Schedule (PANAS)[1] (**Chapter III**).

Literature suggests that there are many factors that are related to collaboration with healthcare professionals that impact the bereavement phase of family caregivers. A focus group study with bereaved family caregivers of advanced cancer patients found that there are several healthcare-related issues that influence the family caregiver's grief: the lack of knowledge from healthcare professionals about the health status of the patient, the access to and the accuracy of information provided to them, and the provision of services[63]. In general, when family caregivers view their caregiving experience positively, they report better quality of life and social engagement, and fewer psychological symptoms and medication usage[64]. Another study found improvements in the quality of care for older persons when nurses in the hospital involved the family caregivers of the patients in the caregiving and the decision-making[65]. Furthermore, two other studies found that the physical and psychological wellbeing of both patients and family caregivers improved with the active involvement of family caregivers[66,67].

Both prior research and our study indicate that the support provided before bereavement has an impact on the post-bereavement phase for family caregivers. However, in practice, collaborative efforts at the end of life are not being consistently implemented. A qualitative interview study showed that family caregivers of individuals with a serious chronic illness report that there are missed opportunities when it comes to collaboration with healthcare professionals in palliative care[3]. In a focus group discussion, healthcare professionals also report challenges when it comes to supporting family caregivers at the end of life; healthcare professionals state that they don't always know the relatives or family caregiver of the patient and report that family caregivers can be demanding or even refuse collaboration entirely[68].

While the importance of family-centered care is widely acknowledged, pediatrics truly recognizes that genuine family-centered care is about healthcare professionals actively collaborating with the families of sick children[69]. Such a collaborative approach as employed by pediatrics, emphasizes the importance of involving family caregivers in the care of the patient, ensuring their perspectives are heard and valued. Healthcare professionals may thus follow the example set by pediatrics where, regardless of the age of the patient, collaboration with and involvement of family caregivers is essential to providing qualitative care.

The DIAdIC interventions also aim to enhance collaboration among patients, family caregivers, and healthcare professionals. In both the iFOCUS and FOCUS+ interventions, dyads are encouraged to ask questions, express concerns, and raise potentially difficult topics with their healthcare professionals. Dyads receive practical tips to make the most out of their medical consultations, such as writing down questions, attending appointments together, and repeating information back to their healthcare professionals to confirm they understand what is being said. The interventions focus on open communication and aim to empower both patients and family caregivers to actively engage in their own care plan.

Further recommendations on how collaboration between healthcare professionals and family caregivers can be improved are described further in this chapter.

Recommendations for research, policy, and practice

Each study in this dissertation has presented diverse findings that have acknowledged that there are areas in the support and wellbeing of patients and family caregivers that could benefit from improvement. In this section, various recommendations are formulated for better support and wellbeing for patients and family caregivers in three domains, namely future research, policy and practice. It is important to note that the recommendations for policy and practice are specifically aimed at Flanders, Belgium, considering the familiarity with the healthcare system and that the survey study was conducted in Flanders, Belgium.

Recommendations for research

Scrutinize the results of the DIAdIC study

As thoroughly described throughout this dissertation, the results of the DIAdIC trial (**Chapter VI**) require additional investigation.

The DIAdIC trial found a significant improvement in self-efficacy in patients in the FOCUS+ intervention group at the 12-week mark. However, as this effect was not present in family caregivers, or at the 24-week mark, it should be investigated how this effect can be more durable and extended to the family caregiver. In a randomized controlled trial conducted by Northouse, that compared a brief (3 sessions) and extensive (6 sessions) version of the FOCUS program, only the extensive program significantly improved dyads' self-efficacy[21]. This suggests that a higher dose of the FOCUS+ intervention might be needed to reach the desired impact on self-efficacy on both parties involved and make the effect more durable.

As emotional functioning did not show significant improvements for any of the interventions for either the patient or the family caregiver, the working mechanisms of the interventions should be investigated. In the future as part of the process evaluation of the DIAdIC study, a qualitative exploration of the experiences of the participants will be conducted to gain insights about the attitudes, behavior, and knowledge deriving from the interventions. This might clarify and enrich the current quantitative findings from the DIAdIC trial. In general, our study has highlighted the importance of having process evaluation data to truly understand what works or doesn't work in an intervention, rather than solely relying on outcome measures to explore effectiveness.

It also raises the question of whether emotional functioning was the right primary outcome for the trial. Emotional functioning is considered a part of the quality-of-life construct, the latter which is commonly used as an outcome measure to evaluate the effectiveness of interventions. Quality of life is frequently chosen as an outcome measure in psychosocial intervention studies because it has many validated instruments. However, formulating a plausible theory in which quality of life is ultimately affected does not guarantee its demonstration in a study. When evaluating quality of life, future studies should employ a mixed-method approach for a more in-depth understanding and context to the effectiveness of the interventions.

Another area for research related to the DIAdIC study is the role of exploratory analyses for the secondary endpoints to achieve a better understanding of the various effects of the interventions. For example, exploring the results of the Client Service Receipt Inventory (CSRI)[70] can provide valuable insights into the cost-effectiveness of the interventions and thus the broader impact of the interventions. There are also many other secondary endpoints that can and will be investigated such as dyadic communication, ways of giving support, and benefits of illness/caregiving.

Given the fact that there already is a lot of support in cancer care settings, it might be opportune to investigate the applicability and effectiveness of the interventions of the DIAdIC trial within a different population, such as people with other chronic illnesses. While adapting these interventions to meet the specific needs of populations with a different diagnosis is crucial, the fundamental principles of enhancing communication within families, reducing uncertainty, managing symptoms, and empowering both patients and family caregivers are transferrable across various populations. For example, individuals living with chronic illnesses such as chronic obstructive pulmonary disease (COPD) often face similar challenges in managing their conditions. Patients with COPD frequently report anxiety and depression, and their family caregivers also report a high emotional burden[71,72]. Support resources for people with such conditions may be comparatively limited or less recognized than in cancer care settings and thus might benefit from the interventions of the DIAdIC trial.

There are also still many subgroup analyses that can be performed within the DIAdIC trial, for example making comparisons within the different sexes of patients and family caregivers, looking at the different relationship types of family caregivers (partners, parent-child, friends,..), and comparisons within countries and socioeconomic status.

Explore the concept and impact of collaboration between healthcare professionals and family caregivers further

Collaboration between healthcare professionals and family caregivers of patients with a serious illness is a relatively new concept that is being investigated. As our study demonstrated an association between pre-bereavement collaboration between healthcare professionals and family caregivers in the last months of life and the emotional wellbeing of family caregivers post-bereavement (**Chapter III**), there seems a lot of value in further investigating the concept of collaboration. There currently is some research on the topic of collaboration in healthcare, but mostly in the context of hospital staff[73–76].

It could be further investigated what constitutes ‘good collaboration’ between family caregivers and healthcare professionals at the end-of-life, further building on the research by Vermorgen et al with family caregivers, which identified five elements in qualitative collaboration at the end-of-life: 1) viewing the family caregiver as part of the care team, 2) the availability and approachability of healthcare professionals, 3) sharing of information and communication, also encompassing concerns related to family caregivers, 4) coordinating care among all involved parties, and 5) contextual factors[3]. Further research can include the perspectives of healthcare professionals and patients, investigate the modes and intensity of collaboration depending on the stage of the illness, and differentiate between patients with different chronic illnesses.

The research described in **Chapter III** measured the emotional wellbeing of family caregivers post-bereavement by the Positive and Negative Affect Schedule (PANAS) at one time point[77]. Further research on collaboration can be conducted including other outcome measures evaluating for example quality of life and other bereavement outcomes. Additionally, studies with a longitudinal design can shed light on the duration of the association found in our research.

Recommendations for policy

Promoting collaborative and dyadic care in end-of-life settings

In **Chapter III**, we discussed the finding that pre-bereavement collaboration between family caregivers and healthcare professionals was significantly associated with the emotional wellbeing of family caregivers post-bereavement. Based on this finding, it is important for healthcare professionals to prioritize collaborative care principles within end-of-life care. Healthcare professionals should receive specialized training and education on how to actively involve and communicate with family caregivers of seriously ill patients throughout the caregiving trajectory. This training should also focus on incorporating principles of palliative care that highlight the needs of not only patients but also their family caregivers. Currently, the incorporation of collaborative practices with family caregivers is inadequately addressed in the education of healthcare professionals. Therefore, it is recommended to enrich the standard curriculum for nurses, general practitioners, and other specialist healthcare professionals with specific lessons focused on fostering effective collaboration with family caregivers. By implementing these measures, healthcare professionals can better support both patients and their families during challenging end-of-life situations, ultimately enhancing the overall quality of care provided.

Access to and early integration of palliative care

In **Chapter II**, we discussed the finding that the use of palliative care among family caregivers of seriously ill patients was the most important predictor for receiving more support for all caregiving tasks. This finding suggests that access to palliative care can play a crucial role in enhancing the level of support available to family caregivers throughout their caregiving trajectory.

The benefit of early integration of palliative care in oncology for patients and family caregivers has been demonstrated in many previous studies. Research shows that early integration of palliative care resulted in improved quality of life for patients[78–84], lower depression rates and stress in family caregivers at the end-of-life decline[85], and higher satisfaction with care among family caregivers[86].

By accessing palliative care services early on, family caregivers may benefit from comprehensive support tailored to their needs, thereby potentially alleviating caregiving burden and improving other caregiving health outcomes.

Furthermore, to address the diverse needs of patients with advanced cancer and their family caregivers, it is also recommended to actively promote the use of alternative support systems beyond professional healthcare services. Policymakers should prioritize initiatives that raise awareness among patients and family caregivers about the availability and benefits of non-professional support resources (e.g. peer support groups, online forums, and local organizations). Healthcare professionals should receive training on how to guide individuals toward utilizing these resources effectively. Funding should be allocated not only to promote these alternative forms of support but also to evaluate their effectiveness.

To achieve this, educational efforts are needed to enhance the knowledge in the general public on palliative care, along with a change in policy to get rid of the stigma and misconceptions surrounding palliative care[87].

Recommendations for practice

Collaborative involvement and empowerment of family caregivers

The population-based survey of bereaved family caregivers of people with serious illnesses (**Chapters II** and **III**) showed that while family caregivers do receive professional support in their caregiving tasks, this support primarily consists of purely sharing information with family caregivers, and a more empowering approach is lacking. Additionally, we found that pre-bereavement collaboration between healthcare professionals and family caregivers was associated with emotional wellbeing in family caregivers post-bereavement. These findings all point to a clear practice recommendation for healthcare professionals to collaborate with, involve, and empower family caregivers.

An empowering approach to supporting family caregivers could enhance their self-efficacy, which can lead to lower caregiver burden, diminished negative mood and increased positive mood, and improved health in the patient they are caring for[88]. Healthcare professionals can involve family caregivers in collaborative decision-making related to the patient's care, such as discussing treatment options, goals of care, and end-of-life preferences. A mixed-method study found that the majority of patients and family caregivers also expect the family caregiver to participate in decision-making regarding the cancer treatment of the patient[89].
The advantages of collaborative involvement and empowerment of family caregivers by healthcare professionals are numerous, benefiting both the family caregivers themselves and the patients under their care.

Screening and addressing sexual health in the oncology population

Our study on sexual satisfaction (**Chapter V**) demonstrated low levels of sexual satisfaction in patients with advanced cancer and their family caregivers (recruited for the DIAdIC trial). Furthermore, we observed a reluctance to disclose their levels of sexual satisfaction, especially in patients. Additionally, we also found that sexual satisfaction in patients and family caregivers could be predicted by health parameters in both; e.g. the physical wellbeing of patients was associated with sexual satisfaction in family caregivers.

Based on these findings, I recommend that healthcare professionals adopt an open approach to addressing sexual health concerns by routinely screening for various aspects of sexual wellbeing, including sexual functioning and satisfaction, within their patient population. Given the observed hesitation within the patient and family caregiver population, healthcare professionals should take the initiative to start an open discussion about sexual health, while refraining from making assumptions about their level of interest in the topic. In doing so, healthcare professionals can aim to reduce the barriers individuals face in disclosing any sexual health issues they may be experiencing and reduce potential feelings of embarrassment or discomfort associated with discussing these topics.

Furthermore, the finding that certain health outcomes in both patients and family caregivers predict sexual satisfaction highlights the interdependence between physical and emotional wellbeing and sexual health outcomes. By addressing the concerns and needs of both parties concurrently, a dyadic approach can improve outcomes for both patients and family caregivers more efficiently and effectively.

Integration of iFOCUS and FOCUS+ intervention in practice

As the FOCUS+ intervention shows promising results, its integration in healthcare practice and oncology care should be considered. Further investigation of the process evaluation data can further strenghten this recommendation. However, integrating the complete intervention into healthcare where nurses deliver the FOCUS+ intervention at the homes of dyads might not be feasible, due to limited time, resources and funding. Alternatively the principles of the interventions can be applied within consultations of oncology nurses or social workers with patients and their family caregivers. So by integrating the five core components of the interventions - Family involvement, Outlook, Coping, Uncertainty, and Symptom management - into routine consultations within existing clinical workflows, while tailoring the content to the specific needs of the dyad, the impact of the intervention can be maximised, while leveraging available resources.

Before recommending integration of iFOCUS in healthcare, a few things should be considered. The iFOCUS intervention could possibly benefit from enhancements to its design and the tailoring format. Also, possibly a purely standalone web-based format is not recommended within this population that has high support needs, but a more hybrid format where face-to-face interactions are combined with continued online support or sessions, might be a good alternative. Such an integrated format might better fit the complex and diverse needs of the advanced cancer population.

Conclusion

This dissertation has revealed that family caregivers of people with a serious chronic illness are an essential part of end-of-life care. Family caregivers take on a unique role in the healthcare system where they are not only providers of care to the patient, but they are also in need of support themselves. This dynamic between patients and their family caregivers should be taken into consideration when providing support to both, as better support for the patient will result in better health outcomes for the family caregiver, and vice versa, supporting the family caregiver can improve the patient’s care. A collaboration between family caregivers and healthcare professionals does not only improve the quality of care for patients, but it also has clear benefits for family caregivers’ wellbeing post-bereavement. Our findings have also highlighted an aspect of quality of life in the context of serious illness that is often overlooked, namely sexual satisfaction. It is a topic that is still overrun with taboo, while problems with sexuality could in fact benefit from more open communication. Psychoeducational interventions, such as FOCUS+ as explored in the DIAdIC trial, show promise in addressing these issues on collaboration, quality of care and sexuality.

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Summaries

English summary

General introduction

The symptoms of advanced cancer can greatly impact the patient's quality of life. But when someone is diagnosed with advanced cancer, it's not just their own life that is affected, but also the lives of those closest to them, especially family caregivers. Family caregivers often also describe cancer as an emotionally and physically demanding condition. Both patients and family caregivers have high unmet support needs, especially when cancer is in an advanced stage.

Psychoeducational interventions can serve as a valuable support strategy for individuals facing advanced cancer and their family caregivers to acquire knowledge, coping strategies, and emotional support. Such programs can alleviate the burden they face and enhance the quality of life for both patients and family caregivers. Literature shows that there is an interdependence between several health aspects within the patient-family caregiver dyad; there is a dynamic where the wellbeing of each person is intricately linked to the other, where each person affects the other. This is why dyadic interventions (i.e. interventions that are offered to patients and their family caregivers together as the unit of care) can be beneficial as they address the issues of patients and family caregivers simultaneously.

Two dyadic psychoeducational interventions that are highly relevant for patients and family caregivers are the face-to-face FOCUS intervention and the web-based FOCUS intervention, developed by Northouse and colleagues in the United States. The face-to-face FOCUS intervention is a dyadic program that was developed for patients with cancer and their family caregivers to enable them to cope with the effects of the illness. FOCUS is an acronym that stands for the five core components that are addressed in the intervention: Family involvement, Optimistic attitude, Coping effectiveness, Uncertainty reduction and Symptom management. The program thus focuses on enhancing effective communication between patients and family caregivers, sustaining hope, employing active coping strategies, acquiring information related to the illness, and managing symptom distress. Patients and their family caregivers are invited for three home visits, each lasting approximately one and a half hours, spread over a period of three months. Each session was structured to address the five core content areas of the FOCUS Program, following an extensive intervention protocol manual with checklist format. While the manual detailed the main content of the FOCUS program, there was still room for tailoring the content to meet the needs of each dyad. Northouse has conducted several randomized controlled trials that have successfully demonstrated the effectiveness of the FOCUS intervention in American populations. Later on, the 'F' component (representing Family involvement) of FOCUS program was converted into a web-based format and showed promising results in a feasibility study. However, the effect of the FOCUS intervention is yet to be determined in a European context and the European healthcare systems. The DIAdIC trial adapted the FOCUS interventions and evaluated its effectiveness.

This dissertation addresses pertinent gaps in the knowledge on the support and wellbeing for both patients with a serious illness (such as advanced cancer) and their family caregivers. Hitherto, little attention has been paid to how family caregivers collaborate with healthcare professionals in the last months of life of the person they are caring for. Research often does not take into account the role of family caregivers in the care team and the professional support they receive during those last months before bereavement. The research conducted as part of this dissertation highlights the importance of family caregivers in end-of-life healthcare and their role of a partner in care. Next, studies on psychoeducational interventions in family caregiving have several shortcomings. They often have small sample sizes, lack clear effectiveness and are not tailored to individual needs of participants. The DIAdIC trial is set up to reach a large sample size across six countries and the multisite randomized controlled trial allows for the most favorable design to study effectiveness of the interventions, that are tailored to mee the dyad's specific needs.

Study objectives and research questions

The main objective of this dissertation is to investigate the support and wellbeing for patients coping with serious illness and their family caregivers. This objective is guided by the following aims and associated research questions:

The first aim is to describe experiences of the population of bereaved family caregivers of people with a serious illness regarding their collaboration with healthcare professionals. The following specific research questions will be answered:

1) How are family caregivers of people with a serious illness supported by healthcare professions in their caregiving tasks?
2) Is pre-bereavement collaboration between family caregivers and healthcare professionals associated with post-bereavement emotional well-being?

The second aim of this dissertation is to describe the protocol of a randomized controlled trial on the evaluation of two psychoeducational interventions for people with advanced cancer and their family caregiver in six European countries. The following research question will be answered:

3) What is the design, methodology and procedure for conducting the DIAdIC trial?

The third aim is to present the findings resulting from the DIAdIC study. The following research questions will be answered:

4) What are the predictors of sexual satisfaction in patients with advanced cancer and their family caregivers who were recruited for the DIAdIC trial?
5) What is the effect of 1) the face-to-face FOCUS+ intervention and 2) the iFOCUS web-based intervention compared to 3) care as usual on the emotional functioning and self-efficacy of the patients with advanced cancer and their family caregivers?

Methods

To answer the research questions of this dissertation, several methods of data collection were employed. First, we conducted a cross-sectional survey among bereaved family caregivers in Flanders, Belgium on their experience with support from and collaboration with healthcare professionals (**Chapter II** and **III**). Additionally, we drafted a research protocol to describe all relevant aspects of the DIAdIC trial (**Chapter IV**). To describe sexual satisfaction of patients and family caregivers and the effect of two dyadic interventions on emotional functioning and self-efficacy of patient-caregiver dyads, we conducted a randomized controlled trial in six European countries (**Chapter V** and **VI**). The methods for each study are briefly described in the following paragraphs.

Study 1: A cross-sectional survey of bereaved family caregivers on the collaboration between healthcare professionals and family caregivers of persons with a serious illness (research questions 1 and 2)

By means of a population-based cross-sectional survey in Flanders, Belgium, data was collected from bereaved family caregivers of individuals with a serious illness. Participants were identified through records from the three largest health insurers in Flanders, which cover approximately 79% of the population. These health insurers keep records of individuals applying for a care budget for persons with significant care needs ('zorgbudget voor zwaar zorgbehoevenden'), as well as the names of their family caregivers. We conducted a random sampling of 3,000 deceased individuals with a serious illness who had applied for a care budget through one of the participating health insurers. The individual registered in the database as the family caregiver was selected. Questionnaires were then distributed by post between November 2019 and January 2020. The questionnaire included items pertaining to the care provided for the patient during the final three months of their life, including demographic items.

Study 2: An international randomized controlled trial on the effectiveness of a nurse-delivered (FOCUS+) and a web-based (iFOCUS) psychoeducational intervention for people with advanced cancer and their family caregivers (DIAdIC) (Research questions 3, 4 and 5)

We conducted an international multicenter trial, the DIAdIC trial, comparing the face-to-face FOCUS+ intervention and the web-based iFOCUS intervention to standard care for patients with advanced cancer and their primary family caregivers. The trial spanned six countries (Belgium, The Netherlands, United Kingdom, Denmark, Italy and Ireland) and recruited participants between February 2021 and September 2023. Randomization (1:1:1 ratio) assigned participants to one of the three study arms. The two interventions were provided in addition to usual care and focused on psychoeducation, aiming to teach dyads optimal strategies for jointly managing the implications of advanced cancer and addressing their priority concerns. FOCUS+ involved two home visits and one online session spread over 12 weeks, while iFOCUS was a self-managed web-based program. While the FOCUS+ and iFOCUS interventions differ in their modes of delivery (face-to-face vs. web-based), they share the same core content, addressing five essential components: (1) supporting family involvement, communication, and mutual support, (2) fostering outlook and meaning, (3) enhancing coping effectiveness, (4) reducing uncertainty, and (5) teaching symptom management. Data collection occurred at baseline, at 3 months and once again at 6 months. For the study on sexual satisfaction, we used two measures: an item from the Functional Assessment of Cancer Therapy – General (FACT-G) for patients and an item of the Caregiver Quality of Life Index-Cancer scale (CQOLC) for family caregivers.

The primary outcomes for the trial were emotional functioning and self-efficacy. Emotional functioning was measured using a 10-item short form (EF10) based on the European Organisation for Research and Treatment of Cancer (EORTC) EF item bank. Self-efficacy was assessed by 17 items from the Lewis Cancer self-efficacy scale. Data on socio-demographic and clinical characteristics were gathered at enrollment and baseline.

Main findings of dissertation

*Support for family caregivers in their caregiving tasks (**Chapter II**)*

We included 1,334 respondents for analysis, who were family caregivers of someone with at least one serious illness and had had contact with them during the last three months of life. Family caregivers commonly facilitated safe mobility inside or outside the house (85%), talked about emotions (73%), promoted social interaction (73%), assisted with administration (71%), provided physical comfort (72%) and managed symptoms (65%). Less than half (47%) talked about end-of-life preferences or made home adjustments for safety and comfort (39%). The majority of respondents (72-93%) had wanted to perform the caregiving tasks themselves. Most family caregivers received support from one or more healthcare professionals so they could perform the task themselves, ranging from 71% for promoting social interaction to 95% for managing symptoms. Home care nurses and GPs most frequently supported family caregivers in their caregiving tasks in the last three months of life. Healthcare professionals mostly explained how family caregivers could perform the task. The majority of family caregivers indicated they had received sufficient support from healthcare professionals for all caregiving tasks, ranging from 78% for promoting social interaction to 89% for facilitating safe mobility. A factor analysis identified three dimensions of support for caregiving tasks, i.e. support for physical, psychosocial and practical tasks. The use of specialised palliative care services was associated with receiving more support across physical (p=.001), psychosocial (p<.001) and practical (p<.001) tasks.

*Collaboration between family caregivers and healthcare professionals (**Chapter III**)*

The mean value of the Positive Affect (PA) sub-scale was 29.38, which was lower compared to the mean in a normative sample (31.31). The mean value of the Negative Affect (NA) sub-scale was 21.7, which was much higher compared to the mean in a normative sample (16.0). The majority of family caregivers evaluated the pre-bereavement collaboration items with healthcare professionals positively. Family caregivers' evaluation of collaboration with healthcare professionals was positively correlated with PA (r=.13 p<.001) and negatively correlated with NA (r=-.13, p<.001). A multivariable multivariate analysis showed a statistically significant association of emotional well-being post-bereavement with collaboration, as well as with the degree of surprise about the patient's death, relationship with patient, patient's decisional capacity, collaboration and patient staying at home.

*The protocol for a randomized controlled trial on the effectiveness of two psychoeducational interventions for patients with advanced cancer and their family caregivers (**Chapter IV**)*

The two interventions of the DIAdIC study offer tailored psychoeducational support for patient-family caregiver dyads. The nurse-led face-to-face intervention (FOCUS+) consisted of two home visits and one online video session; and the web-based intervention (iFOCUS) was completed independently by the patient-family caregiver dyad in four online sessions. The interventions were based on the FOCUS intervention, developed in the USA, both which addressed the same five core components: family involvement, optimistic outlook, coping effectiveness, uncertainty reduction, and symptom management. The FOCUS interventions were adapted to fit the needs of the European population.

To evaluate the interventions, we have set up an international multicenter parallel-group three-arm randomized controlled trial in Belgium, Denmark, Ireland, Italy, The Netherlands, and the United Kingdom. All patient-family caregiver dyads were randomized to one of the study arms: 1) the iFOCUS+ program, 2) the FOCUS+ program or 3) a control group (care as usual). The primary outcomes were emotional functioning and self-efficacy of the patient and the family caregiver. The secondary outcomes were quality of life, benefits of illness, coping, dyadic communication, and ways of giving support of the patient and family caregiver. These endpoints were chosen as the DIAdIC interventions were designed to provide support in the five F O C U S domains (see above). These five areas are expected to have a direct effect on appraisal factors (appraisal of illness/caregiving, uncertainty,..) and coping resources (coping, self-efficacy, dyadic communication).

*Sexual satisfaction in patients and family caregivers of the DIAdIC trial (**Chapter V**)*

The sample consisted of 431 patients and 431 family caregivers who participated in the DIAdIC trial. 42% of patients and 33% of family caregivers indicated to be not at all satisfied with their sex life (mean score of respectively 1.21, SD=1.21 vs 1.43, SD=1.21). One out of three patients (34.3%) preferred not to answer the question about sexual satisfaction. The 'prefer-not-to-answer' option was not offered to family caregivers but the latter had more missing values to the sexual satisfaction question compared to patients (respectively 8.6% and 1.2%).

Patients with prostate and gynecological cancer reported lower sexual satisfaction compared to patients with gastrointestinal cancer (respectively B=-.267, 95% confidence interval [CI] -1.674, -.594, p<.001 and B=-.196, CI -2,103, -.452, p=.003). When adjusted for confounders, higher sexual satisfaction in patients was associated with higher emotional (B=.278 CI .024, .057, p<.001), physical (B=.305, CI .012, .025, p<.001) and social functioning (B=.151, CI .001, .013, p=.032), global health (B=.356, CI .007, .013, p<.001) and social wellbeing (B=.161, .013, .082, p=.008).

In family caregivers, sexual satisfaction was lower as age increased (B= -.142, CI -.022, -.004, p=.005). Family caregivers who were not the patient's partner reported higher levels of sexual satisfaction compared to family caregivers who were the patient's partner (B= .257, CI .481, 1.056, p<.001). Family caregivers of patients with gynecological or prostate cancer reported lower levels of sexual satisfaction compared to family caregivers of patients with gastrointestinal cancer but only if the family caregiver was partner to the patient (respectively B=-1.310, CI -2.179, -.442, p=.003 and B=-1.088, CI -1.652, -.523, p<.001). Family caregivers with higher emotional functioning reported higher sexual satisfaction (B=.177, CI .011, .043, p=.001). Higher quality of life was associated with higher sexual satisfaction (B=.165, CI -.165, .716, p=.002). Family caregivers of patients, whose physical functioning was higher, reported higher sexual satisfaction (B=.110, CI .001, .013, p=.032).

*Effectiveness of two dyadic psychoeducational interventions for advanced cancer (**Chapter VI**)*

We enrolled 431 dyads into the DIAdIC study. Dyads were randomized to the iFOCUS intervention (n=148), FOCUS+ intervention (n=140) or the control group (n=143).

Patient outcomes

Emotional functioning did not show a significant difference between the iFOCUS intervention group and control group at 12 weeks (T1) (baseline-adjusted mean difference, -·27; 95% CI, -2·11 to 1·57; P = .774). No significant difference was observed in the FOCUS+ intervention group compared to the control group at T1 (baseline-adjusted mean difference, ·12; 95% CI, -1·65 to 1·89; P = ·897). Non-significant differences for emotional functioning for both intervention groups persisted at 24 weeks (T2). We did not find a significant difference for the second primary outcome, self-efficacy, between the iFOCUS intervention group and control group at T1 (baseline-adjusted mean difference, ·49; 95% CI, -6·21 to 7·19; P = ·887). A statistically significant difference was found between the FOCUS+ intervention group and control group at T1 for self-efficacy (baseline-adjusted mean difference, 9·02; 95% CI, 2·45 to 15·58; P = ·007). Non-significant differences were found at T2.

Family caregiver outcomes

Emotional functioning did not differ significantly between the iFOCUS intervention group and control group at T1 (baseline-adjusted mean difference, ·30; 95% CI, -1·41 to 2·00; P = ·732). Similarly, no significant difference was found between the FOCUS+ intervention group and control group at T1 (baseline-adjusted mean difference, ·17; 95% CI, 1·45 to 1·79; P = ·834). Non-significant differences for emotional functioning persisted at T2. For self-efficacy, we did not find a significant difference between the iFOCUS intervention group and control group at T1 (baseline-adjusted mean difference, 3·66; 95% CI, -3·36 to 10·68; P = ·306). Similarly, no significant difference was found between the FOCUS+ intervention group and control group at T1 for self-efficacy (baseline-adjusted mean difference, 3·88; 95% CI, -2·84 to 10·61; P = ·258). No significant differences were found at T2.

Interpretation and discussion of findings

This dissertation has compiled insights on available support and wellbeing for bereaved family caregivers of patients with serious illness, the development of the DIAdIC study, sexual satisfaction in patients with advanced cancer and their family caregiver and the effectiveness of two psychoeducational interventions.

The taboo on sexuality in oncology

An important finding in this dissertation is the taboo around sexuality among individuals coping with cancer. In the baseline data of the DIAdIC trial when evaluating sexual satisfaction, the inclusion of a 'prefer not to answer' option seemed to serve as an escape route for respondents, a route that many patients chose to take, emphasizing the sensitivity associated with the topic of sexual satisfaction. Despite the sensitivity of the topic, there are many studies that show that sexuality is an important part of quality of life and wellbeing. However, introducing a ‘prefer not to answer’ option for the sexual satisfaction question may inadvertently signal our own sensitivity as researchers toward the topic of sexuality and thus could have unintentionally contributed to the perpetuation of the taboo surrounding sexuality in this population. Research also shows that healthcare professionals also feel hesitant when discussing sexuality with patients. The researchers involved in the DIAdIC study regularly had interactions with the nurses who delivered the FOCUS+ intervention, further confirming this issue. There thus seems to be room for improvement for educating healthcare professionals in oncology settings on the topic of sexuality.

Effectiveness of iFOCUS and FOCUS+ in the DIAdIC trial

The DIAdIC trial demonstrated a significant improvement in self-efficacy in patients in the FOCUS+ intervention group at the 12-week mark (T1) compared to the control group. This improvement did not sustain at 24 weeks (T2) and was not found in family caregivers. Across all other comparisons, no significant improvements were observed. It is surprising that we didn't find any impact of the interventions on the primary outcomes for the family caregiver, despite it being a dyadic interventions. However, family caregivers might have still benefitted from the interventions, albeit indirectly. The increased self-efficacy in patients can lead to other improved health outcomes, which can in its turn result in less burden or stress in the family caregiver. So indirectly, the family caregivers might have still benefitted from the FOCUS+ intervention, this indirect effect may require more time to become apparent. Future research will explore secondary outcomes such as coping mechanisms, dyadic support, and quality of life, potentially demonstrating significant effects for family caregivers.

Next, as the DIAdIC trial was conducted in the middle of the COVID-19 pandemic, a rerun of the DIAdIC trial without the context of a global pandemic, can possibly yield different results.

While Northouse found that the tailored web-based FOCUS program led to improvements in several outcomes in a pre- to post-intervention assessment, the web-based iFOCUS intervention of the DIAdIC trial did not find any statistical significant improvements on the primary outcomes. While literature shows that web-based interventions are often well-received, the delivery of support or care through online format does not suit every individual's needs or preferences. Because of the varied experiences and personal preferences of patients and family caregivers, the trial results may not have demonstrated consistent enough results that reflect significant improvements from the iFOCUS web-based program in the DIAdIC trial.

The limited effectiveness of the FOCUS+ intervention cause critical reflection regarding the implementation. Despite demonstrating a positive impact on patient self-efficacy in the short term, its limited effectiveness in other areas and over time raises questions about its overall efficacy and sustainability. Implementing an intervention that demonstrated improvements in only one aspect and for a restricted amount of time may not justify the resources and efforts required for implementation. Instead, further exploration and refinement of the FOCUS+ intervention may be warranted to enhance its effectiveness across a broader range of outcomes and to ensure prolonged benefits for both patients and family caregivers.

Collaboration as an important contributor to post-bereavement wellbeing in family caregivers

In this dissertation, we found that family caregivers' evaluation of collaboration with healthcare professionals in the last three months pre-bereavement was associated with emotional wellbeing. Both prior research and our study indicate that the support provided before bereavement has an impact on the post-bereavement phase for family caregivers. However, in practice, collaborative efforts at the end-of-life are not being consistently implemented. Recommendations on how collaboration between healthcare professionals and family caregivers can be improved are described below.

Recommendations

Various recommendations can be formulated for better support and wellbeing for patients and family caregivers in three domains, namely practice, policy, and future research.

Recommendations for research

- Scrutinize the results of the DIAdIC trial
    - Continue the trial so until we attain the intended sample size
    - Look into a higher dosage of FOCUS+
    - Investigate the working mechanisms of the original FOCUS intervention
    - Explore the experiences of the participants by means of qualitative research
    - Explore secondary outcomes
    - Investigate the impact of the iFOCUS and FOCUS+ interventions outside of oncology population
    - Perform subgroup analyses

- Explore the concept and impact of collaboration between healthcare professionals and family caregivers
    - Investigate what constitutes 'good collaboration' between family caregivers and healthcare professionals at the end-of-life
    - Include the perspectives of healthcare professionals and patients
    - Investigate the modes and intensity of collaboration depending on the stage of the illness
    - Differentiate between patients with different chronic illnesses
    - Conduct longitudinal studies investigating the association between collaboration and emotional wellbeing on the long term

Recommendations for policy

- Promote collaborative and dyadic care in end-of-life settings
- Promote and provide access to and early integration of palliative care

Recommendations for practice

- Collaborate with, involve and empower family caregivers in serious illness care
- Screen and address sexual health in the oncology population
- Implement principles of FOCUS interventions in healthcare

Nederlandstalige samenvatting

Algemene inleiding

De symptomen van gevorderde kanker kunnen de levenskwaliteit van de patiënt enorm beïnvloeden. Maar wanneer iemand de diagnose kanker krijgt, wordt niet alleen zijn of haar eigen leven beïnvloed, maar ook dat van zijn of haar naasten, met name de mantelzorger. Mantelzorgers beschrijven kanker vaak als een emotioneel en fysiek veeleisende aandoening. Zowel patiënten als mantelzorgers hebben veel ondersteuningsbehoeften, vooral wanneer de kanker zich in een vergevorderd stadium bevindt.

Psycho-educatieve interventies kunnen dienen als een waardevolle ondersteuningsstrategie voor mensen die worden geconfronteerd met gevorderde kanker en hun mantelzorgers om kennis op te doen, manieren te ontdekken om om te gaan met de ziekte en emotionele steun te krijgen. Dergelijke programma's kunnen de last waarmee ze geconfronteerd worden verlichten en de kwaliteit van leven voor zowel patiënten als mantelzorgers verbeteren. De literatuur toont aan dat er een onderlinge afhankelijkheid is tussen verschillende gezondheidsaspecten binnen de patiënt-mantelzorger dyade; er is een dynamiek waarbij het welzijn van de ene persoon nauw verbonden is met de ander, waarbij elke persoon de ander beïnvloedt. Daarom kunnen dyadische interventies (d.w.z. interventies die worden aangeboden aan patiënten en hun mantelzorgers samen) nuttig zijn omdat ze de problemen van patiënten en mantelzorgers tegelijkertijd aanpakken.

Twee dyadische psycho-educatieve interventies die zeer relevant zijn voor patiënten en mantelzorgers zijn de face-to-face FOCUS interventie en de web-based FOCUS interventie, ontwikkeld door Northouse en collega's in de Verenigde Staten. De face-to-face FOCUS interventie is een dyadisch programma dat werd ontwikkeld voor patiënten met kanker en hun mantelzorgers om hen in staat te stellen om te gaan met de gevolgen van de ziekte. FOCUS is een acroniem dat staat voor de vijf kerncomponenten die in de interventie aan bod komen: Family involvement (betrekken van familie), Optimistic outlook (Optimistische houding), Coping effectiveness (Coping effectiviteit) , Uncertainty reduction (verminderen van onzekerheid) en Symtom management (omgaan met symtomen). Het programma richt zich dus op het verbeteren van effectieve communicatie tussen patiënten en mantelzorgers, het behouden van hoop, het toepassen van actieve copingstrategieën, het verkrijgen van informatie over de ziekte en het omgaan met symptoomklachten. Patiënten en hun mantelzorgers worden uitgenodigd voor drie huisbezoeken, die elk ongeveer anderhalf uur duren, verspreid over een periode van drie maanden. Elke sessie was gestructureerd om de vijf kerncomponenten van het FOCUS-programma te behandelen, waarbij een uitgebreide handleiding met interventieprotocol en checklists werd gevolgd. Hoewel de handleiding de belangrijkste inhoud van het FOCUS-programma bevatte, was er nog ruimte om de inhoud aan te passen aan de behoeften van elke dyade. Northouse heeft verschillende gerandomiseerde gecontroleerde studies uitgevoerd die met succes de effectiviteit van de FOCUS-interventie in Amerikaanse populaties hebben aangetoond. Later werd de 'F'-

component (die staat voor ‘Family involvement’ of betrekken van familie) van het FOCUS-programma omgezet naar een web-based format en liet veelbelovende resultaten zien in een haalbaarheidsstudie. Het effect van de FOCUS-interventie moet echter nog worden aangetoond worden in een Europese context en de Europese gezondheidszorgsystemen. De DIAdIC trial paste de FOCUS interventies aan en evalueerde de effectiviteit ervan.

Dit proefschrift richt zich op belangrijke hiaten in de kennis over de ondersteuning en het welzijn van zowel patiënten met een ernstige ziekte (zoals gevorderde kanker) als hun mantelzorgers. Tot nu toe is er weinig aandacht besteed aan hoe mantelzorgers samenwerken met professionele zorgverleners in de laatste levensmaanden van de persoon voor wie zij zorgen. Onderzoek houdt vaak geen rekening met de rol van mantelzorgers in het zorgteam en de professionele ondersteuning die zij krijgen tijdens die laatste maanden voor het overlijden. Het onderzoek dat is uitgevoerd als onderdeel van dit proefschrift benadrukt het belang van mantelzorgers in de zorg rond het levenseinde en hun rol als partner in de zorg. Daarnaast hebben andere onderzoeken naar psycho-educatieve interventies bij mantelzorg vaak verschillende tekortkomingen. Ze hebben vaak een kleine steekproefgrootte, hebben geen duidelijke conclusies omtrent effectiviteit, en zijn niet afgestemd op de individuele behoeften van de deelnemers. De DIAdIC trial is opgezet om een grote steekproefgrootte te bereiken in zes landen en de multisite gerandomiseerde gecontroleerde trial biedt de meest gunstige opzet om de effectiviteit van de interventies te onderzoeken en aan te tonen, die zijn afgestemd op de specifieke behoeften van de dyade.

Doelstellingen van het onderzoek en onderzoeksvragen

Het hoofddoel van dit proefschrift is het onderzoeken van de steun en het welzijn voor patiënten met een ernstige aandoening en hun mantelzorgers. Dit hoofddoel wordt gevormd door de volgende concrete doelstellingen en bijbehorende onderzoeksvragen:

De eerste doelstelling is het beschrijven van ervaringen van de populatie mantelzorgers van mensen met een ernstige ziekte die overleden zijn met betrekking tot hun samenwerking met professionele zorgverleners. De volgende specifieke onderzoeksvragen zullen worden beantwoord:

1) Hoe worden mantelzorgers van mensen met een ernstige ziekte ondersteund door professionele zorgverleners in hun zorgtaken?
2) Is samenwerking vóór de rouw tussen mantelzorgers en professionele zorgverleners geassocieerd met emotioneel welzijn na de rouw?

De tweede doelstelling van dit proefschrift is het beschrijven van het protocol van een gerandomiseerde gecontroleerde trial over de evaluatie van twee psycho-educatieve interventies voor mensen met gevorderde kanker en hun mantelzorger in zes Europese landen. De volgende onderzoeksvraag zal worden beantwoord:

3) Wat is het design, de methodologie en het protocol voor het uitvoeren van de DIAdIC trial?

De derde doelstelling is om de bevindingen van de DIAdIC-studie te presenteren. De volgende onderzoeksvragen zullen worden beantwoord:

4) Wat zijn de voorspellers van seksuele tevredenheid bij patiënten met gevorderde kanker en hun mantelzorgers die werden gerekruteerd voor de DIAdIC studie?

5) Wat is het effect van 1) de face-to-face FOCUS+ interventie en 2) de iFOCUS web-gebaseerde interventie vergeleken met 3) standaardzorg op het emotioneel functioneren en zelfredzaamheid (self-effficacy) van de patiënten met gevorderde kanker en hun mantelzorgers?

Methoden

Om de onderzoeksvragen van dit proefschrift te beantwoorden, werden verschillende methoden van dataverzameling gebruikt. Ten eerste voerden we een cross-sectionele studie uit onder nabestaanden in Vlaanderen, België over hun ervaring met steun van en samenwerking met professionele zorgverleners (**Hoofdstuk II** en **III**). Daarnaast stelden we een onderzoeksprotocol op om alle relevante aspecten van de DIAdIC trial te beschrijven (**Hoofdstuk IV**). Om de seksuele tevredenheid van patiënten en mantelzorgers en het effect van twee dyadische interventies op emotioneel functioneren en zelfredzaamheid van patiënt-mantelzorger dyades te beschrijven, voerden we een gerandomiseerde gecontroleerde trial uit in zes Europese landen (**Hoofdstuk V** en **VI**). De methoden van elke studie worden kort beschreven in de volgende paragrafen.

Studie 1: Een cross-sectionele studie onder nabestaanden over de samenwerking tussen professionele zorgverleners en mantelzorgers van personen met een ernstige aandoening (onderzoeksvragen 1 en 2)

Door middel van een populatie-gebaseerd cross-sectioneel onderzoek in Vlaanderen, België, werden gegevens verzameld van nabestaanden van personen met een ernstige ziekte. De deelnemers werden geïdentificeerd aan de hand van gegevens van de drie grootste zorgverzekeraars in Vlaanderen, die ongeveer 79% van de bevolking dekken. Deze zorgverzekeraars houden gegevens bij van personen die een zorgbudget voor zwaar zorgbehoevenden aanvragen, evenals de namen van hun mantelzorgers. We hielden een aselecte steekproef van 3,000 overledenen met een ernstige ziekte die een zorgbudget hadden aangevraagd bij een van de deelnemende zorgverzekeraars. De persoon die in de database geregistreerd stond als mantelzorger werd geselecteerd. Vervolgens werden tussen november 2019 en januari 2020 vragenlijsten per post verspreid. De vragenlijst bevatte items met betrekking tot de zorg die was verleend aan de patiënt gedurende de laatste drie maanden van hun leven, waaronder ook enkele demografische items.

Studie 2: Een internationale gerandomiseerde gecontroleerde trial naar de effectiviteit van een face-to-face (FOCUS+) en een webgebaseerde (iFOCUS) psycho-educatieve interventie voor mensen met kanker in een gevorderd stadium en hun mantelzorgers (DIAdIC) (onderzoeksvragen 3, 4 en 5)

We voerden een internationale multicenter trial uit, de DIAdIC trial, waarin de face-to-face FOCUS+ interventie en de web-based iFOCUS interventie werden vergeleken met standaardzorg voor patiënten met gevorderde kanker en hun primaire mantelzorgers. De studie ging door in zes landen (België, Nederland, het Verenigd Koninkrijk, Denemarken, Italië en Ierland) en wierf deelnemers aan tussen februari 2021 en september 2023. Door randomisatie (ratio 1:1:1) werden de deelnemers toegewezen aan een van de drie studiearmen. De twee interventies werden aangeboden als aanvulling op standaardzorg en waren gericht op psycho-educatie, met als doel het aanleren van optimale strategieën voor het gezamenlijk omgaan met de gevolgen van gevorderde kanker en het aanpakken van hun prioritaire zorgen. FOCUS+ bestond uit 2 huisbezoeken en 1 online sessie, verspreid over 12 weken, terwijl iFOCUS een zelfgestuurd webgebaseerd programma was. Hoewel de interventies van FOCUS+ en iFOCUS verschillen in de manier waarop ze worden uitgevoerd (face-to-face vs. web-based), delen ze dezelfde kerninhoud en richten ze zich op dezelfde vijf kerncomponenten: (1) het ondersteunen van familiebetrokkenheid, communicatie en wederzijdse steun, (2) het bevorderen van uitzicht en betekenis, (3) het verbeteren van coping effectiviteit, (4) het verminderen van onzekerheid, en (5) het aanleren van symptoombestrijding. De gegevens werden verzameld op baseline, na 3 maanden en opnieuw na 6 maanden. Voor het onderzoek naar seksuele tevredenheid gebruikten we twee maten: een item van de Functional Assessment of Cancer Therapy - General (FACT-G) voor patiënten en een item van de Caregiver Quality of Life Index-Cancer scale (CQOLC) voor mantelzorgers. De primaire uitkomsten voor de trial zelf waren emotioneel functioneren en zelfredzaamheid. Emotioneel functioneren werd gemeten met een korte 10-item-schaal (EF10) gebaseerd op de EF-itembank van de European Organisation for Research and Treatment of Cancer (EORTC). Zelfredzaamheid werd gemeten met 17 items van de Lewis Cancer self-efficacy scale. Gegevens over socio-demografische en klinische kenmerken werden verzameld bij inschrijving tot de studie en bij baseline.

Belangrijkste bevindingen van proefschrift

*Ondersteuning van mantelzorgers bij hun zorgtaken (**Hoofdstuk II**)*

We includeerden 1,334 respondenten voor analyse, die mantelzorgers waren van iemand met ten minste één ernstige aandoening en contact met hen hadden gehad tijdens de laatste drie levensmaanden. Mantelzorgers zorgden vaak voor veilige mobiliteit binnen of buiten het huis (85%), praatten over emoties (73%), bevorderden sociale interactie (73%), assisteerden bij de administratie (71%), boden fysiek comfort (72%) en hielpen bij het bestrijden van symtomen (65%). Minder dan de helft (47%) sprak over voorkeuren voor het levenseinde of maakte aanpassingen in huis voor veiligheid en comfort (39%). De meerderheid van de respondenten (72-93%) had de zorgtaken zelf willen uitvoeren. De meeste mantelzorgers kregen ondersteuning van een of meer professionele zorgverleners zodat ze de taak zelf konden uitvoeren, variërend van 71% voor het bevorderen van sociale interactie tot 95% voor symptoombestrijding. Thuiszorgverpleegkundigen en huisartsen ondersteunden mantelzorgers het vaakst bij hun zorgtaken in de laatste drie levensmaanden. Professionele zorgverleners legden meestal uit hoe mantelzorgers de taak konden uitvoeren. De meerderheid van de mantelzorgers gaf aan voldoende ondersteuning te hebben gekregen van professionele zorgverleners voor alle zorgtaken, variërend van 78% voor het bevorderen van sociale interactie tot 89% voor het vergemakkelijken van veilige mobiliteit. Een factoranalyse identificeerde drie dimensies van ondersteuning voor zorgtaken, namelijk ondersteuning voor lichamelijke, psychosociale en praktische taken. Het gebruik van gespecialiseerde palliatieve zorgdiensten hing samen met het ontvangen van meer ondersteuning voor lichamelijke (p=.001), psychosociale (p<.001) en praktische (p<.001) taken.

*Samenwerking tussen mantelzorgers en professionele zorgverleners (**Hoofdstuk III**)*

De gemiddelde waarde van de subschaal Positief Affect (PA) was 29.38, wat lager was vergeleken met het gemiddelde in een normatieve steekproef (31.31). De gemiddelde waarde van de subschaal Negatief Affect (NA) was 21.7, wat veel hoger was vergeleken met het gemiddelde in een normatieve steekproef (16.0). De meerderheid van de mantelzorgers beoordeelde de items voor samenwerking met professionele zorgverleners voorafgaand aan de rouw positief. De evaluatie door mantelzorgers van de samenwerking met professionele zorgverleners was positief gecorreleerd met PA (r=.13 p<.001) en negatief gecorreleerd met NA (r=-.13, p<.001). Een multivariabele analyse toonde een statistisch significante associatie van emotioneel welbevinden na overlijden met samenwerking, evenals met de mate van verrassing over het overlijden van de patiënt, de relatie met de patiënt, de beslissingsbevoegdheid van de patiënt, samenwerking en thuisblijven van de patiënt.

*Het protocol voor een gerandomiseerde gecontroleerde trial naar de effectiviteit van twee psycho-educatieve interventies voor patiënten met gevorderde kanker en hun mantelzorgers (**Hoofdstuk IV**)*

De twee interventies van de DIAdIC-studie bieden op maat gemaakte psycho-educatieve ondersteuning voor patiënt-mantelzorger dyades. De face-to-face interventie onder leiding van een verpleegkundige (FOCUS+) bestond uit twee huisbezoeken en één online videosessie; en de webgebaseerde interventie (iFOCUS) werd zelfstandig door de patiënt-mantelzorger dyade voltooid in vier online sessies. De interventies waren gebaseerd op de FOCUS-interventie, ontwikkeld in de VS, die beide gericht waren op dezelfde vijf kerncomponenten: betrokkenheid van de familie, optimistisch vooruitzicht, effectiviteit van coping, onzekerheidsreductie en symptoombestrijding. De FOCUS-interventies werden aangepast aan de behoeften van de Europese populatie.

Om de interventies te evalueren, hebben we een internationale multicenter parallel-groep drie-armige gerandomiseerde gecontroleerde studie opgezet in België, Denemarken, Ierland, Italië, Nederland en het Verenigd Koninkrijk. Alle patiënt-mantelzorger dyades werden gerandomiseerd naar één van de studiearmen: 1) het iFOCUS+ programma, 2) het FOCUS+ programma of 3) een controlegroep (standaardzorg). De primaire uitkomsten waren emotioneel functioneren en zelfredzaamheid van de patiënt en de mantelzorger. De secundaire uitkomsten waren kwaliteit van leven, voordelen van ziekte, coping, dyadische communicatie en manieren van steun geven van de patiënt en de mantelzorger.

*Seksuele tevredenheid bij patiënten en mantelzorgers van de DIAdIC trial (**Hoofdstuk V**)*

De steekproef bestond uit 431 patiënten en 431 mantelzorgers die deelnamen aan de DIAdIC trial. 42% van de patiënten en 33% van de mantelzorgers gaven aan helemaal niet tevreden te zijn met hun seksleven (gemiddelde score van respectievelijk 1.21, SD=1.21 vs 1.43, SD=1.21). Eén op de drie patiënten (34.3%) gaf er de voorkeur aan de vraag over seksuele tevredenheid niet te beantwoorden. De 'liever niet beantwoorden' optie werd niet aangeboden aan mantelzorgers, maar deze laatsten hadden meer missende waarden op de seksuele tevredenheid vraag in vergelijking met patiënten (respectievelijk 8,6% en 1,2%).
Patiënten met prostaat- en gynaecologische kanker rapporteerden een lagere seksuele tevredenheid in vergelijking met patiënten met gastro-intestinale kanker (respectievelijk B=-.267, 95% betrouwbaarheidsinterval [CI] -1.674, -.594, p<.001 en B=-.196, CI -2.103, -.452, p=.003). Wanneer gecorrigeerd voor confounders, was hogere seksuele tevredenheid bij patiënten geassocieerd met hogere emotionele (B=.278 CI .024, .057, p<.001), fysieke (B=.305, CI .012, . 025, p<.001) en sociaal functioneren (B=.151, CI .001, .013, p=.032), algemene gezondheid (B=.356, CI .007, .013, p<.001) en sociaal welzijn (B=.161, .013, .082, p=.008).
Bij mantelzorgers was de seksuele tevredenheid lager naarmate de leeftijd toenam (B= -.142, CI -.022, -.004, p=.005). Mantelzorgers die niet de partner van de patiënt waren rapporteerden hogere niveaus van seksuele tevredenheid vergeleken met mantelzorgers die wel de partner van de patiënt waren (B= .257, CI .481, 1.056, p<.001). Mantelzorgers van patiënten met gynaecologische of prostaatkanker rapporteerden lagere niveaus van seksuele tevredenheid vergeleken met mantelzorgers van patiënten met gastro-intestinale kanker, maar alleen als de mantelzorger partner was van de patiënt (respectievelijk B=-1.310, CI -2.179, -.442, p=.003 en B=-1.088, CI -1.652, -.523, p<.001). Mantelzorgers met een hoger emotioneel functioneren rapporteerden een hogere seksuele tevredenheid (B=.177, CI .011, .043, p=.001). Hogere kwaliteit van leven was geassocieerd met hogere seksuele tevredenheid

(B=.165, CI -.165, .716, p=.002). Mantelzorgers van patiënten van wie het lichamelijk functioneren hoger was, rapporteerden een hogere seksuele tevredenheid (B=.110, CI .001, .013, p=.032).

*Effectiviteit van twee dyadische psycho-educatieve interventies voor gevorderde kanker (**Hoofdstuk VI**)*

431 dyades werden geïncludeerd voor de DIAdIC studie. De dyades werden gerandomiseerd naar de iFOCUS interventie (n=148), FOCUS+ interventie (n=140) of de controlegroep (n=143).

Uitkomsten patiënten

Emotioneel functioneren vertoonde geen significant verschil tussen de iFOCUS interventiegroep en controlegroep op 12 weken (T1) (voor baseline gecorrigeerd gemiddeld verschil, -.27; 95% CI, -2.11 tot 1.57; P = .774). Er werd geen significant verschil waargenomen in de FOCUS+ interventiegroep vergeleken met de controlegroep op T1 (voor baseline gecorrigeerd gemiddeld verschil, .12; 95% CI, -1.65 tot 1.89; P = .897). Niet-significante verschillen voor emotioneel functioneren voor beide interventiegroepen bleven bestaan op 24 weken (T2). We vonden geen significant verschil voor de tweede primaire uitkomst, zelfredzaamheid, tussen de iFOCUS interventiegroep en controlegroep op T1 (baseline-gecorrigeerd gemiddeld verschil, .49; 95% CI, -6.21 tot 7.19; P = .887). Er werd een statistisch significant verschil gevonden tussen de FOCUS+ interventiegroep en de controlegroep op T1 voor zelfredzaamheid (voor baseline gecorrigeerd gemiddeld verschil, 9.02; 95% CI, 2.45 tot 15.58; P = .007). Op T2 werden geen significante verschillen gevonden.

Uitkomsten voor mantelzorgers

Emotioneel functioneren verschilde niet significant tussen de iFOCUS interventiegroep en de controlegroep op T1 (voor baseline gecorrigeerd gemiddeld verschil, .30; 95% CI, -1.41 tot 2.00; P = .732). Er werd ook geen significant verschil gevonden tussen de FOCUS+ interventiegroep en de controlegroep op T1 (voor basislijn gecorrigeerd gemiddeld verschil, .17; 95% CI, 1.45 tot 1.79; P = .834). Niet-significante verschillen voor emotioneel functioneren bleven bestaan op T2. Voor self-efficacy vonden we geen significant verschil tussen de iFOCUS interventiegroep en de controlegroep op T1 (voor baseline gecorrigeerd gemiddeld verschil, 3.66; 95% CI, -3.36 tot 10.68; P = .306). Er werd ook geen significant verschil gevonden tussen de FOCUS+ interventiegroep en de controlegroep op T1 voor zelfredzaamheid (voor baseline gecorrigeerd gemiddeld verschil, 3.88; 95% CI, -2.84 tot 10.61; P = .258). Op T2 werden geen significante verschillen gevonden.

Interpretatie en discussie van bevindingen

In dit proefschrift zijn inzichten verzameld over beschikbare ondersteuning voor en het welzijn van nabestaanden van patiënten met een ernstige ziekte, de ontwikkeling van de DIAdIC studie, seksuele tevredenheid bij patiënten met gevorderde kanker en hun mantelzorger en de effectiviteit van twee psycho-educatieve interventies.

Het taboe op seksualiteit in de oncologie

Een belangrijke bevinding in dit proefschrift is het taboe rondom seksualiteit onder mensen die te maken hebben met kanker. Op basis van de baseline bevraging van de DIAdIC studie leek bij het evalueren van seksuele tevredenheid het aanbieden van een 'liever niet antwoorden' optie te dienen als ontsnappingsroute voor respondenten, een route waar veel patiënten voor kozen, wat de gevoeligheid benadrukt die geassocieerd wordt met het onderwerp seksuele tevredenheid. Ondanks de gevoeligheid van het onderwerp, zijn er veel onderzoeken die aantonen dat seksualiteit een belangrijk onderdeel is van de kwaliteit van leven en welzijn. Het introduceren van een 'liever niet antwoorden' optie voor de vraag over seksuele tevredenheid kan echter onbedoeld een signaal zijn van onze eigen gevoeligheid als onderzoekers ten opzichte van het onderwerp seksualiteit en kan dus onbedoeld hebben bijgedragen aan het in stand houden van het taboe rondom seksualiteit in deze populatie. Uit onderzoek blijkt ook dat professionele zorgverleners in de gezondheidszorg zich terughoudend voelen wanneer ze seksualiteit met patiënten bespreken. De onderzoekers die betrokken waren bij de DIAdIC-studie hadden regelmatig interacties met de verpleegkundigen die de FOCUS+-interventie uitvoerden, wat dit probleem verder bevestigt. Er lijkt dus ruimte te zijn voor verbetering in het opleiden van professionele zorgverleners in oncologische settings over het onderwerp seksualiteit.

Effectiviteit van iFOCUS en FOCUS+ in de DIAdIC studie

De DIAdIC trial toonde een significante verbetering in zelfredzaamheid bij patiënten in de FOCUS+ interventiegroep na 12 weken (T1) in vergelijking met de controlegroep. Deze verbetering hield niet aan na 24 weken (T2) en werd niet gevonden bij mantelzorgers. In alle andere vergelijkingen werden geen significante verbeteringen waargenomen. Het is verrassend dat we geen effect vonden van de interventies op de primaire uitkomsten voor de mantelzorger, ondanks dat het een dyadische interventie was. Het is echter mogelijk dat mantelzorgers toch baat hebben gehad bij de interventies, zij het indirect. De toegenomen zelfredzaamheid bij patiënten kan leiden tot andere verbeterde gezondheidsuitkomsten, wat weer kan resulteren in minder belasting of stress bij de mantelzorger. Dus indirect kunnen de mantelzorgers nog steeds baat hebben gehad bij de FOCUS+ interventie, maar dit indirecte effect kan meer tijd nodig hebben om zichtbaar te worden. Toekomstig onderzoek zal secundaire uitkomsten onderzoeken, zoals copingmechanismen, dyadische steun en kwaliteit van leven, en mogelijk significante effecten aantonen voor mantelzorgers.

Aangezien de DIAdIC-studie midden in de COVID-19 pandemie werd uitgevoerd, kan een herhaling van de DIAdIC-studie zonder de context van een wereldwijde pandemie mogelijk andere resultaten opleveren.

Terwijl Northouse vond dat de web-gebaseerde versie van het FOCUS-programma leidde tot verbeteringen in verschillende uitkomsten in een haalbaarheidstudie, zorgde de webgebaseerde iFOCUS-interventie van de DIAdIC-studie niet voor statistisch significante verbeteringen op de primaire uitkomsten. Hoewel uit de literatuur blijkt dat webgebaseerde interventies vaak goed worden ontvangen, sluit het bieden van ondersteuning of zorg in online vorm niet altijd aan bij de behoeften of voorkeuren van ieder individu. Vanwege de wisselende ervaringen en persoonlijke voorkeuren van patiënten en mantelzorgers kunnen de onderzoeksresultaten mogelijks niet consistent genoeg zijn geweest om significante verbeteringen van het iFOCUS programma in de DIAdIC trial te weerspiegelen.

De beperkte effectiviteit van de FOCUS+ interventie geeft aanleiding tot kritische reflectie over de implementatie. Ondanks het aantonen van een positieve impact op de zelfredzaamheid van patiënten op de korte termijn, roept de beperkte effectiviteit op andere gebieden en de beperkte duurzaamheid van het effect vragen op implementatie mogelijkheden. Het implementeren van een interventie die slechts op één aspect en voor een beperkte tijd verbeteringen liet zien, rechtvaardigt mogelijk niet de middelen en inspanningen die nodig zijn voor de implementatie. In plaats daarvan kan verder onderzoek en verfijning van de FOCUS+ interventie gerechtvaardigd zijn om de effectiviteit ervan te verbeteren voor een breder scala aan uitkomsten en om ervoor te zorgen dat de voordelen voor zowel patiënten als mantelzorgers blijven bestaan.

Samenwerking als belangrijke bijdrage aan welbevinden na verlies bij mantelzorgers

In dit proefschrift vonden we dat de evaluatie door mantelzorgers van de samenwerking met professionele zorgverleners in de laatste drie maanden vóór de rouw geassocieerd was met emotioneel welbevinden na het overlijden. Zowel eerder onderzoek als onze studie geven aan dat de ondersteuning die vóór de rouwperiode wordt geboden impact heeft op de fase na het overlijden voor mantelzorgers. In de praktijk worden samenwerkingsverbanden aan het einde van het leven echter niet consequent uitgevoerd. Hieronder worden aanbevelingen beschreven over hoe de samenwerking tussen zorgverleners en mantelzorgers kan worden verbeterd.

Aanbevelingen

Er kunnen verschillende aanbevelingen worden geformuleerd voor betere ondersteuning en welzijn voor patiënten en mantelzorgers op drie gebieden, namelijk praktijk, beleid en toekomstig onderzoek.

Aanbevelingen voor onderzoek

- Onderzoek de resultaten van de DIAdIC trial
    - Verder zetten van de trial totdat we de beoogde steekproefgrootte hebben bereikt
    - Kijken naar een hogere dosering van FOCUS+
    - Onderzoek de werkingsmechanismen van de oorspronkelijke FOCUS-interventie
    - De ervaringen van de deelnemers onderzoeken door middel van kwalitatief onderzoek
    - Secundaire uitkomsten onderzoeken
    - Onderzoeken van de impact van de iFOCUS en FOCUS+ interventies buiten de oncologiepopulatie
    - Subgroepanalyses uitvoeren

- Het concept en de impact van samenwerking tussen zorgverleners en mantelzorgers onderzoeken
    - Onderzoeken wat een 'goede samenwerking' is tussen mantelzorgers en professionele zorgverleners aan het einde van het leven
    - De perspectieven van professionele zorgverleners en patiënten betrekken
    - De wijze en intensiteit van samenwerking onderzoeken, afhankelijk van de fase van de ziekte
    - Onderscheid maken tussen patiënten met verschillende chronische ziekten
    - Longitudinale studies uitvoeren die de associatie tussen samenwerking en emotioneel welzijn op lange termijn onderzoeken

Aanbevelingen voor beleid

- Bevorder samenwerking en dyadische zorg aan het einde van het leven
- Bevorder en bied toegang tot en vroegtijdige integratie van palliatieve zorg

Aanbevelingen voor de praktijk

- Werk samen met mantelzorgers, betrek hen bij de zorg voor ernstige ziekten en geef hen meer inspraak
- Screen en benader seksuele gezondheid in de oncologische populatie
- Integreer de principes uit de FOCUS interventies in de gezondheidszorg

Curriculum vitae and list of publications of Orphé Matthys

Curriculum vitae

Orphé Matthys, born January 27, 1992 (Eeklo, Belgium), obtained her Master's degree in Clinical Psychology with honours in 2015 from Ghent University and obtained an additional Master's degree in Marketing Management from Vlerick Business School Ghent in 2016. After graduating, Orphé worked at Intuo, a talent management software company as a customer marketeer. Next, she worked as a communication manager at New Balls Please, an event agency. In January 2019, she joined the End-of-Life Care Research Group of Ghent University and Vrije Universiteit Brussel (VUB) as a doctoral researcher.

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“Effect of two dyadic psychoeducational interventions for advanced cancer: the DIAdIC randomized controlled trial”, Oncopoint Symposium, Ghent, 29 April 2024.

“Is Pre-bereavement Collaboration between Family Caregivers and Healthcare Professionals Associated with Post-bereavement Emotional Wellbeing? A Population-based Survey”, World Congress of the European Association for Palliative Care, Rotterdam, 15 June 2023.

“Good collaboration with professionals as predictor for emotional wellbeing of bereaved family carers”, International Conference on Communication in Healthcare, Glasgow, 8 September 2022.

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Appendix