

eHealth support for people with serious illness and their family caregivers

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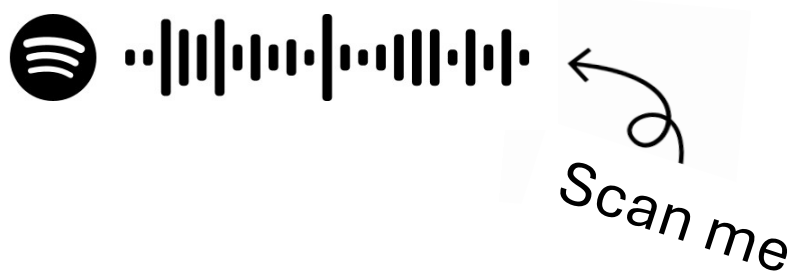
Als het leven een heelal is zijn jullie de sterren en ik heb een rijkge vulde sterrenhemel. Ik maak mijn afwezigheid van de voorbije maanden nog goed!

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(Vincent tegen Ruben, 2019 voor het begin van het doctoraat)

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(Ruben tegen Vincent, 2019 voor het begin van het doctoraat)



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Vandaar **ga naar Spotify, klik op zoeken en klik dan op het camera icoontje rechts bovenaan.** Door dit te scannen kom je dan (normaal) op een liedje uit.

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List of chapters

Chapters 1-7 in parts two, three and four of this dissertation are based on the following publications.

Chapter 1:

Van Goethem V, Dierickx S, Deliens L, De Vleminck A, Lapeire L, Cohen J. *Size and characteristics of family caregiving for people with serious illness: A population-based survey*. Palliative and Supportive Care. 2022;21(4):634-643. doi:10.1017/S1478951522001079 [2022 Web of Science impact factor: 2,2; journal ranking Q2; ranking n° 45/117 in Health policy & Services]

Chapter 2:

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Chapter 3:

Matthys, O., De Vleminck, A., Dierickx, S., Deliens, L., **Van Goethem, V.**, Lapeire, L., ... & 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, 1-18. [2021 Web of Science impact factor: 2,113; journal ranking Q2; ranking n° 37/88 in Health policy & Services]

Chapter 4:

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Chapter 5:

Matthys, O., Turola, E., Dierickx, S., Dombrecht, L., **Van Goethem, V.**, Deliens, L., ... & Cohen, J., (2024) *Impact of nurse-led and web-based psychoeducation for advanced cancer patients and their caregivers on emotional function and self-efficacy: the DIAdIC randomized controlled trial* [Submitted]

Chapter 6:

De Vleminck, A. & **Van Goethem, V.**, Dierickx, S., Matthys, O., Beernaert, K.,... & Cohen, J., (2024) *Developing and implementing a nurse-delivered and a web-based dyadic psychoeducational program for people with advanced cancer and their family caregivers: sharing experiences from a three-arm international randomized controlled trial (DIAdIC)*. [Submitted]

Chapter 7:

Van Goethem, V., Dierickx, S., Matthys, O., Beernaert, K., Guerin, S., Deliens, L., ... & Cohen, J., *Implementation of dyadic psychoeducational support programs at home for people with advanced cancer and their family caregivers: Stakeholder perspectives on barriers, facilitators, risks and opportunities*. [Submitted]

List of abbreviations

eHealth	Electronic health
DIAdIC	Dyadic psychoeducational Intervention for people with advanced cancer and their informal caregivers
FOCUS	Family involvement, outlook, coping, uncertainty reduction, symptom management
RCT	Randomized controlled trial
DC	Dyadic coping
CM	Congruence model
RFM	Relationship-focused model
CCM	Communal coping model
STM	Systemic-transaction model
RCCM	Relation-cultural coping model
DCCM	Development-contextual coping model
WHO	World health organization
SCC	Social cultural changes survey
PCA	Principal component analysis
ANOVA	Analysis of variance
CEO	Chief executive officer
IT	Information technology
ICT	Information communication technology
DAG	Directed acyclic graphs
EF	Emotional functioning
EORTC	European organization for research and treatment of cancer
ITT	intention-to-treat
PP	Per-protocol
FCS	Fully conditional specification
CAPI	Computer assisted personal interviewing
MRC	Medical research council
NPT	Normalization Process Theory

SPIRIT	Standard Protocol Items Recommendations for Interventional Trials
GDPR	General Data Protection Regulation
ANCOVA	Analysis of covariance
FS	Fixed sequence
QoL	Quality of Life
CONSORT	Consolidated standards of reporting trials
RA	Research assistant
TIDieR	Template for intervention description and replication
PIPFLA	Participatory and iterative process framework for language adaptation
NATC	National adaptation and translation coordinator
PROMs	Patient Reported Outcome Measures
GP	General Practitioner

Key concepts within the dissertation

In order to fully understand the findings of this dissertation, several key concepts presented in the dissertation are defined and operationalised below.

Patients with advanced cancer

Patients with advanced cancer have been diagnosed with a progressive form of cancer that is locally recurrent or metastatic and is unlikely to be cured or is incurable. These patients no longer receive curative treatment; instead, their treatment focuses on controlling symptoms, slowing disease progression and managing pain.

Family caregiver

Family caregivers are informal care providers such as relatives, partners, friends, or neighbours who provide a significant amount of support in a non-contractual relationship that develops naturally and does not have formally agreed working hours, breaks or holidays. In the DIAdIC trial, family caregivers who participate are identified as such by the patient with advanced cancer.

eHealth

Health services and information delivered or enhanced through the internet and related technologies.

The FOCUS program

An American face-to-face psychoeducational support programme developed by Professor Northouse (early 2000s) that has been shown to improve the quality of life and well-being of people with cancer and their carers. FOCUS is an acronym that stands for: Family Involvement (F), Outlook (O), Coping (C), Uncertainty Reduction (U) and Symptom Management (S).

DIAdIC:

An international multicentre trial to develop and evaluate two dyadic psychoeducational programmes: The face-to-face FOCUS+ programme and the eHealth iFOCUS programme. Both programmes are based on Professor Northouse's FOCUS programme. Most of the results of the eHealth (iFOCUS) programme discussed in this dissertation are derived from the DIAdIC study.

Self-efficacy (primary outcome): Refers to one's ability to manage the symptoms, side effects, and challenges associated with cancer and its treatments. Self-efficacy is a construct known for

having a positive influence on other outcomes¹. The selection of this primary endpoints is based on available evidence and aligns with the goals of the DIAdIC interventions, which aim to offer support in the five FOCUS domains outlined above.

Emotional functioning (primary outcome): The ability to recognize, understand, manage and adequately express emotions in various situations. The selection of the primary endpoints is based on available evidence and aligns with the goals of the DIAdIC interventions, which aim to offer support in the five FOCUS domains outlined above.

Dissertation outline

This PhD dissertation will start with a general introduction. After the introduction the background provides an overview of essential concepts for understanding the context of the dissertation. The background begins by examining the impact of advanced cancer on patients and family caregivers. Next the interdependent relationship between patients and family caregivers is explored, emphasizing reciprocal challenges and resilience within patient-family caregiver dyads. Key models of dyadic coping strategies are discussed, underscoring their role in managing illness-related stressors and fostering mutual support. Following, the concept of palliative care is elaborated, highlighting its importance in care and support for patients with advanced cancer and their family caregivers. The background section also addresses eHealth interventions as a promising way to provide psychoeducational support. Following the eHealth section, I also describe how promising interventions were identified to serve as the foundation for the development of iFOCUS and the DIAdIC trial is introduced. The background chapter closes by identifying research gaps. After the background, the objectives and research questions of the dissertation follow. The methods section provides a brief description of the designs with their respective methods, used to address the research questions.

Part 2,3 and 4 of this dissertation draw upon articles that have been published, accepted, or submitted for publication. Each chapter is designed to be comprehensible on its own. Vincent Van Goethem, author of this dissertation was the first author of each chapter EXCEPT FOR chapter 3 (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), and chapter 5 (Impact of nurse-led and web-based psychoeducation for advanced cancer patients and their caregivers on emotional function and self-efficacy: the DIAdIC randomized controlled trial). These chapters were written by a colleague also working on the DIAdIC project (Orphé Matthys). Vincent Van Goethem, listed as the FIFTH AUTHOR on these two papers, was involved in the data collection of the trial and participated in the review process of these articles prior to its submission. These articles have been added to provide additional background information or to facilitate a discussion on the effectiveness of eHealth. Papers further exploring the effects of the eHealth iFOCUS program on secondary outcomes and identifying agents of change are forthcoming.

The scientific research presented in Chapter 3 and Chapter 5 is also included in the PhD dissertation of the first author, Orphé Matthys.

In part 2, **CHAPTER 1** I explore the size and characteristics of family caregivers for individuals with serious illnesses, comparing them with other family caregivers and non-family caregivers.

In part 3, **CHAPTER 2** describes the development of a self-management psychoeducational eHealth program to support and empower patients with advanced cancer and their family caregivers. **CHAPTER 3** delineates the protocol, describing how the iFOCUS program was part of the international DIAdIC trial.

In part 4, **CHAPTER 4** I describe the results of the DIAdIC trial. Specifically in this chapter I examine the impact of digital competence on participation and retention in trials with an eHealth component. In **CHAPTER 5** I describe effectiveness results from the iFOCUS program on the main trial outcomes; Self-efficacy and emotional functioning in patients and family caregivers with advanced cancer. **CHAPTER 6** delineates our experiences and a critical reflection on the development and implementation of two psychoeducational home-based programs (eHealth iFOCUS and face-to-face FOCUS+) as part of an international multicentre trial. I close this part with **CHAPTER 7** which assesses the barriers, facilitators, risks and opportunities in relation to the sustainability of psychoeducational home-based programs such as iFOCUS and FOCUS+.

In part 5, I provide a summary of the main findings from each study, methodological considerations, strengths and limitations, a discussion of findings in light of current challenges and the state of knowledge.

The dissertation concludes with recommendations for research, policy, and practice.

PART 1

GENERAL INTRODUCTION

1. INTRODUCTION

A significant portion of the adult population lives with a serious life-limiting illness. It affects around 90 million people in the United States, and around 14% of individuals aged 50 or older in England^{2,3}. As the population continues to age, these numbers are expected to increase^{2,4}. People with serious illness suffer from one or multiple conditions which significantly impact their life-expectancy, functioning and quality of life and put strain on family caregivers⁵. While a minority of patients with a serious illness prioritize extending their life, most patients with a serious illness and their family caregivers often have complex and diverse care needs which encompass functional, psychological, physical, practical, social and spiritual aspects, focused on improving quality of life, symptom control and education and empowerment^{6,7}.

Advanced cancer is considered a serious illness as the diagnosis, treatment and disease trajectory can have a profound impact on both the individual with cancer and their family caregivers^{8,9}. Both parties may experience high levels of distress and reduced quality of life (QoL), which is strongly interrelated due to co-suffering^{9,10}. However, patients with advanced cancer and their family caregivers not only experience distress and burden in common. It is also important to recognize the shared resilience and strength within the patient-family caregiver dyad (a two-person relationship), with patients and family caregivers being an important sources of care and support for each other¹¹. Psychoeducational dyadic eHealth programs could be a feasible way to provide additional support for patients and family caregivers who are coping with the impact of advanced cancer¹². Nevertheless, little to no research on this topic has been performed^{12,13}.

The primary objective of this dissertation is to describe the development and evaluation of a home-based psychoeducational eHealth program called iFOCUS for patient-caregiver dyads in an advanced cancer trajectory. iFOCUS was developed and evaluated during the DIAdIC trial, which involved six countries: Belgium, the Netherlands, Denmark, Italy, the United Kingdom, and Ireland. The development of iFOCUS was based on the face-to-face FOCUS+ program, which was also developed as part of the DIAdIC trial¹⁴. Both iFOCUS and FOCUS+ were based on the proven effective FOCUS program, developed by Northouse. FOCUS is an acronym and stands for Family involvement (F), Outlook (O), Coping effectiveness (C), Uncertainty reduction (U), and Symptom management (S)¹⁵. Given that factors such as delivery mode and cultural fit can significantly impact program effectiveness, a thorough adaptation process was essential for developing the eHealth iFOCUS program^{16,17}. This adaptation involved modifying the original

FOCUS program and FOCUS+ to better suit a European context and accommodate the eHealth format. The FOCUS, (and by extension) FOCUS+ and iFOCUS programs are all founded upon the Transactional Model of Stress and Coping by Lazarus and Folkman¹⁸ and adopt a salutogenic approach, prioritizing the promotion of health and well-being over the mere treatment of illness. Furthermore, the Scrum method was used during development of iFOCUS¹⁹, which facilitated iterative and flexible development cycles.

In addition to the primary objective, three sub-aims were identified: (1) to describe the numbers, characteristics and experiences of family caregivers of people with serious illness, (2) to describe the development of a psychoeducational eHealth program (iFOCUS) to support patients with advanced cancer and their family caregivers and its implementation in an international randomized controlled trial (RCT), and (3) to describe the results of the DIAdIC trial, focusing on trial recruitment and retention, effectiveness of iFOCUS and FOCUS+ on primary outcomes (self-efficacy and emotional functioning), our experiences with the implementation of these programs within the trial, and the feasibility of sustainable implementation of iFOCUS and FOCUS+ beyond the trial setting.

2. BACKGROUND

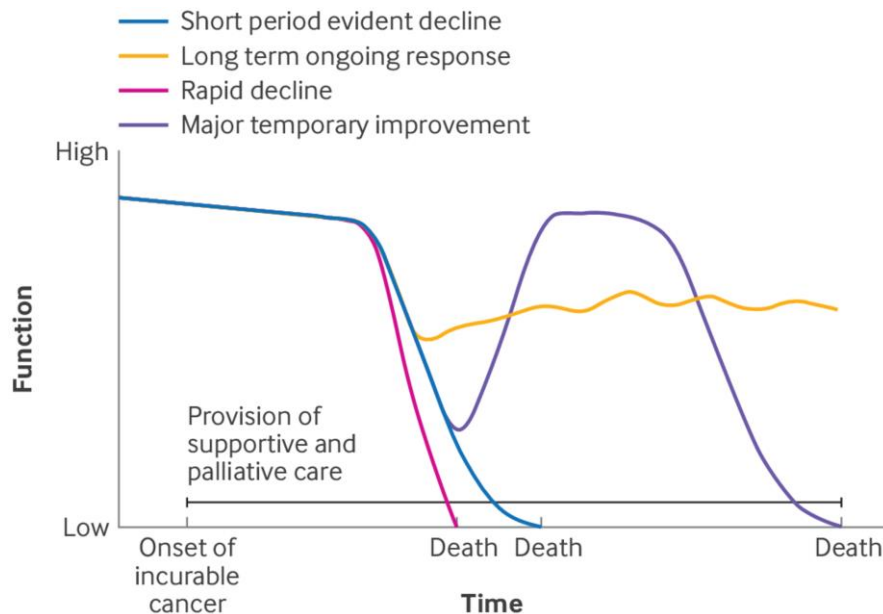
2.1. The impact of advanced cancer on patients and family caregivers

Incidence and mortality rates

Cancer is the second leading cause of death globally and has a significant impact on the QoL of both people with cancer and their family caregivers^{8,20}. Cancer is a general term for a heterogeneous group of diseases that can originate in any part of the body and in any kind of cell type. Cancer is characterized by the abnormal and uncontrolled proliferation of cells, which may exceed their typical boundaries and/or invade adjoining parts of the body or spreading to other organs²¹. Advanced cancer can be defined as a progressive, locally recurrent or metastatic type of cancer that is unlikely to be cured or is incurable^{22,23}. In 2022, over 2.7 million individuals in Europe were diagnosed with cancer, and nearly 1.3 million individuals died from cancer. These numbers are projected to continue to increase, with an estimated 3.2 million new cancer diagnoses and over 1.6 million cancer-related deaths by 2040^{24,25}. The majority (90%) of all new cases of cancer are solid cancer types, including breast, lung, colorectal and prostate cancers²⁶.

Traditionally, the disease trajectory of individuals with advanced cancer has been typified by a prolonged period of relative comfort and maintained functioning, followed by a rapid decline. However, the disease trajectory can vary significantly depending on the type of cancer and the response to the treatments (Figure 1)^{27,28}. Furthermore, the early diagnosis of cancer due to the implementation of comprehensive primary and secondary prevention measures and the development of more efficient screening technologies, coupled with advancements in treatments such as systemic anti-cancer therapies, has led to an increase in the number of individuals surviving for extended periods of time^{28,29}. Consequently, advanced cancer is increasingly being classified as a chronic rather than an acute disease^{28,29}.

Figure 1: Disease trajectories of advanced cancer and the provision of supportive and palliative care by Geijteman et al., (2024)



The impact of advanced cancer on patients

Research indicates that the experiences of patients with advanced cancer differ greatly from those of patients in a non-advanced condition and from patients with other chronic disease^{30,31}. A substantial body of evidence indicates that individuals with advanced cancer may experience considerable distress across multiple domains, including physical (fatigue, pain, dyspnea, appetite loss, constipation, diarrhea, insomnia...), psychological (depression, anxiety, fear, anger...), social (loneliness, isolation...), and existential or spiritual (hopelessness, helplessness, demoralization...) domains. These experiences have been shown to significantly impact functioning, increase distress, and reduce QoL³²⁻³⁵. This distress can already manifest at the initial diagnosis but typically intensifies as the disease progresses, increasing the burden and reducing the patient's QoL exponentially^{9,32,36}.

Impact of advanced cancer on family caregivers

The impact of advanced cancer extends beyond the individual diagnosed with the disease and also adversely affects family caregivers³⁷. Family caregivers are informal care providers who provide a significant level of support to the individual with the diagnosis, albeit physically, socially, emotionally, or practically. This care is provided in a non-contractual relationship that

develops naturally and does not have formally agreed work hours, breaks, or holidays^{38,39}. The importance of family caregiving as a cornerstone for long-term care is evident when considering that in 2016, it was estimated that family caregivers across Europe collectively spent a total of 72,301.5 million hours providing care, which is estimated to have an economic value of €576,000 million or 3.63% of Europe's gross domestic product⁴⁰. Moreover, the importance of family caregiving is likely to increase further due to the mounting pressure on formal healthcare which is attributable to factors such as the rising prevalence of cancer, the aging population, constrained healthcare expenditures, and a shortage of professional care providers^{41,42}. While family caregivers are most commonly recognized for their role as care providers, they also need to be acknowledged for their role as facilitators of care and experts on the patient's condition, daily functioning, wishes and needs^{43,44}. Additionally, family caregivers can also experience physical, psychological, social distress, existential or spiritual distress and other types of distress which potentially gives them the role of potential care recipient^{8,39}. Research indicates that family caregivers exhibit comparable levels of adjustment difficulties and emotional distress to patients, with anxiety and depression occurring in up to 40% of cases⁴⁵.

The interrelatedness of burden...and resilience in dyads

Based on the aforementioned we can state that both patients with advanced cancer and their family caregivers can experience serious distress^{32,45}. Initially, stress and burden were perceived as individual experiences, overlooking the interconnected dynamics within their social context¹¹. However, over the last two decades a more systemic perspective has emerged, acknowledging that both the patient and their family caregiver can encounter stressors that affect one partner and spill over into the relationship, and/or stressors which affect both^{11,46}. Consequently, research indicates a positive correlation between the distress of the patient with cancer and their family caregivers, identifying a level of co-suffering^{10,13,47}. Therefore it is likely that due to co-suffering, the distress in the family caregiver increases as the disease of the patient progresses. Population-based data that delineates the characteristics and burden of family caregivers for people with serious, life-limiting illness, such as advanced cancer, is crucial for quantifying the extent of their experienced health challenges and for developing appropriate responses⁴⁸. However population-based studies that describe the characteristics and burden of family caregivers are scarce^{48,49}.

Nevertheless, not only the distress, but also the strength and resilience of patients with cancer and their family caregivers is interconnected, as patient-family caregiver dyads can provide

mutual support to each other which positively impacts the relationship, the wellbeing of both and has been shown to mitigate depressive symptoms^{11,50,51}. Coping with the disease as a dyad creates a sense of interdependence allowing concerns and challenges to be shared and resolved jointly⁵². A number of different forms of positive dyadic coping have been identified, including *supportive dyadic coping* (providing empathetic understanding), *delegate dyadic coping* (sharing responsibilities), and *common dyadic coping* (taking action together)¹¹. While some studies have indicated that positive dyadic coping may result in exhaustion, the majority of research has demonstrated its beneficial impact on various aspects of the relationship, emotional well-being, couple cohesion, stress reduction, improved communication, and overall QoL^{11,51,53,54}.

2.2. A dyadic way of coping with the disease

To gain insights into the interrelationship between stress and coping in patient-family caregivers, dyadic coping (DC) models are explored. As described in the introduction, the eHealth program discussed in this dissertation (iFOCUS), along with the programs it is based on (FOCUS and FOCUS+), are all founded on the Transactional Model of Stress and Coping by Lazarus and Folkman¹⁸. While the Transactional Model of Stress and Coping by Lazarus and Folkman is not inherently a dyadic model, it is an important theoretical framework in psychological research and the basis for many DC models. Within the Transactional Model of Stress and Coping, stressors lead to two distinct appraisals: primary (identification of threat) and secondary (identification of coping resources). These appraisals subsequently inform the selection of problem focused or emotion-focused coping strategies. Based on the effectiveness of these coping efforts, the situation or the individual's perception of stress is reappraised, and the outcomes become apparent¹⁸.

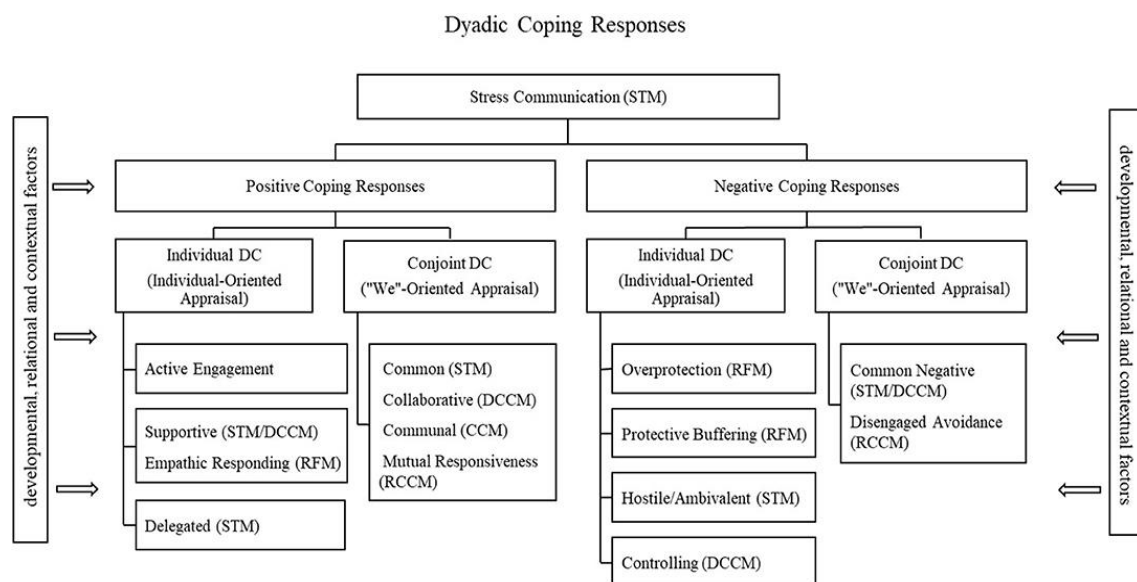
As awareness grew that cancer affects not only the individual but also their family caregivers, several DC models emerged in the 1990s¹¹, and DC research has often been guided by these models⁵⁵. Below, we provide a brief overview of the most prominent models and their contributions to DC research.

- The Congruence Model (CM) is one of the earliest DC models. This model examines the interaction of partners' individual coping styles, recognizing the interpersonal context of stress and coping in couples⁵⁶. Primarily applied in studies of couples coping with stress, the CM uniquely emphasizes the interaction of individual partners' coping strategies, and explores how individual coping influences couple functioning¹¹.

- The Relationship-Focused Model (RFM) shifts the focus from individual coping to relationship-centered strategies for managing stress⁵⁷. Primarily used in studies of couples coping with illness, the RFM emphasizes partners' support for each other's coping efforts^{11,58}. In addition the RFM introduces active engagement in helping partners express their thoughts and feelings about illness as a coping strategy, but does not describe how partners cope conjointly or the influence of contextual factors, such as cultural differences¹¹.
- The Communal Coping Model (CCM) introduced the notion of communal coping, emphasizing shared collaborative coping where challenges are managed collectively across individual boundaries⁵⁹. Initially studied in couples coping with a partner's illness, CCM emphasizes the importance of perceiving, communicating, and addressing medical issues within the relationship⁶⁰. However, this model primarily focuses on medical or individual stressors rather than addressing common or dyadic stressors^{11,60}.
- The Systemic-Transaction Model (STM) focuses on couples navigating daily challenges or minor chronic stressors, rather than focusing on couples coping with serious illness⁴⁶. Within this framework, couples use both individual and DC strategies and may seek support from external sources⁴⁶. Originally developed for general stress coping in couples, the STM has been used extensively in research on couples facing illness, particularly cancer because of its comprehensive understanding of coping^{61,62}. However, this model relies heavily on the Dyadic Coping Inventory (DCI), which only assesses coping strategies and does not consider appraisal of stress or concepts such as overprotection, protective buffering, or active engagement¹¹.
- The Relation-Cultural Coping Model (RCCM) builds further on the STM by adding relational and cultural components to their model, which they argue are factors that shape behaviour⁶³. Unique to this model is that couples are placed on a continuum of four cultural dimensions that may influence coping: family boundaries, gender roles, personal control and independence^{11,64}.
- The Development-Contextual Coping Model (DCCM) was developed specifically to understand the process of stress and coping in couples with chronic illness⁶⁵. Within the DCCM, particular emphasis is placed on partner responses, which are categorized along a continuum ranging from underinvolvement to overinvolvement⁶⁵. Moreover, the model recognizes that couples' coping strategies may fluctuate depending on the stage of the illness, or they may cope differently even when faced with the same stressor^{11,65}.

As previously stated, these models do not contradict one another and, in fact demonstrate significant overlap. Each model builds upon the theoretical framework established by Lazarus and Folkman, yet each also highlights certain aspects, therefore providing a partial view of the DC process^{11,66}. Consequently Falconier and Kuhn suggest integrating the aforementioned models to gain a more in-depth understanding of DC and to create comprehensive oversight of dyadic stress appraisal and coping (Figure 2)⁶⁶. This model acknowledges the impact of both positive and negative DC, as well as the influence of individual, dyadic, and contextual factors⁶⁶. However, further research is needed to gain a deeper understanding of DC in other types of dyads (e.g., same-sex couples) or with different cultural backgrounds⁶⁶.

Figure 2: Integration model chart by Falconier and Kuhn (2021)



In developing and implementing the eHealth program examined in this dissertation, we drew from the theoretical framework of Lazarus and Folkman, while not strictly adhering to any specific model or framework. This approach aligns with prior research, serving as the foundation for the trial outlined in this dissertation.

2.3. Palliative care for patients with advanced cancer and their family caregivers and the role of psychoeducation

The definition of palliative care

Rather than curing cancer, oncological treatments in advanced cancer mainly focuses on therapies to reduce symptom burden and medical complications while prolonging the life of

patients and oncologists were traditionally responsible for guiding patients in their treatment decisions^{67,68}. Non-curative aspects of care, pertaining to physical, psychological, existential, social, and practical needs in relation to living and coping with the impact of the disease were less frequently addressed in oncological care^{8,69}. To address these needs in patients with advanced cancer and their family caregivers, early and systematic integration of palliative care in oncology is recommended⁷⁰. The World Health Organization (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. It prevents and relieves suffering through the early identification, correct assessment and treatment of pain and other problems, whether physical, psychosocial or spiritual’*⁷¹. More specifically, palliative care:

- *provides relief from pain and other distressing symptoms;*
- *affirms life and regards dying as a normal process;*
- *intends neither to hasten nor postpone death;*
- *integrates the psychological and spiritual aspects of patient care;*
- *offers a support system to help patients live as actively as possible until death;*
- *offers a support system to help the family cope during a patient’s illness and their own bereavement;*
- *uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated;*
- *will enhance quality of life, and may also positively influence the course of illness; and*
- *is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications*⁷¹.

Models of palliative care

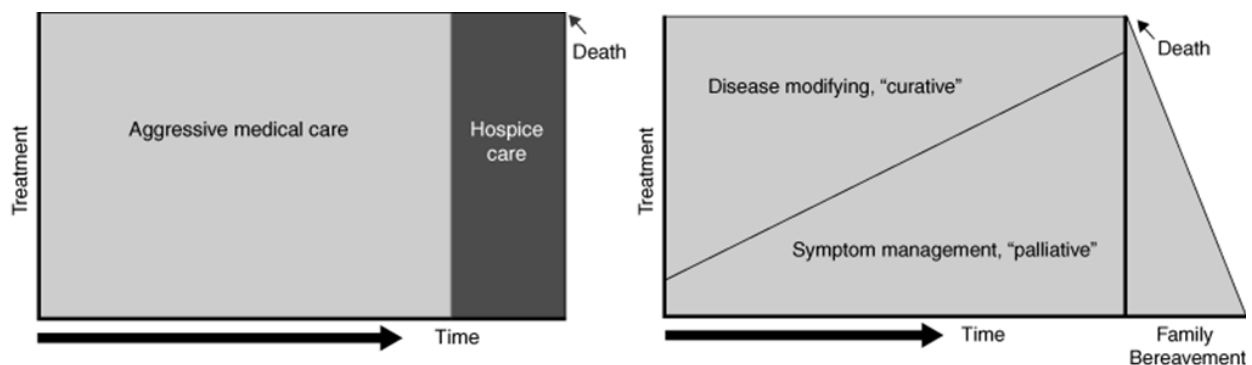
There are many different palliative care models internationally, each influenced by cultural, religious, legal and institutional differences^{72,73}. As they are pertinent to the dissertation topic we will briefly discuss the level of palliative care (generalist or specialist) and the timing of palliative care (early integrated palliative care or late palliative care).

Specialist or specialized palliative care encompasses care provided by a multidisciplinary team with specialized training in palliative care provision⁷⁴. General palliative care encompasses symptom management, psychosocial support, goal setting, and care discussions, typically

provided by people who are not exclusively specialized in palliative care⁷⁵. While both types of care are important, each having their specific strengths and challenges, they are inherently complementary⁷⁵⁻⁷⁷. Therefore a coordinated model integrating generalist and specialist care is recommended to effectively address various palliative care needs, enhance care accessibility, and manage care costs⁷⁵⁻⁷⁷. The eHealth program discussed in this dissertation employs an approach that is both specialized and generalist.

With regard to the timing of palliative care figure 3 illustrates the transition from the Transition Model of Palliative Care (an older model dating back to the 1960s) to the Trajectory Model of Palliative Care as proposed by Lynn & Adamson (2003). The Transition Model depicts a clear-cut phase of biomedical 'cure' followed by a phase of 'care', the trajectory model illustrates the early integration of palliative care in care³⁰. Within the model of Lynn and Adamson palliative care can start as early as at the diagnose and becomes increasingly important as the disease progresses. The model considers the complementary nature of palliative and curative care are complementary in responding to the needs of patients and family caregivers³⁰. In practice, both models are still applied in the context of the healthcare system.

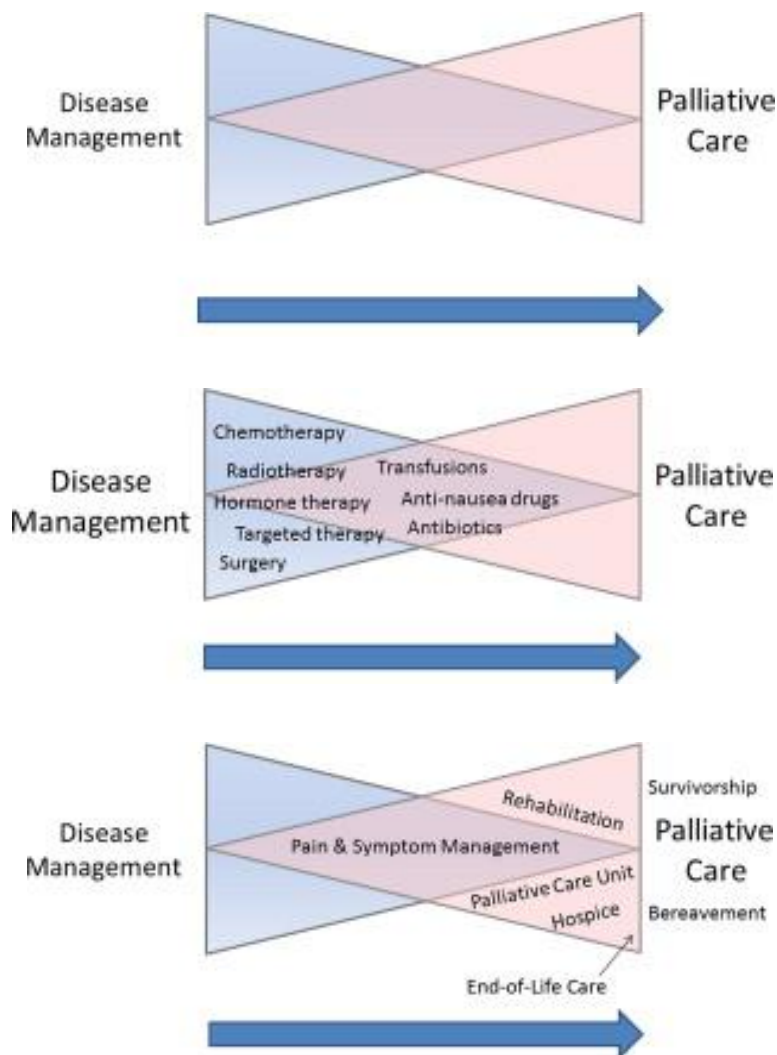
Figure 3: The 'Transition Model' (left) vs. the 'Trajectory Model' of palliative care (right), from Lynn and Adamson (2003)



While the trajectory model serves its purpose in clarifying the need for early involvement of palliative care within the cancer trajectory it may unintentionally have a fatalistic approach. This is because it places a strong emphasis on patient death as an endpoint, which may deter patients, family caregivers, and healthcare providers from adopting palliative care early in the trajectory⁷⁸. The "Bow Tie" Model of the 21st century palliative care by Hawley (2013) as shown in figure 4, while sharing similarities with the approach to early integrated palliative care, diverges from the explicit focus on death as an endpoint. Instead, it emphasizes the description of an early and integrated palliative care process. The arrow at the bottom indicates a dynamic process that

facilitates a shift in focus between disease management and palliative care. Furthermore, the Bow Tie model furthermore incorporates aftercare or support for bereaved family caregivers. In operationalizing survivorship, the model defines it as “a person who survives, especially a person remaining alive after an event in which others have died”^{78,79}.

Figure 4: The ‘Bow tie’ Model from Hawley (2013)



Palliative care for patients with advanced cancer and their family caregivers

The accumulation of evidence indicates that early dyadic palliative care for patients with advanced cancer and their family caregivers could result in positive outcomes for both patients and family caregivers. These outcomes may include greater emotional engagement between the patient and the family caregiver, reduced distress, improved QoL, enhanced dyadic communication and potentially greater cost-effectiveness compared to single-target

interventions⁸⁰⁻⁸⁴. Therefore, it can be assumed that early palliative care aimed at both patients and family caregivers is fully integrated in regular care. It is surprising to note that there are few rigorously developed intervention programs that provide early integrated palliative care to patients and family caregivers as one unit of care, also called dyads⁸¹.

Home-based palliative care

The eHealth program developed and evaluated in this dissertation will be accessible by patients and family caregivers at home. Therefore we briefly explore the concepts of home-based palliative care. There is substantial evidence that palliative care provided at home may have many benefits, including reduced healthcare expenditures⁸⁵ and higher quality of care^{86,87}. Furthermore, home-based palliative care is likely to enhance the patient and the family caregiver involvement, engagement, and governance in the treatment trajectory⁸⁸. This results in improved symptom burden, increased satisfaction with care, reduced burden and improved the QoL^{88,89}.

Psychoeducation as a part of palliative care

Psychoeducation, which can be defined as *“a brief process of therapy focused on the communication of varied aspects of disease- and/or treatment-related information”*⁹⁰ is a flexible approach to provide care and support⁹¹. Psychoeducational programs offer support and information related to managing or coping with a serious illness, helping patients and family caregivers adapt to the impact of the disease, enhancing communication and supporting informed decision-making⁹¹. Psychoeducational programs have been identified as a common and effective way to provide support to family caregivers, and patients with advanced cancer^{82,92}. These programs have shown to improve the emotional well-being, reduce depressive symptoms and stress and to stimulate an open communication in patients with cancer⁹³⁻⁹⁶. In family caregivers of patients with advanced cancer psychoeducational programs have been demonstrated to reduce depressive symptoms, improve emotional well-being, enhance communication, and foster relational intimacy^{97,98}. Furthermore dyadic psychoeducational interventions in patients with advanced cancer and their family caregivers have been shown to enhance self-efficacy, the dyadic communication, and the QoL while reducing emotional distress and negative appraisal of illness^{82,99-102}.

2.4. eHealth for patients with advanced cancer and their family caregivers

eHealth support to cope with pressure in healthcare

The majority of psychosocial care and psychoeducational interventions for patients with advanced cancer and their family caregivers are delivered in person¹⁰³. Face-to-face programs are typically more expensive due to the need to identify and remunerate facilitators who systematically provide this support¹⁰⁴. Due to high costs of these types of programs (to both the deliverer and the recipient), these types of programs are seldom sustainably implemented⁸⁰. In light of the challenges to formal healthcare due to the aging population and budgetary constraints, new formats of care and support that are accessible, affordable, scalable and sustainable are required^{41,42}. In light of the difficulties that formal healthcare systems face, eHealth has been proposed as a means of providing care in addition to existing care^{105,106}. While there is no consensus on a single definition of eHealth, it can be defined as *“health services and information delivered or enhanced through the Internet and related technologies”*¹⁰⁷.

One of the benefits of eHealth support at home is that it could reduce the pressure on professional caregivers and reduce the feeling of intrusiveness patients and family caregivers could experience linked to face-to-face home-based support^{88,108}. eHealth as a mode of delivery facilitates remote monitoring and follow-up, effectively reducing the travel time for professionals and potentially making psychoeducation available in remote or rural areas^{108,109}. While the development of eHealth programs may entail a significant initial cost, low ongoing program costs and reduced labor costs suggest that the long-term cost-effectiveness of digital interventions may be more favorable than that of face-to-face support^{12,110}. Furthermore, eHealth allows for a certain degree of flexibility for both the care provider and recipient. It also reduces the risk of infection due to the reduced exposure associated with face-to-face contact and could lower the threshold to accessing psychosocial care by eliminating the need for someone to visit the home^{108,111}. Research also indicates that at the level of patients and family caregivers, eHealth programs could improve information-sharing, support decision-making and communication within the dyad and towards healthcare providers^{109,112}. Furthermore, eHealth has demonstrated the potential to enhance self-efficacy, informed decision-making, and the reduction of burden and distress, thereby improving the overall QoL of patients^{102,113}.

Nevertheless, research also indicates potential drawbacks associated with the utilization of eHealth. The use of eHealth as a means of support may be more accessible to younger individuals who have more experience and interest in digital components, while excluding older populations^{114,115}. Additionally, individuals with lower income levels may encounter limited availability and access to the internet, thereby hindering their effective engagement with these programs¹¹⁶. Moreover, individuals with lower educational levels are less likely to access eHealth support and demonstrate lower adherence to eHealth programs¹¹⁷. While there is substantial evidence supporting the positive impact of eHealth support, it's crucial to recognize that there is also research suggesting little or no significant effect on psychological well-being, depression, anxiety, and decision-making¹⁰⁹. Moreover, the evidence regarding the physical and functional well-being of patients with cancer who used eHealth is either lacking or inconsistent^{118,119}. Systematic reviews analyzing the effect of eHealth support are also limited, indicating a lack of evidence for this population¹²⁰. Therefore, given its potential benefits for patients with advanced cancer and their family caregivers, and the incoherence or lack of evidence, further research is warranted¹²¹.

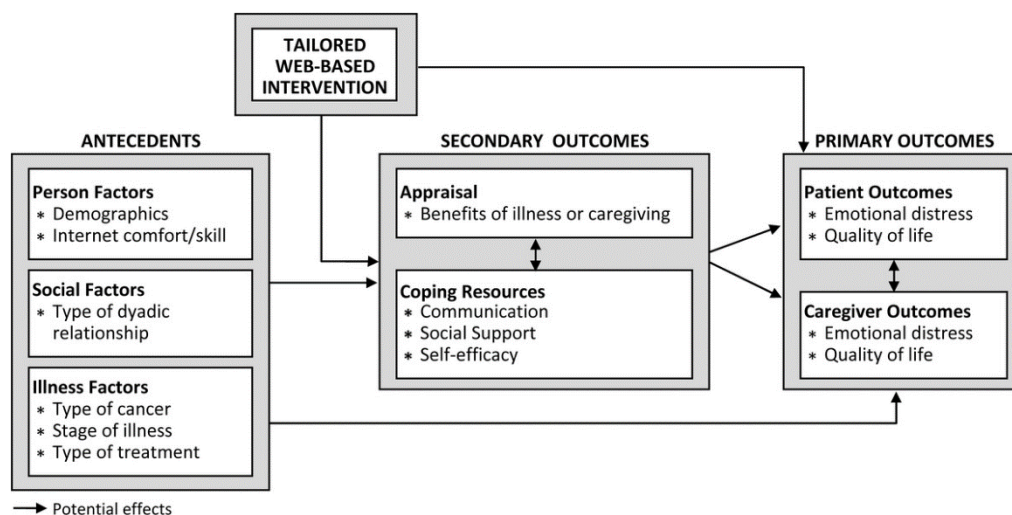
2.5. Identifying promising interventions for the development of a dyadic psychoeducational programs

For the H2020 DIAdIC (“Dyadic psychoeducational Interventions for people with Advanced cancer and their Informal Caregivers”) project, we developed the face-to-face FOCUS+ program and the web-based iFOCUS program. Both programs were evaluated as part of the DIAdIC trial, a large-scale international three-arm superiority trial which investigated the effectiveness, cost-effectiveness, and mechanisms of change of iFOCUS and FOCUS+¹⁴.

To increase the likelihood of program effectiveness, we sought to base the development of iFOCUS and FOCUS+ on existing, proven programs. In order to select the most promising and innovative early palliative care dyadic interventions for patients with advanced cancer and their family caregivers, the DIAdIC research consortium reviewed the available evidence about dyadic interventions, and evaluated the potential ‘fit’ and relevance of these interventions to a European context, based on the strategic health objectives outlined in the white paper “*Together for Health: A Strategic Approach for the EU 2008-2013*”¹²². Based on the review of the DIAdIC consortium, the FOCUS intervention developed by Northouse et al.⁸² in the early 2000s was identified as among the most effective and potentially relevant for the European context. The FOCUS

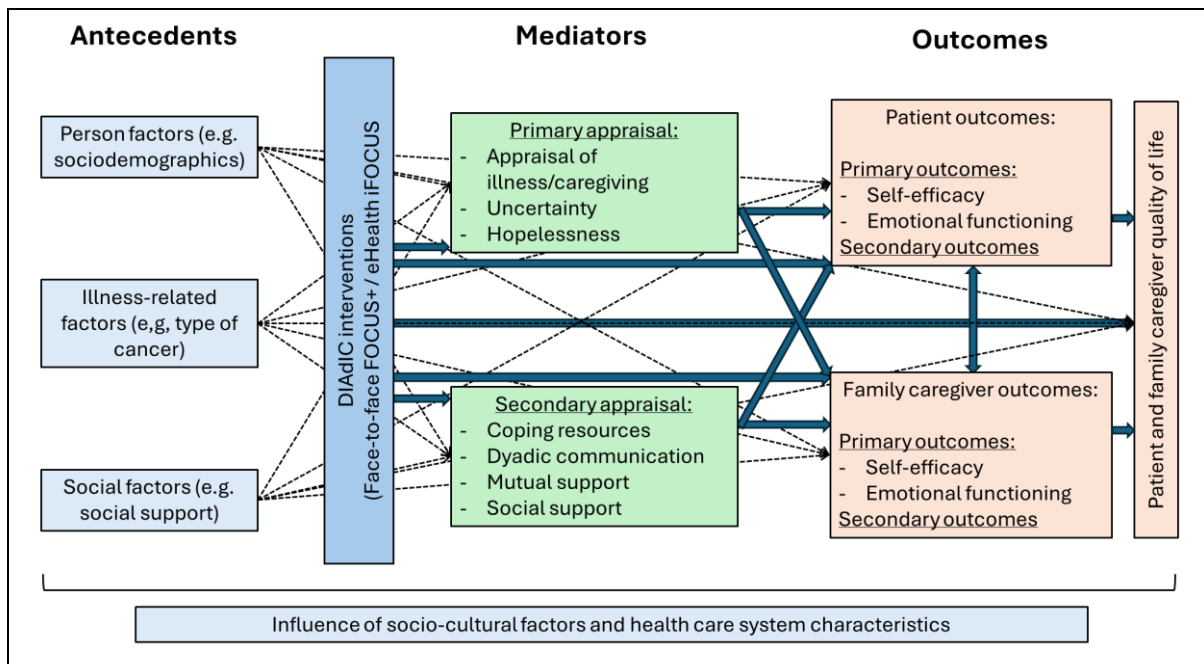
intervention is a nurse-led psychoeducational dyadic intervention for patient-caregiver dyads in a cancer trajectory consisting of five modules: Family involvement (F), Optimistic outlook (O), Coping effectiveness (C), Uncertainty reduction (U), and Symptom management (S).¹⁵ FOCUS is delivered simultaneously to patients and family caregivers by a nurse and has shown to improve the quality of life, self-efficacy and, dyadic communication whilst reducing emotional distress, negative appraisal of illness and caregiving, uncertainty, and hopelessness in dyads in a cancer trajectory.^{82,99,101,123} The F-component (family involvement) of the face-to-face program was translated into a tailored, web-based format and was associated with better patient and family caregiver quality of life, emotional distress, perceived benefits of illness/caregiving, and improved caregiver self-efficacy.¹⁰² Within her research Northouse indicates that personal, societal, and illness-related stressors (antecedents) influence the appraisal of the illness and coping resources of patients and family caregivers, which in turn affects emotional distress and quality of life. In this model, she adds a tailored web-based intervention to intersect on appraisal, coping resources and patient and family caregiver outcomes¹⁰². Additionally, the outcomes for patients and family caregivers significantly influence each other's outcomes (Figure 5).

Figure 5: Model of factors that predict patient and spouse adjustment by Northouse et al., (2014)



Based on the Transactional Model of Stress and Coping by Lazarus and Folkman and trials of Northouse, a conceptual model for iFOCUS and FOCUS+ was developed. (Figure 6). Based on the aforementioned evidence, self-efficacy and emotional functioning at T1 (further described in CHAPTER 3 – DIAdIC protocol) were selected as the primary outcomes.

Figure 6. Conceptual model of iFOCUS and FOCUS+ as part of the DIAdIC trial



2.6. Research gaps in relation to psychoeducational home-based eHealth support for people with advanced cancer and their family caregivers

Patients with advanced cancer and their family caregivers both experience significant distress as result a of the illness and its treatment, manifesting in high levels of physical, psychological, social, and existential challenges^{32,124,125}. While the number of patients with advanced cancer is clearly described, population-based research describing the size and characteristics of family caregivers for someone with a serious illness is lacking^{49,126}.

Research shows that the burden and resilience of patients with advanced cancer and their family caregivers are interconnected^{11,13,47,50}. Early integrated palliative care may be a suitable approach to provide care and support to both patients with advanced cancer and their family caregivers^{80,81}. While there are various models of palliative care, there is substantial evidence suggesting that a combination of specialist and generalist palliative care which is early integrated could contribute to the QoL of patients with advanced cancer and their family caregivers^{70,75,77}. In light of the mounting evidence suggesting the benefits of the aforementioned approaches, one

might assume that early integrated palliative care supporting dyads with advanced cancer is a common practice. However, this is not the case, and there are few rigorously developed early integrated palliative care dyadic interventions⁸¹.

The demand for formal healthcare is set to increase as a result of the rising prevalence of cancer, the aging population, constrained healthcare spending, and a shortage of qualified healthcare professionals^{41,42}. Home-based programs and psychoeducational programs have been proposed as cost-effective strategies for delivering sustainable and high-quality care for patients with advanced cancer and their family caregivers^{86,100}. One approach to providing this type of home-based psychoeducational support is through the use of eHealth. There is mounting evidence that eHealth support could improve the information-sharing, support decision-making and communication for patients with cancer and/or their family caregivers^{109,112}. While there is some evidence indicating potential benefits such as enhanced psychological well-being, decision-making, and physical functioning for patients with cancer and/or their family caregivers through eHealth, these findings remain inconclusive or are not specifically applicable for patients with advanced cancer and their family caregivers^{109,118,119}. Therefore, further research is needed to determine the effectiveness of eHealth programs in patients with advanced cancer and their family caregivers.

3. OBJECTIVES AND RESEARCH QUESTIONS

The primary objective of this dissertation is to develop and evaluate a psychoeducational home-based eHealth program for patient-caregiver dyads in an advanced cancer trajectory. Specifically we address three aims:

The **first aim** is to describe the numbers, characteristics and experiences of family caregivers of people with serious illness. To this end, we will answer the following research questions:

- 1) What proportion of the adult population provides family care for a person with serious illness, what are the sociodemographic and caregiving characteristics of family caregivers of someone with serious illness and how do they compare to other family caregivers on these characteristics? (Chapter 1)

The **second aim** is to describe the development of a psychoeducational eHealth program (iFOCUS) to support patients with advanced cancer and their family caregivers and its implementation in an international RCT. This chapter addresses the following research question:

- 1) How did we develop the psychoeducational eHealth iFOCUS program, what were our challenges during development, and how was the initial acceptability and usability of the eHealth iFOCUS program? (Chapter 2)
- 2) How was the psychoeducational eHealth program for patients with advanced cancer and their family caregivers (iFOCUS) implemented in an international RCT, evaluating its effect on the primary outcomes emotional functioning and self-efficacy? (Chapter 3)

The **third aim** is to describe the results of the DIAdIC trial, focusing on trial recruitment and retention, the effectiveness of iFOCUS and FOCUS+ on primary outcomes (self-efficacy and emotional functioning), our experiences with the implementation of these programs within the trial, and the feasibility of sustainable implementation of iFOCUS and FOCUS+ beyond the trial setting. To this end, we address the following research questions:

- 1) How often did eligible patients and family caregivers explicitly mention Information and Communication Technology (ICT) as a reason for non-participation, what is the self-reported digital competence and what are associated sociodemographic characteristics in participants, and to what extent does self-reported digital competence predict retention in trial with an eHealth component? (Chapter 4)

- 2) How does the iFOCUS psychoeducational eHealth program affect the self-efficacy and emotional functioning in patients with advanced cancer and their family caregivers? (Chapter 5)
- 3) What were our experiences with the development and implementation of the eHealth iFOCUS and face-to-face FOCUS+ program within the international DIAdIC trial? (Chapter 6)
- 4) What are barriers, facilitators, risks or opportunities for sustainable implementation of psychoeducational home-based programs like iFOCUS? (chapter 7)

4. METHODS

The aforementioned objectives and aims are addressed through the use of different study designs including a secondary data analysis of a cross-sectional survey (Chapter 1), an international three-arm superiority trial comparing two interventions (the eHealth iFOCUS and face-to-face FOCUS+ program) to a control group (Chapter 2, Chapter 3, Chapter 4, Chapter 5 and Chapter 6) and a qualitative research study with interviews with stakeholders involved in the implementation of psychoeducational programs (Chapter 7). In the context of the international three-arm superiority trial, which compares two interventions, a variety of methodologies have been employed to address the research questions at hand.

Methods to answer the first aim: to describe the numbers, characteristics and experiences of family caregivers of people with serious illness.

Research question 1: What proportion of the adult population provides family care for a person with serious illness, what are the sociodemographic and caregiving characteristics of family caregivers of someone with serious illness and how do they compare to other family caregivers on these characteristics? (Chapter 1)

In order to provide an answer to this research question a secondary analysis was performed on data from the 19th Social-Cultural Changes survey (SCC) in Flanders, conducted from March to July 2014 by the Study Service of the Flemish Government. The 2014 SCC was the latest edition to contain an extensive module on family caregiving and was therefore chosen for the analyses. A random sample of 2,581 Dutch-speaking individuals aged between 18 and 95, residing in Flanders or the Brussels-Capital Region, was drawn from the national population register. Participants were chosen through a stratified two-step sample, with clusters of postal sectors as the primary sampling unit.

Sociodemographic measurements included age, gender, education, household composition, marital status, employment situation, and perception of net monthly income. The characteristics of family caregiving included the relationship between the care provider and the care recipient, the gender, age, living situation and proximity of the care recipient, and frequency, intensity, duration, and content of caregiving. Family caregiving experiences were evaluated through Likert scale questions assessing the perceived impact of caregiving, satisfaction, and meaningfulness

of caregiving, as well as scales measuring burden and appreciation, alongside an assessment of the interference of caregiving with job demands.

Participants were categorized into three groups: caregivers for people with serious illness, caregivers for people with other conditions, and non-caregivers. Descriptive statistics highlighted the sociodemographic characteristics, while Pearson chi-square tests and Mann-Whitney U tests revealed differences between groups. Principal Component Analysis (PCA) elucidated underlying structures of caregiving experiences, followed by one-way ANOVA to identify group differences. Variables significantly associated with caregiver groups were further examined through multivariable ANOVA. More details on the method in chapter 1.

Methods to answer the second aim: to describe the development of a psychoeducational eHealth program (iFOCUS) to support patients with advanced cancer and their family caregivers and its implementation in an international RCT.

Research question 1: How did we develop the psychoeducational eHealth iFOCUS program, what were our challenges during development, and how was the initial acceptability and usability of the eHealth iFOCUS program? (Chapter 2)

To answer the question, we created a report detailing the development of the iFOCUS eHealth program using the Scrum methodology¹⁹. The development process followed four phases of the Scrum methodology: design, development, go-live, and maintenance & support. Five groups were involved during the development: the core development group (1), the web development team (2); the international consortium (3), experts on videos and visualization (4) and potential end-users (5). The seven-step development process, based on the Scrum methodology, included the following steps: concept design (1), development of mock-ups (2) and feedback of the consortium (3) (Scrum, Design phase), Technical development of the iFOCUS program (4), Creating iFOCUS versions for six participating countries (5) and preliminary testing of iFOCUS (6) (Scrum, Development phase) and Implementing the final version in an RCT (7) (Scrum, Go-Live & Maintenance). A detailed description of the method can be found in Chapter 2.

Research question 2: How was the psychoeducational eHealth program for patients with advanced cancer and their family caregivers (iFOCUS) implemented in an international RCT,

evaluating its effect on the primary outcomes emotional functioning and self-efficacy? (Chapter 3)

Chapter 3 outlines the study protocol for the DIAdIC trial, an international multicenter trial comparing face-to-face (FOCUS+) and web-based (iFOCUS) interventions to standard care for patients with advanced cancer and their family caregivers. Both interventions (FOCUS+ and iFOCUS) were administered in the homes of the patient-caregiver dyads (or in the location of the dyad's preference). The interventions were conducted in six countries (Belgium, Denmark, Ireland, Italy, the Netherlands, and the United Kingdom). Data was collected three times from patient-caregiver dyads; (1) baseline measure before randomization to the study arms (T0), (2) first follow-up at 12 weeks (T1) and (3) second follow-up at 24 weeks (T2). The primary endpoints include emotional functioning and self-efficacy, while the secondary endpoints encompass QoL, coping, communication, and healthcare utilization. The process evaluation includes qualitative interviews with participants and nurses. Additional information can be found in Chapter 3.

Methods to answer the third aim: to describe the results of the DIAdIC trial, focusing on trial recruitment and retention, effectiveness of iFOCUS and FOCUS+ on primary outcomes (self-efficacy and emotional functioning), our experiences with the implementation of these programs within the trial, and the feasibility of sustainable implementation of iFOCUS and FOCUS+ beyond the trial setting.

Research question 1: How often do eligible patients and family caregivers explicitly mention Information and Communication Technology (ICT) as a reason for non-participation, what is the self-reported digital competence and what are associated sociodemographic characteristics in participants, and to what extent does self-reported digital competence predict retention in trial with an eHealth component?

To address the first question, we conducted an analysis of recruitment files and data from baseline and first follow-up questionnaires from all participating countries. Research staff documented information pertaining to the screening, recruitment, and participation in an Excel log file. Individual who met the eligibility criteria but declined participation and did not sign an informed consent form were considered non-participants. We analysed recruitment logs from all countries, identifying ICT-related keywords and quantitatively assessing their frequency. Furthermore, data collected as part of the baseline and first follow-up questionnaires were

utilized. Digital competence was quantified by calculating the mean score of two items in the baseline questionnaire. Additionally, sociodemographic data were collected at baseline.

Descriptive statistics were employed to summarize sociodemographic variables and self-reported digital competence. Pearson chi-square tests were utilized to compare responses between patients and caregivers, and t-tests were employed to assess differences in digital competence. Potential predictors of digital competence were identified through a comprehensive literature review and directed acyclic graphs (DAGs). Multivariable linear regressions and logistic regressions were conducted, adjusting for relevant confounders. The methodology is further described in chapter 4.

Research question 2: How does the iFOCUS psychoeducational eHealth program affect the self-efficacy and emotional functioning in patients with advanced cancer and their family caregivers? (Chapter 5)

To address this research question we analysed data from patient-caregiver dyads at baseline, at T1 (first follow-up, 12 weeks after baseline), and at T2 (second follow-up, 24 weeks after baseline). 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. Self-efficacy was measured with 17 items from the Lewis Cancer Self-Efficacy Scale. Sociodemographic and clinical characteristics were collected during enrollment or at baseline through a questionnaire.

The primary analysis was an intention-to-treat (ITT) analysis, while a per-protocol (PP) analysis was conducted as a sensitivity analysis. Multiple imputations (n=50) were performed for missing data using the Fully Conditional Specification (FCS) method for the ITT analysis. 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. The method is further described in chapter 5.

Research question 3: What were our experiences with the development and implementation of the eHealth iFOCUS and face-to-face FOCUS+ program within the international DIAdIC trial? (Chapter 6)

In order to provide an answer to this questions, a reflexive report was written which delineates the experiences o the authors during the development and implementation of the dyadic face-to-face FOCUS+ and web-based iFOCUS program. The narrative chronological structure of the report first outlines the intended development process of FOCUS+ and iFOCUS alongside our experiences. Additionally, it describes the implementation of these programs in an international RCT, together with the authors' reflections. Further details can be found in Chapter 6.

Research question 4: What are barriers, facilitators, risks or opportunities for sustainable implementation of psychoeducational home-based programs like iFOCUS? (chapter 7)

To address this question, we conducted online semi-structured in-depth interviews with external stakeholders as part of the DIAdIC trial's process evaluation. During these interviews we focused on context (MRC Framework), maintenance (RE-AIM framework), and cognitive participation, collective action, and reflexive monitoring (Normalization Process Theory, NPT). The interviews were conducted in Flanders, Belgium between November 2022 and March 2023.

A non-exhaustive list of healthcare professionals and stakeholders involved in delivering psychoeducational support to patients with advanced cancer and their family caregivers was compiled using stratified sampling. This targeted individuals experienced in implementing such interventions, including clinical leads, principal psychologists, and senior oncologists. A framework outlining roles and settings was designed and purposive sampling ensured representation across each segment. The objective of the interviews was to gain insight into the involvement of stakeholders in the implementation of home-based psychoeducational programs, the factors influencing the sustainability of such programs, and the roles of various actors. Data analysis followed a thematic analysis approach, with iterative coding generating codes inductively and organizing them into themes and subthemes. A two-step iterative coding process was employed, initially using NVivo 1.7 for coding, with subsequent cross-checking by another researcher. The final themes and subthemes were reviewed by a multidisciplinary team. Further details on this methodology can be found in Chapter 7.

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PART 2

FAMILY CAREGIVING FOR PEOPLE WITH SERIOUS ILLNESS

CHAPTER 1

Size and characteristics of family caregiving for people with serious illness: A population-based survey

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ABSTRACT

Objectives: Family caregivers play a vital role in care for people with serious illness. Reliable population-level information on family caregiving is scarce. We describe the sociodemographic and family caregiving characteristics and experiences of family caregivers of people with serious illness in the adult population.

Methods: We performed a secondary analysis of the cross-sectional population-based 19th Social-Cultural Changes survey. A random sample of 2,581 Dutch-speaking people aged 18 to 95, living in Flanders or Brussels, were surveyed between March and July 2014 using a stratified two-step sample. Differences between groups are described using Pearson chi-square tests and analysis of variance.

Results: Response rate was 59% (1,515/2,581). Over a 12-month period, 7.6% of participants provided family care for someone with serious illness. They were most often aged 55-74 (36.0%), women (57.9%), worked full-time (42.3%); 31.8% provided at least ten hours of family care each week. Family caregivers of people with serious illness, compared with family caregivers of people with other conditions, provided more medical and nursing care (33.3% vs 22.5%, $p=0.027$), and experienced a higher burden of family caregiving ($p=0.038$) but a similarly high meaningfulness of family caregiving.

Significance of results: A considerable part of the adult working population provides family care for someone with serious illness. While family caregiving for someone with serious illness shows similarities with family caregiving for people with other conditions in terms of caregiver characteristics and the impact of caregiving on work-life balance and the meaning derived from it, it is also associated with increased burden.

1. INTRODUCTION

Family care plays a pivotal role in care provision for people with serious illness with family caregivers often being the main care providers^{1,2}. Family caregivers are relatives, partners, friends or neighbours who provide support in a non-contractual relationship that develops naturally and does not have formally agreed work hours, breaks or holidays³⁻⁵. Family caregivers can occupy four distinct roles. Firstly, they can act as care providers by assisting people with serious illness in a range of physical, social, emotional or practical tasks including routine activities of daily living such as bathing, instrumental activities of daily living such as transport, psychosocial support, and medical and nursing tasks⁶⁻⁸. Secondly, they can be facilitators of care due to their involvement in organising professional patient care⁹. Thirdly, they can be experts on the patient's care situation due to their relationship with the patient. Family caregivers generally spend much more time with a patient than do professional caregivers^{1,10}. Fourthly, family caregivers can also be considered care clients due to the impact family caregiving can have on their own health and well-being¹¹.

Providing family care for people with serious illness can have benefits for both the patient and the family caregiver, such as a stronger relationship and a sense of satisfaction, accomplishment, and personal growth¹²⁻¹⁴. However, providing family care can also negatively impact family caregivers in terms of lower quality of life and increased distress and anxiety, not only during caregiving but also after bereavement^{15,16}. Research shows that family caregivers report increased distress, anxiety and burden which is moderated by various sociodemographic characteristics such as age, sex, socio-economic status, role within the family, impact on work and daily life and social support^{17,18}. Disease progression and symptoms the patient experiences can also impact caregiver wellbeing due to a change in intensity of care tasks and possible behavioural changes in the patient such as irritability, depression and anxiety^{16,19}.

Describing family caregiving within the entire population is vital to inform policy and practice in order to support family caregivers adequately. Studies describing family caregiving for people with a serious illness on a population level are however, scarce. Moreover, previous research has mainly focused on family caregivers' needs and roles and the economic value of family caregiving²⁰⁻²².

This study therefore aims to describe the numbers, characteristics, and experiences of family caregivers of people with serious illness using population-based data. We address the following research questions:

- 1) What proportion of the adult population, within a time period of 12 months, provide family care for a person with serious illness?
- 2) What are the sociodemographic characteristics of family caregivers of people with serious illness, compared with family caregivers of people with other conditions or disabilities and people not providing family care?
- 3) What are family caregiving characteristics of family caregivers of people with serious illness, compared with family caregivers of people with other conditions or disabilities?
- 4) How do family caregivers of people with serious illness experience being a caregiver compared with family caregivers of people with other conditions or disabilities?

2. METHODS

2.1. Study design, setting and participants

We performed a secondary analysis on data from the 19th Social-Cultural Changes (SCC) in Flanders survey conducted from March to July 2014 by the Study Service of the Flemish Government²³. The Social-Cultural Changes survey is a face-to-face computer-assisted cross-sectional survey that is repeated every year in a random sample of the Dutch-speaking adult population in Flanders and Brussels-Capital Region, Belgium to assess changes in beliefs and values. As such, the Social-Cultural changes survey is an important instrument to measure the social-cultural environment in Flanders²⁴. The 2014 Social-Cultural Changes survey was the most recent edition to contain an extensive module about family caregiving and was therefore chosen for analyses.

A random sample of 2,581 Dutch-speaking people between the ages of 18 and 95 living in Flanders (the northern Dutch-speaking part of Belgium) or Brussels (the Capital Region of Belgium) was selected from the national population register. People living in collective households and nursing homes were excluded. The participants were selected using a stratified two-step sample. Clusters of postal sectors were the primary sampling unit. The number of clusters in each province was proportional to the total population size. For the second step, random clusters within postal sectors were formed depending on the population size of the postal sector. Participants were randomly recruited from these random clusters^{23,24}.

2.2. Questionnaire and measures

The questionnaire, originally developed in 1996, is revised annually by the Study Service of the Flemish Government and a scientific guidance committee consisting of researchers from several Flemish universities.

Sociodemographic measurements include age, sex, education, household composition, marital status, employment situation and perception of net monthly income. Characteristics of family caregiving include relationship to the care provider, sex, age, living situation and proximity of the care recipient, and frequency, intensity, duration, and content of caregiving. Family caregiving experiences were measured using questions on the perceived physical or psychological impact of providing care, the impact of providing care on time for family or themselves and satisfaction

with and meaningfulness of providing care, using a 5-point Likert scale (1=completely disagree to 5=completely agree). The extent to which participants experienced family caregiving as burdensome and felt appreciated for providing care was measured on a scale from 0 (not at all burdensome/not at all appreciated) to 10 (very burdensome/very appreciated). The extent to which family caregiving hindered the respondent's job demands or vice-versa was measured on a scale ranging from 1 (never) to 4 (always).

2.3. Statistical analysis

The data are weighted by province, sex, age and nationality to be representative of the adult population of Dutch-speaking people in Flanders and Brussels. We divided participants into three groups: 1) family caregivers of people with serious illness, 2) family caregivers of people with other conditions or disabilities and 3) people not providing family care. We identified family caregivers using the question 'are you currently, or have you been during the past 12 months, supporting a sick, disabled or elderly family member, acquaintance or neighbour?' People who answered 'yes, I currently provide support' or 'yes, I have provided support during the last 12 months but not currently' were identified as family caregivers. Those who indicated they provide/have provided support to someone with chronic and/or terminal illness were classified as 'family caregivers of people with serious illness'. Those who indicated they provide/have provided support to someone with physical disability, mental disability, early stage dementia/cognitive decline, psychological difficulties, general decline due to old age, or acute illness/accidents were classified as 'family caregivers of people with other conditions'. All data were analysed using SPSS 27.0 (IBM).

We used descriptive statistics to report sociodemographic characteristics of family caregivers of people with serious illness, family caregivers of people with other conditions and people not providing family care. We conducted Pearson chi-square tests to compare 1) sociodemographic characteristics between family caregivers of people with serious illness vs family caregivers of people with other conditions and people not providing family care and 2) family caregiving characteristics of people with serious illness vs family caregivers of people with other conditions. We tested differences in experiences of family caregiving between those caring for people with serious illness and others using Mann-Whitney U tests. To reveal underlying structures of family caregiving experiences we performed a Principal Component Analysis (PCA) with varimax rotation on all items concerning family caregiving experiences. Items loading higher than 0.70 on

a component were retained in that component. Internal consistency of the items within the underlying constructs was checked using Cronbach's α (Table 1).

Table 1: Principal component analysis, component loadings per construct

Item	Burden of family caregiving	Meaningfulness of family caregiving	Work-family conflict
The care I provide is physically demanding	0.744	-	-
The care I provide is psychologically demanding	0.798	-	-
I experience family care as meaningful	-	0.916	-
I get satisfaction from the care tasks I take on	-	0.932	-
I have insufficient time for myself due to the care I provide	0.787	-	-
I have insufficient time for my family due to the care I provide	0.705	-	-
How burdensome is providing family care to you?	0.808	-	-
How appreciated by society do you feel for providing family care. *	-	-	-
Job demands hinder(ed) my family caregiving tasks	-	-	0.912
Family caregiving tasks hinder(ed) my job demands	-	-	0.914
Cronbach's Alpha	0.771	0.861	0.882
Nr of items	5	2	2
* This item scored low on all components which is why we made the executive decision to remove it from the model.			

To identify differences between the two family caregiver groups on the constructs revealed through the PCA, a preliminary one-way analysis of variance (ANOVA) was conducted with the family caregiver group as independent variable and the constructs identified through PCA as dependant variables. Means, mean difference, F-value and p-value are reported. Constructs that were significantly associated with the family caregiver group ($p < 0.05$) were included in

multivariable ANOVA. We included the variables for which we found a statistically significant difference ($p < 0.05$) between family caregiver groups as confounders. Mean, 95% confidence interval and p-value were reported on interaction effects between the family caregiver group and other independent variables.

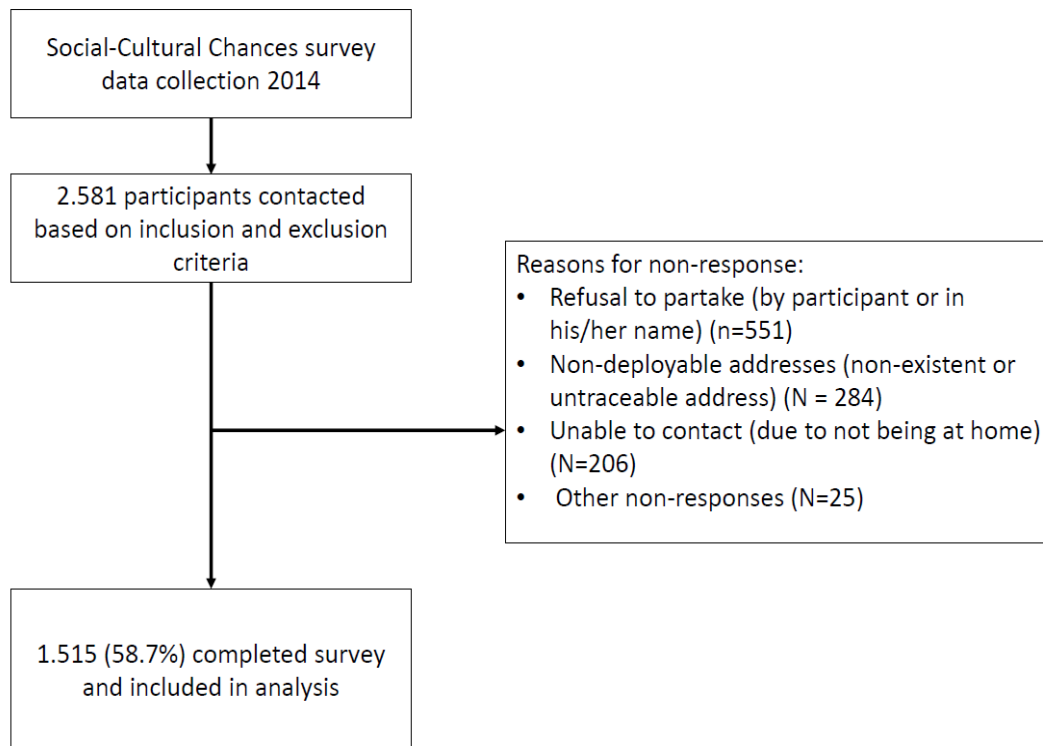
2.4. Ethical considerations

Participants were informed of the goal and content of the survey. Participants were free to refuse participation without any negative effects and were free to withdraw from the study at any time. Data used for this study was made available by the study service of the Flemish government. No further personal data were sought or collected, therefore ethical approval was not required.

3. RESULTS

Of the 2,581 participants who were contacted, 1,515 completed the questionnaire resulting in a response rate of 58.7%. The most frequent reason for non-response was refusal to take part in the survey (Figure 1). Within a 12-month period, 7.6% of the total population provided family care to someone with serious illness, 18.1% provided family care to a person with another condition, and 74.3% did not provide family care.

Figure 1: Flowchart participation Social Cultural Changes survey



3.1. Sociodemographic characteristics of respondents

More than one third of family caregivers were aged 35 to 54 or 55 to 74 (family caregivers of people with serious illness: 34.2% and 36.0%; family caregivers of people with other conditions: 34.9% and 36.4%) (Table 2). Family caregivers of people with serious illness were more often women (57.9%) compared with people who did not provide family care (47.8%, $p=0.040$). More than one out of three family caregivers were full-time employed or self-employed (family caregivers of people with serious illness: 42.3%; family caregivers of people with other conditions: 35.4%) and 62.9% were married or legally cohabiting.

Table 2. Characteristics of family caregivers of people with serious illness, family caregivers of people with other conditions and people not providing family care.

	A: Serious illness	B: Other conditions	C: Not providing family care	P-value for A vs B*	P-value for A vs C**
	n (%)	n (%)	n (%)		
Total	114 (7.6%)	272 (18.1%)	1117 (74.3%)		
Characteristics					
Sex				0.177	0.040
Woman	66 (57.9%)	137 (50.4%)	534 (47.8%)		
Man	48 (42.1%)	135 (49.6%)	583 (52.2%)		
Age				0.997	0.067
18 – 34	24 (21.1%)	55 (20.2%)	283 (25.3%)		
35 – 54	39 (34.2%)	95 (34.9%)	357 (32.0%)		
55 – 74	41 (36.0%)	99 (36.4%)	302 (27.0%)		
75+	10 (8.8%)	23 (8.5%)	175 (15.7%)		
Educational attainment				0.439	0.137
None	3 (2.6%)	6 (2.2%)	33 (3.0%)		
Primary school	10 (8.8%)	34 (12.5%)	167 (14.9%)		
Secondary school	53 (46.5%)	138 (50.9%)	567 (50.7%)		
Higher education	48 (42.1%)	93 (34.3%)	350 (31.3%)		
Other	0 (0.0%)	0 (0.0%)	1 (0.1%)		
Job situation				0.619	0.438
Full-time (self-) employed	47 (42.3%)	96 (35.4%)	430 (38.6%)		
Part-time (self-) employed	18 (16.2%)	52 (19.2%)	128 (11.5%)		
Unemployed	10 (9.0%)	36 (13.3%)	114 (10.2%)		
Retired	27 (24.3%)	67 (24.7%)	334 (30.0%)		
Other	9 (8.1%)	20 (7.4%)	108 (9.7%)		
Perception of net monthly family income				0.078	0.454

	A: Serious illness	B: Other conditions	C: Not providing family care	P-value for A vs B*	P-value for A vs C**
(Very) hard to make ends meet with current income	25 (21.9%)	35 (12.9%)	190 (17.2%)		
Current income sufficient to make ends meet	53 (46.5%)	137 (50.4%)	539 (48.9%)		
Comfortable life led with current income	36 (31.6%)	100 (36.8%)	374 (33.9%)		
Marital status				0.359	0.121
Married/Legal cohabitation	77 (67.5%)	171 (62.9%)	681 (61.0%)		
Unmarried/Separated or divorced	34 (29.8%)	85 (31.3%)	352 (31.5%)		
Widowed	3 (2.6%)	16 (5.9%)	83 (7.4%)		
Information on family caregiving status was missing for n=26 cases (1.7%). Missing values family caregivers of people with serious illness: Educational attainment N=1 (0.9%) and job situation N=4 (3.5%) Missing values family caregiver of people with other conditions: Job situation N= 3 (1.1%) Missing values of people not providing family care: Job situation N= 3 (0.3%), perception of net monthly family income N= 14 (1.3%), marital status N= 1 (0.1%) * Pearson Chi-square test testing for differences in sociodemographic characteristics between family caregivers of people with serious illness and family caregivers of people with other conditions or disabilities. ** Pearson Chi-square test testing for differences in sociodemographic characteristics between family caregivers of people with serious illness and people not providing family care.					

3.2. Family caregiving characteristics

Nearly half (47.8%) of the family caregivers of people with serious illness provided care to parents or parent in-law (Table 3). Compared with care recipients with other illness, those with serious illness were more often men (29.5% and 46.5% resp., $p=0.001$), aged 35-54 (6.6% and 13.0% resp., $p<0.001$) or aged 55-74 (19.2% and 36.5% resp., $p<0.001$) and more often lived with relatives other than the participating family caregiver (28.7% and 48.2% resp., $p<0.001$). Nearly one in three (32.5%) family caregivers of people with serious illness provided care on a daily basis

and 44.7% provided family care one or more times a week; 31.8 percent provided care for more than ten hours a week. Family caregivers of people with serious illness provided emotional support (92.1%), assistance in household chores (69.3%), transportation and guidance (64.0%), supervision (56.1%), assistance with administration (46.5%) and personal care (24.3%). Compared with family caregivers of people with other conditions, family caregivers of people with serious illness more often provided medical and nursing care (33.3% and 22.5% resp., $p=0.027$).

Table 3. Family caregiving characteristics of family caregivers of people with serious illness compared to family caregivers of people with other conditions.

	People with serious illness (n=114)	Other conditions (n=272)	P-value*
Characteristics	n (%)	n (%)	
The care recipient is the family caregiver's...			0.192
Parent (in law)	55 (47.8%)	128 (47.1%)	
Partner	17 (14.8%)	19 (7.0%)	
Other family member	16 (13.9%)	46 (16.9%)	
Not family member	13 (11.3%)	46 (16.9%)	
Sister/brother (in law)	8 (7.0%)	19 (7.0%)	
Child (in law)	6 (5.2%)	14 (5.1%)	
Sex of the care recipient			0.001
Man	53 (46.5%)	80 (29.5%)	
Woman	61 (53.5%)	191 (70.5%)	
Age of the care recipient			<0.001
Younger than 18	2 (1.7%)	12 (4.4%)	
18 – 34	4 (3.5%)	15 (5.5%)	
35 – 54	15 (13.0%)	18 (6.6%)	
55 – 74	42 (36.5%)	52 (19.2%)	
75 or older	52 (45.2%)	174 (64.2%)	
	People with serious illness	Other conditions (n=272)	P-value*

	People with serious illness (n=114)	Other conditions (n=272)	P-value*
	illness (n=114)		
Living situation of the care recipient**			<0.001
Lives with relatives (partner, parent or child)	55 (48.2%) 29 (25.4%)	78 (28.7%) 108 (39.7%)	
Lives with participating family caregiver	27 (23.7%)	51 (18.8%)	
Lives alone	3 (2.6%)	33 (12.1%)	
Institution (e.g., nursing home)	0 (0.0%)	2 (0.7%)	
Other			
Proximity of the care recipient (i.e. travelling time)			0.484
0 min (part of household)	27 (23.7%)	51 (19.1%)	
1 – 15 min	57 (50.0%)	150 (56.2%)	
16 – 30 min	17 (14.9%)	39 (14.6%)	
31 – 60 min	8 (7.0%)	22 (8.2%)	
>60 min	5 (4.4%)	5 (1.9%)	
Frequency of family caregiving			0.556
Daily	37 (32.5%)	79 (29.0%)	
Once or more/week	51 (44.7%)	132 (48.5)	
Once or more/month	23 (20.2%)	47 (17.3%)	
Once or more/year	3 (2.6%)	14 (5.1%)	
Intensity of family caregiving			0.821
10h/week or less	77 (68.1%)	187 (71.1%)	
>10h - <20h/week	17 (15.0%)	34 (12.9%)	
>20h/week or more	19 (16.8%)	42 (16.0%)	
Duration of family caregiving			0.477
<3 months	5 (4.4%)	25 (9.2%)	
3 – 6 months	11 (9.6%)	21 (7.7%)	
7 – 12 months	13 (11.4%)	23 (8.4%)	
13 – 24 months	13 (11.4%)	32 (11.7%)	

	People with serious illness (n=114)	Other conditions (n=272)	P-value*
> 2 years	72 (63.2%)	172 (63.0%)	
Family caregiving tasks**			
Emotional support	105 (92.1%)	235 (86.7%)	0.133
Household chores	79 (69.3%)	180 (66.4%)	0.583
Transport and guidance	73 (64.0%)	166 (61.3%)	0.608
Supervision	64 (56.1%)	125 (46.0%)	0.068
Administration	53 (46.5%)	133 (48.9%)	0.666
Personal care	28 (24.3%)	64 (23.5%)	0.863
Medical and nursing care	38 (33.3%)	61 (22.5%)	0.027
Information on family caregiving status was missing for n=16 cases (4.1%). Missing values family caregivers of people with serious illness: Intensity of family caregiving N=1 (0.9%) Missing values family caregiver of people with other conditions: Sex of the care recipient N=1(0.4%), proximity of the care recipient N= 5 (1.83%), intensity of family caregiving N=9 (3.3%) * Pearson χ^2 test for differences in family caregiving characteristics between family caregivers of people with serious illness and family caregivers of people with other conditions. ** Percentages do not add to 100% because multiple answers were possible.			

3.3. Family caregiver's experience of being a family caregiver

Among family caregivers of people with serious illness, 22.8% reported that the care they provided is physically demanding and 45.6% reported that it was psychologically demanding (Table 4). A minority of respondents felt that they didn't have time for themselves (13.9%) or their family (9.0%) due to the care they provided, though providing family care did not interfere with their professional occupation (94.2%) or vice versa (87.1%). Compared with family caregivers of people with other conditions, they more often reported that providing care is psychologically demanding (45.6% and 28.7% resp., $p=0.001$) and meaningful (97.4% and 93.7% resp., $p=0.019$).

Table 4. <i>Family caregivers' experiences of being a family caregiver.</i>							
	Serious illness (N=114)			Other conditions (N=272)			P-value *
	(Completely) agree, %	Neutral, %	(Completely) disagree, %	(Completely) agree, %	Neutral, %	(Completely) disagree, %	
The care I provide is physically demanding	22.8	9.6	67.5	16.9	9.9	73.2	0.119
The care I provide is psychologically demanding	45.6	11.4	43.0	28.7	13.2	58.1	0.001
I experience family care as meaningful	97.4	1.8	0.9	93.7	2.6	3.7	0.019
I get satisfaction from the care tasks I take on	87.8	7.8	4.3	83.8	11.4	4.8	0.633
I have insufficient time for myself due to the care I provide	13.9	16.5	69.6	15.8	9.2	75.0	0.180
I have insufficient time for my family due to the care I provide	9.0	11.7	79.3	11.6	8.6	79.8	0.449
	High, %	Neutral, %	Low, %	High, %	Neutral, %	Low, %	
How burdensome is providing family care to you?	17.5	37.7	44.7	15.4	29.8	54.8	0.169
How appreciated by society do you feel for providing family care?	55.7	35.7	8.7	56.9	35.3	7.8	0.974
	Never to sometimes, %	Often to always, %		Never to sometimes, %	Often to always, %		

Job demands hinder(ed) my family caregiving tasks	87.1	12.9	81.0	19.0	0.893
Family caregiving tasks hinder(ed) my job demands	94.2	5.8	90.2	9.8	0.913
<i>Missing values for family caregivers of people with serious illness: I have insufficient time for my family due to the care I provide N=3 (2.6%), job demands hinder(ed) my family caregiving tasks N=44 (38.6%), Family caregiving tasks hinder(ed) my job demands N=55 (39.5%),</i> <i>Missing values family caregivers of people with other conditions: I have insufficient time for my family due to the care I provide N=5 (1.8%), How appreciated by society do you feel for providing family care N=3 (1.1%), job demands hinder(ed) my family caregiving tasks N=119 (43.8%), Family caregiving tasks hinder(ed) my job demands N=119 (43.8%)</i> <i>*Mann-Whitney-u test for family caregiver's experiences between family caregivers of people with serious illness and family caregivers of people with other conditions</i>					

The PCA performed to identify underlying constructs in family caregiver experiences resulted in three components i.e., burden of family caregiving (Cronbach's $\alpha = 0.771$), meaningfulness of family caregiving (Cronbach's $\alpha = 0.861$) and work-family conflict (Cronbach's $\alpha = 0.822$). Family caregivers of people with serious illness experienced higher burden than family caregivers of people with other conditions (mean difference -0.226, $p=0.038$) but did not differ in experienced meaningfulness (mean difference 0.159, $p=0.138$) and work-life conflict (mean difference=0.074, $p=0.503$) (Table 5).

Table 5: Association between family caregiver type and experienced burden, experienced meaningfulness of family caregiving, and work-life conflict

Items	Family caregivers of people with serious illness (n=114) Mean (SD)	Family caregivers of people with other conditions (n=272) Mean (SD)	Mean Difference	F-Value	p-value*
Experienced burden	0.187 (0.972)	-0.039 (1.007)	-0.226	4.333	0.038
Experienced meaningfulness of family caregiving	0.126 (0.859)	-0.033 (1.034)	-0.159	2.207	0.138
Work-life conflict	-0.040 (0.921)	0.033 (1.043)	0.074	0.449	0.503

Missing values N=12 (3.1%)

*Univariate analysis of variance test

Note: The items were originally assessed using Likert scales ranging from 1 to 5. Factor scores derived from Principal Component Analysis were standardized to have a mean of 0 and a standard deviation of 1. The values in the table represent standardized scores, reflecting standard deviation mean differences across factors.

Table 5 shows that family caregivers for people with a serious illness experience significantly higher burden than family caregivers for people with other conditions. However, as shown in table 6, the experienced burden of family caregivers could be influenced by whether family caregivers provide medical and nursing care. For caregivers who provide medical and nursing care, both caregiving groups experience elevated burden. Family caregivers of people with other conditions report a higher mean burden (mean = 0.400, 95% CI = 0.008 – 0.793) compared to caregivers of people with serious illnesses (mean = 0.261, 95% CI = -0.211 – 0.733), however, this difference is not statistically significant. Conversely, for family caregivers providing no medical or nursing tasks, the burden is significantly higher for those caring for people with a serious illness (mean=0.116, 95%CI=-0.283 - 0.516 vs mean =-0.290, 95%CI =-0.620 - 0.039).

Table 6: Association between family caregiver type and experienced burden controlled for family caregiving characteristics

Items	Burden experienced by family caregivers of people with serious illness (n=114)	Burden experienced by family caregivers of people with other conditions (n=272)	p-value*
	Mean (95%CI)	Mean (95%CI)	
Parameter**			
Sex of the care recipient			0.867
Man	0.219 (-0.224 - 0.661)	0.067 (-0.306 - 0.439)	
Woman	0.159 (-0.258 - 0.575)	0.044 (-0.295 - 0.382)	
Age of the care recipient			0.455
Younger than 18	0.334 (-0.794 - 1.466)	-0.041 (-0.641 - 0.559)	
18 – 34	-0.597 (-1.555 - 0.361)	0.064 (-0.500 - 0.629)	
35 – 54	0.542 (-0.016 - 1.099)	0.277 (-0.241 - 0.794)	
55 – 74	0.330 (-0.072 - 0.731)	0.042 (-0.339 - 0.423)	
75 or older	0.334 (0.020 - 0.648)	-0.066 (-0.374 - 0.241)	
Living situation of the care recipient			0.494
Lives alone	0.450 (0.034 - 0.866)	0.550 (0.299 - 0.802)	
Lives with participating family caregiver	0.143 (-0.321 - 0.606)	0.070 (-0.221 - 0.361)	
Lives with relatives (partner, parent, or child)	-0.155 (-0.526 - 0.217)	0.162 (-0.113 - 0.437)	
Institution (e.g., nursing home)	0.316 (-0.699 - 1.331)	0.410 (0.023 - 0.798)	
Other	***	-0.917 (-2.243 - 0.409)	
Family caregiving task provided:			
Medical and Nursing care			0.026
Yes	0.261 (-0.211 - 0.733)	0.400 (0.008 - 0.793)	
No	0.116 (-0.283 - 0.516)	-0.290 (-0.620 - 0.039)	
Missing values N=12 (3.1%)			
*Two-way Analysis of Variance with interaction effect between type of family caregiver and parameters.			
** Interaction effects reported between type of family caregiver and another parameter			
*** This level of combination of factors is not observed			

4. DISCUSSION

4.1. Main findings

This population-based survey indicates that, within a period of 12 months, 7.6% of the adult population provided family care for someone with a serious illness. Almost half of these family caregivers are a child of the ill person and work full-time, and a third provide ten hours or more of family care each week. Compared with family caregivers of people with other conditions, family caregivers of people with serious illness seemed to incur similar experiences in terms of work-life balance and the meaning derived from care but experienced a higher burden. In terms of caregiving tasks, family caregivers of people with serious illness more often take on medical and nursing care than family caregivers of people with other conditions.

4.2. Strengths and limitations

A particular strength of this study is that it uses a representative sample of the adult population in Flanders, Belgium. This allows generalizability of the findings about family caregiving in serious illness to the entire adult population and, hence, provides a clear profile of family caregiving. Response rate to the survey is satisfactory and several measures have been implemented to enhance data quality, including the use of computer-assisted personal interviewing (CAPI) by trained interviewers, regular quality checks of interviews and control for interviewer-variance ²³.

Limitations include: only participants from private households are included, which means that participants in e.g., nursing homes are not included which could have impacted the findings about characteristics of caregivers and/or the caregiving situation. Additionally, selection bias due to non-response cannot be ruled out. However, non-response has been analysed taking into account sociodemographic variables such as living area, age and sex. There is also a possible social-desirability bias in the responses due to the expectations that you should look after your partner or parent. Finally, because family caregiving was not the primary focus of the SCV survey, ascertainment bias for the caregiving outcomes may be limited.

4.3. Interpretation and implications of the findings

According to our study, 7.6% of the adult population in Flanders and Brussels provides family care for someone with serious illness every year, which corresponds to about 494,000 people of the 6,500,000 adult inhabitants. While our operationalization of caregiving in serious illness was not limited to caregiving for the imminently dying or in terminal illness, we could broadly describe it as informal palliative care. Research shows that, depending on the estimation methods, 38% to 74% of decedents had a need for palliative care prior to their death²⁵. For Flanders this means that annually approximately 22,800 to 44,400 of the 60,000 dying people require palliative care. However, palliative care also intends to provide support to family caregivers²⁶. Our study therefore indicates that a substantially larger population than just the estimated number of patients can benefit from some kind of palliative care support and that family caregivers may well be one of the most overlooked groups in medical care in general. Family caregivers are both care providers and care receivers and could benefit from comprehensive assessment as a base for a pro-active support plan. Furthermore education of family caregivers such as skill training aimed at increasing medical skills and mental resilience, which reduces hopelessness and increases self-efficacy and social recognition, could empower them^{27,28}.

Our findings reveal a higher burden for family caregivers of people with serious illness compared to family caregivers for people with other conditions but also reveal an interaction effect between the type of family caregiving (caregiver for people with a serious illness versus caregivers for people with other conditions) and the specific caregiving tasks provided (medical and nursing care versus not providing such care). When providing medical and nursing care, both caregiving groups experience elevated burden but this burden is not significantly different. When not providing medical and nursing care, only family caregivers for people with serious illness experience elevated burden, which is significantly different than the burden experienced by other family caregivers. These results align with existing research, which suggests that the type and intensity of care can significantly impact caregiver burden^{29,30}. Nevertheless, regardless of the type of care provided, research also suggests that additional factors such as physical symptoms and complaints like sleep deprivation and pain^{31,32} may also contribute to the experienced burden of family caregivers. Family caregivers might develop a passive attitude towards self-care because caring for the patient is their main focus, and may choose to minimise or ignore their own symptoms and complaints³³.

Furthermore our results show that family caregivers of people with a serious illness significantly more often found the care they provided to be psychologically demanding and other research indicates that up to 40% of family caregivers who provide palliative care experience depressive symptoms³⁴. The significantly higher psychological and overall burden in family caregivers of people with serious illness may be influenced by the concept of co-suffering, wherein the decline in the patient's physical, psychological and emotional well-being contributes to elevated distress^{35,36}. Elevated psychological burden might also be related to a decrease in leisure time, even though family caregivers did not report having too little time for themselves in one particular study³⁷. Nevertheless, we have to take into consideration that family caregivers might underreport on the actual time available for themselves or their families and the psychological burden that a lack of personal time might cause³³. On the other hand, we found that family caregivers also generally find providing family caregiving to be meaningful. Family caregivers can enhance the relationship with the care recipient, effectively creating meaning in the palliative care situation³⁸.

Family care will become increasingly important due to continuous strain on the accessibility and workability of formal care because of current demographic and socio-economic developments. The proportion of the world's population aged 65 and older is expected to increase from 5% in 2015 to 16% in 2050 which implies an increase in people with chronic illness or comorbidities including heart disease, stroke and cancer^{39,40}. The need for, and numbers of, family caregivers is therefore likely to grow. Yet our findings indicate that more than half of family caregivers of people with serious illness combine family caregiving with a full- or part-time job, putting them under increasing strain. Future research could study the constructs put in place to support family caregivers of people with serious illness or family caregivers in general and how often these constructs are used, whether or not they are sufficient and if they decrease experienced burden or strain.

Some of the aspects the current study was not able to look at and which may be specifically relevant in the 'palliative family caregiving' group relate to how much family caregivers feel competent, confident and supported in performing the caregiver tasks. Research indicates that communication between the healthcare team and the family caregiver is not only the basis of but essential to increasing feelings of competence and confidence in the family caregiver. Therefore a participatory approach where the family caregiver is recognised as a part of the team is recommended⁴¹.

In conclusion, we found that family caregivers who provide palliative family care spend a lot of time providing this care and can experience burden yet find family care to be meaningful. Our findings suggest the importance of tools and programs not only aimed at supporting patient well-being but also family caregiver wellbeing and self-efficacy in the context of serious illness.

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Conflicts of interest: None.

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PART 3

THE DEVELOPMENT AND IMPLEMENTATION OF AN EHEALTH SUPPORT PROGRAM AS PART OF AN INTERNATIONAL RANDOMIZED CONTROLLED TRIAL

CHAPTER 2

A self-management psychoeducational eHealth program to support and empower people with advanced cancer and their family caregivers: Development using the scrum methodology

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ABSTRACT

Background: eHealth programs could be a flexible and scalable resource to support and empower people with advanced cancer and their family caregivers. A face-to-face intervention that has demonstrated effectiveness is the “FOCUS” program, developed and tested in the USA. Recently the FOCUS program was translated and adapted to the European context as part of an international study in six European countries, resulting in the “FOCUS+” program. FOCUS+ served as the basis for development of the web-based iFOCUS program.

Objective: We aim to (1) describe the development process of the iFOCUS program, (2) outline the challenges we encountered and how they were overcome, and (3) present findings regarding the acceptability and usability of iFOCUS.

Methods: We used the four phased agile Scrum methodology to develop iFOCUS and applied set timeframes of rapid program development and evaluation (sprints). Five teams were involved in the development i.e. a core development group, a web development team, an international consortium, audio-visual experts, and potential end-users.

Results: Development followed seven steps, integrated across the four phases of Scrum: (1) concept design, (2) development of mock-ups, (3) Feedback from the international consortium, (4) technical development of iFOCUS, (5) creating versions for the six participating countries, (6) preliminary testing of iFOCUS and (7) implementing the final version in a randomized controlled trial. User testing included 42 participants (twenty patient-family caregiver dyads and two bereaved family caregivers) who reviewed the iFOCUS program. Users found the iFOCUS program to be acceptable and usable. Feedback mainly focused on text size and fonts. Minor changes to the content, tailoring, and program flow were required. During development we encountered program specific and general challenges. Using the Scrum methodology facilitated iterative development to address these issues. For some challenges, such as tailoring, we had to make pragmatic choices due to time and resource limitations.

Conclusions/discussion: The development of a tailored, self-managed psychoeducational eHealth program for people with advanced cancer and their family caregivers is an intense process and requires pragmatic choices. By keeping the emphasis on the target population during development, no specific remarks pertaining to advanced cancer were identified. Some challenges we encountered are common to eHealth development, others were related to program specific requirements. Using the Scrum methodology allows teams to efficiently collaborate during program development and increases the flexibility of the development process. Interpersonal contact between research staff and potential end-users is recommended during and after the development of eHealth programs.

1. INTRODUCTION

Technological advancements, such as eHealth, are increasingly being recommended to address the challenges faced in healthcare¹. eHealth refers to the use of technology, such as computers, to engage, inform, support, and empower users such as patients and family caregivers². By providing a cost-effective means of expanding the reach of clinical care and facilitating efficient patient communication and support, eHealth can improve quality of life in patients and family caregivers and reduce healthcare costs³, as well as reduce travel time and intrusive home visits for formal healthcare⁴. Considering that most care for people living with serious illness is offered at home by family caregivers, eHealth could be considered as a potential way to provide psychoeducational support to patients with advanced cancer and their family caregiver (i.e. dyads) in how to cope with the impact of the disease on their lives⁵. However, a recent systematic review found that only nine psychosocial eHealth interventions have focused on dyads in which the care recipient had cancer⁶. The review does not specify how many of these interventions have a specific emphasis on people with advanced cancer.

Emphasizing research into eHealth development for people with advanced cancer and their family caregivers is justifiable as people with advanced cancer and their family caregivers might have unique experiences related to the disease progression and treatment in comparison to patients and family caregivers involved in a non-advanced setting^{7,8}. Research shows that people with advanced cancer can experience reduced quality of life, which can worsen as the disease progresses^{9,10}. Family caregivers of people with advanced diseases also experience higher levels of distress compared to other family caregivers¹¹, and there is a positive correlation between distress levels in both cancer patients and their family caregivers¹², affecting their overall quality of life^{13,14}.

In order to cope with the unique experiences of patients with advanced cancer and their family caregivers the Transactional Model of Stress & Coping¹⁵ states that enhancing the dyad's self-efficacy, problem-solving, and communication skills can lead to a more favourable response to stressors related to the illness. Research supports this theory, showing that increasing knowledge about the illness, self-efficacy, coping skills, decision-making involvement, improved communication, and mutual understanding can help the patient-caregiver dyad to better manage illness-related stressors^{2,16}. Research also shows that adopting a salutogenic approach towards dyads, which focuses on improving health and social coherence rather than reducing illness can reduce distress and increase their quality of life¹⁷.

The FOCUS program, developed in the USA in the early 2000s, is a nurse-led psychoeducational dyadic intervention designed for people with cancer and their family caregivers¹⁸ based on the Transactional Model of Stress & Coping¹⁵. FOCUS consists of five modules: Family involvement, Optimistic outlook, Coping effectiveness, Uncertainty reduction, and Symptom management. The program is simultaneously delivered to the patient and family caregiver by a nurse and has been shown to improve quality of life and self-efficacy, and reduce emotional distress in dyads in an advanced cancer trajectory^{18,19}. A self-managed web-based format of the “Family involvement” component of the FOCUS program was developed in the USA²⁰. Development of content and program design happened simultaneously for the original FOCUS program. A multidisciplinary team was involved in the process of development encompassing three stadia namely ideation and prototyping (1), iterative design and development (2), and internal testing and final development (3). For usability testing four focus groups and four patient-caregiver dyads per session reviewed the sessions and found the programs structure, design and content favorable²¹. Dyads with advanced cancer who completed this web-based format as part of a phase II feasibility trial reported a decrease in emotional distress, improved quality of life, and more benefits from illness and caregiving²⁰.

As part of the international DIAdIC project which involves six European countries (Belgium, The Netherlands, Denmark, Italy, The United Kingdom, and Ireland) we developed two adaptations of the US-based FOCUS program, namely a face-to-face program named FOCUS+ and a web-based program iFOCUS and will determine whether these two adaptations could effectively improve the emotional well-being and self-efficacy of people with advanced cancer and their family caregivers²². In the present article we specifically report on the development process of the iFOCUS program. Development of the FOCUS+ program has been reported elsewhere²³.

The aim of this article is three-fold:

1. To describe the process of development of the eHealth iFOCUS program.
2. To outline the challenges encountered during the development of the eHealth iFOCUS program and how they were overcome.
3. To present the results of the acceptability and usability of the eHealth iFOCUS program through user testing.

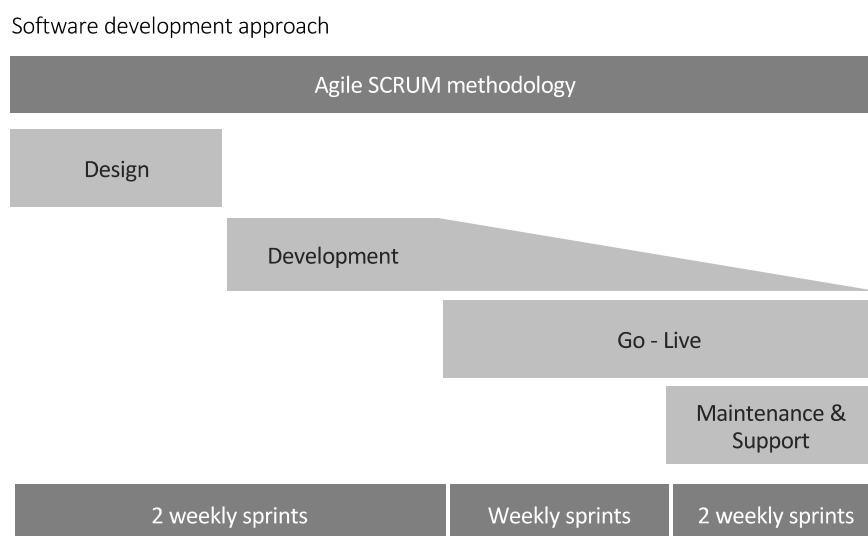
2. METHODS

2.1. Study design

Predating the actual development of iFOCUS the FOCUS program and its materials were evaluated from both an etic (outsider; i.e. scientist) and emic (insider; i.e. user) perspective to identify necessary modifications and additional features for translation to the European context. In a next phase FOCUS was adapted and translated to a face-to-face program for people with advanced cancer and their family caregivers namely FOCUS+. This process is extensively described elsewhere²³. FOCUS+ served as the foundation for the development of the iFOCUS program.

We developed the iFOCUS program using the four phases of the Scrum methodology, which are: design, development, go-live, and maintenance & support²⁴ (Figure A). To support agile software development, we utilized “sprints”, which are periods of rapid program development and evaluation^{24,25}. During each sprint, the team responsible for the technical development decides on the deliverables and related tasks and meets on a daily base to synchronize their work, to discuss the progress and plan the next days. Each sprint is ended by a retrospective evaluation of that sprint²⁶. We applied sprints of two weeks throughout the process of design, development, and maintenance & support. During the go-live period, we had weekly sprints. Using the agile Scrum methodology allowed us to instantly and efficiently resolve emerging problems²⁶.

Figure A: Scrum model



The core development group designed a seven-step development process (Figure B). These steps can be integrated into the four phases outlined in the Scrum model. The seven steps are followed in a sequential, yet flexible manner, allowing for revisiting previous steps for continuous refinement and correction²⁷. During the Scrum phases of design and development (step one to six) an iterative process was used within each step. The iterative process of development involved cycles of brainstorming, development and evaluation within each phase. Multiple feedback rounds were conducted before concluding a particular phase. Each feedback round provided insights which shaped subsequent iterations of development. This approach allowed for continuous refinement and improvement based on user feedback and evaluation.

Figure B: iFOCUS Development flow

SCRUM	Steps taken	Tasks performed	Teams involved
Design	Prior to iFOCUS development		
	Original FOCUS intervention	- Review of the original FOCUS intervention - Conceptualization and operationalization, aims, theoretical framework, key components, materials - Identification of teams necessary for development of the iFOCUS program - Update materials and content to contemporary, European version - Write the intervention manual for the face-to-face version (FOCUS+)	International consortium Core Development group
	The European FOCUS+ program		
	During iFOCUS development		
	1. Concept design May '19 – Sept '19	- Identification and translation of key components to features, principles and pedagogic techniques - Review of previous studies and consultation with development team of original FOCUS program - Result: First PowerPoint-based concept	Core development group International consortium
Development	2. Development of mock-ups Sept '19 – Oct '19	- Present first PowerPoint based concept to web-development team - Development of various materials and functionalities - Result: First digital mock-ups	Core development group Experts on video and visualisation Core development group Web development team
	3. Feedback from the international consortium Nov '19	- Organised moment where the international consortium can provide feedback - Feedback on program flow and log-in procedure	Core development group International consortium
	4. Technical development of the iFOCUS program Nov '19 – Jan '20	- Calculation on required time and cost of development - Development of a functioning back-end - Inputting materials in the iFOCUS program back-end - Result: iFOCUS V1.0 in one language available	Web development team Core development group
	5. Creating iFOCUS versions for the six participating countries Jan '20 – Aug '20	- Providing international translations of core materials - Result: Fully functioning iFOCUS Version V2.0 in six languages	International consortium Core development group
	6. Preliminary testing of iFOCUS Aug '20 – March '21	- National and international functional testing - Result: V2.1 - User testing of iFOCUS (30 dyads spread over 6 countries – 5 dyads per country) - Result: V3.0	International consortium
Go-live & Maintenance	7. Implementing the final version in an RCT Feb '21	- Onboarding procedure	International consortium

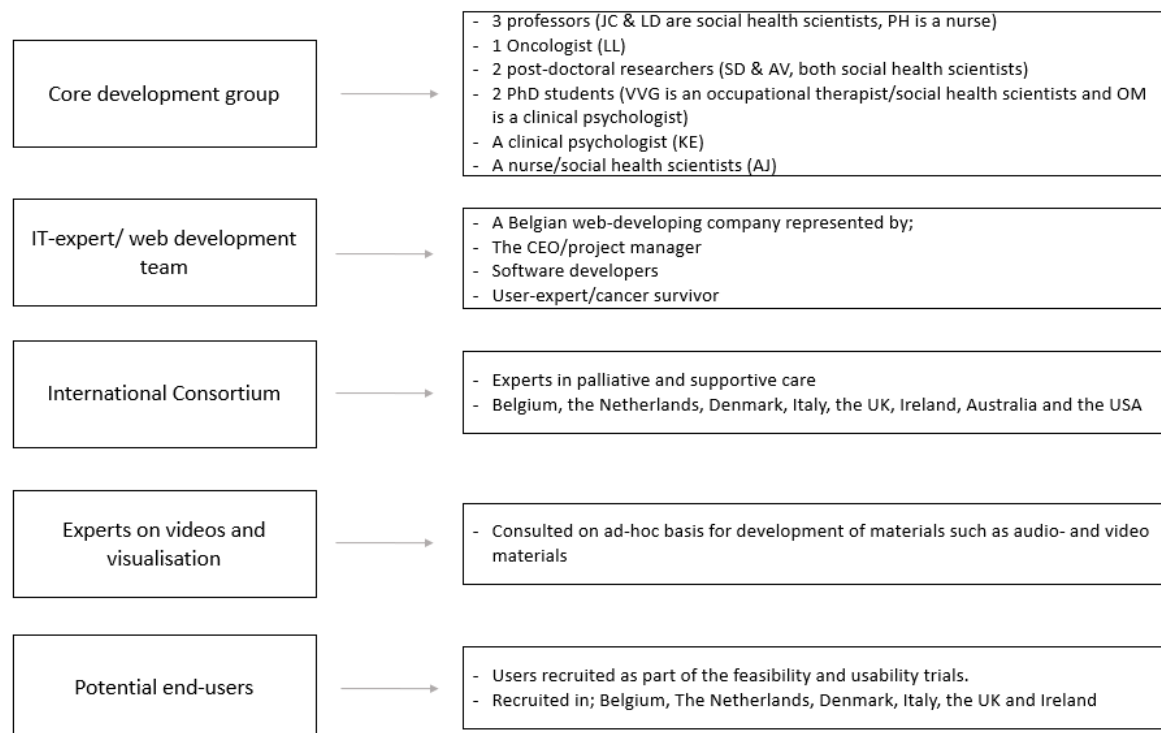
2.2. STUDY PROCEDURE

Groups involved in the development

Five groups participated in the development process (Figure C). The core development group (1) consisted of academics, clinicians, and healthcare professionals who were actively involved in the daily development of program content and flow. The web development team (2) was made up of software developers, a user expert/cancer survivor, and the CEO of the IT firm who acted

as the technical project manager and handled all technical and administrative tasks. The international consortium (3) involved in the DIAdIC project comprising researchers and experts in palliative and supportive care provided oversight, input, and feedback on the program development. Experts on videos and visualization (4) were consulted as needed. Finally, potential end-users (5) from each participating country provided input and feedback during the feasibility and usability evaluation.

Figure C: iFOCUS Development flow



Step 1: Concept design

Two earlier studies that modified one module of the original FOCUS program to a web-based format were analysed to gain insight into the procedures and tailoring^{20,28}. Based on these findings, the core development group created a visual representation of the proposed web program using MS PowerPoint, with each slide corresponding to a screen of the intended program. They also identified the technical requirements. Justifications for the choices regarding program flow, slide design, and technical requirements were documented and added to the slides, referencing the philosophy of the FOCUS+ program. During the phase of concept design we continued to be aware of the intended end-users, being patients with advanced cancer and

their family caregivers. In light of this, we conscientiously considered functionalities which could mediate program difficulties due to side effects resulting from the disease or treatment trajectory of patients with advanced cancer and their family caregivers. Feedback was sought from the international DIAdIC consortium.

Step 2: Development of mock-ups

The web development team created digital mock-ups based on the MS PowerPoint presentation as a first draft representation of iFOCUS. As part of the functional and technical analysis, there were several meetings between the web development team and the core development group to discuss the main functionalities required and the technical specifications. At the same time, the core development group, in collaboration with the video and visualization experts, prepared various materials, such as videos, written text, external resources, and references, to be included in iFOCUS.

Step 3: Feedback from the international consortium

A workshop was held to gain more perspectives on the form and content of the program. During this meeting, the consortium members discussed the proposed content, concepts, functionalities, and materials. The core development group presented the initial MS PowerPoint concept and the first digital mock-ups. Throughout the subsequent development steps, the international DIAdIC consortium was consulted to provide feedback on language, cultural significance, and additional materials.

Step 4: Technical development of the iFOCUS program

The web development team calculated the time and cost required for the technical development of iFOCUS. A digital platform was created which allowed the core development group to input videos, images, and certain functionalities, such as exercises and tailored feedback. This resulted in the first web-based version (V1.0) of iFOCUS in English.

Step 5: Creating an iFOCUS version for the six participating countries

To implement iFOCUS in each of the six participating countries, country-specific versions were created. The core development group asked the international consortium for translations of all written text, spoken text, and references to external local resources

into their respective languages. This process involved both translators and professionals with experience in palliative and supportive care. The core development group then systematically added all translated information and materials to the digital platform, resulting in a viable version (V2.0) of iFOCUS in six languages: Dutch (Belgium), Dutch (The Netherlands), English (The United Kingdom), English (Ireland), Italian, and Danish.

Step 6: Preliminary testing of iFOCUS

To validate the functionality and user experience of iFOCUS, both professionals and end-users were consulted through functional and user testing. The results were used to identify and fix any bugs or errors and to further optimize the program to meet current technological standards and user requirements.

Functional testing

Version 2.0 of the iFOCUS program underwent functional testing from August to October 2020. Functional testing evaluates the performance of a device across its various modes of operation and verifies that the application's features and operational behaviour match its specifications²⁹. Initially, seven members of the core development group acted as dyads going through iFOCUS. Next, five teams from the international consortium (UK, Ireland, The Netherlands, Denmark, and Italy) accessed the web sessions in their respective language and performed functional testing in the same manner as the core development group. The procedure for analysing the data can be found in Appendix 1. Based on the feedback obtained from this functional testing, the core development group resolved all identified bugs and errors, resulting in Version 2.1.

User testing

User testing of Version 2.1 of iFOCUS took place between October 2020 and March 2021. User testing involves evaluating a program by its potential end-users³⁰. As part of the user testing, we wanted to assess the preliminary acceptability and usability of the iFOCUS program as well as control the program for bugs and look for potential improvements to the program as defined by potential end users. We considered a program acceptable when the content and the program structure were agreeable³¹ and satisfactory to the dyads after having engaged with the program (retrospective acceptability)³². We aimed to conduct online semi-structured interviews with people with advanced cancer and their family caregivers to assess their evaluations of the user-friendliness, content, and layout of iFOCUS. Interviews were conducted using an interview guide with questions and probes (Appendix 2). Questions such as “What was your experience logging

in”, “What are your experiences going through this chapter X” and “What did you think going through chapter X” were asked and participants were encouraged to think aloud and express their thoughts as they went through the program³³. The core development team analysed the data and made necessary adaptations to the program.

Based on a diminishing return analysis model, a participant population of five to fifteen is considered sufficient to detect defects³⁴. Considering that the technical functionalities are the same across countries we aimed to recruit five dyads (10 participants) per country participating in the international RCT, resulting in 30 dyads (60 participants) across six countries, through purposive sampling. Participants were dyads similar to those planned for inclusion within the international RCT. Patients were over 18 years old and had been diagnosed with advanced cancer, i.e. were no longer receiving curative treatment. Patients with brain cancer or non-solid cancer, a prognosis of fewer than three months, or without a family caregiver were excluded. Family caregivers were over 18 years old, were appointed by the patient as the main family caregiver, and did not receive a cancer diagnosis 12 months prior to study participation. We aimed to include a diverse range of participants in terms of sociodemographic characteristics such as age, sex, and patient-family caregiver relationship.

As the COVID-19 pandemic affected participant recruitment, we allowed some flexibility by 1) recruiting four dyads instead of five; 2) using alternative recruitment methods such as Patient and Public Involvement, self-referral, contacting dyads involved in the testing of FOCUS+, existing groups or networks of patients and family caregivers, 3) recruiting dyads where the patient was not in an advanced stage of cancer, and 4) recruiting bereaved family caregivers.

Step 7: Implementing the final version in an RCT

Feedback gathered from the functional and user testing resulted in the final version of the iFOCUS program (V3.0).

Ethical Considerations

This study is performed following the Declaration of Helsinki. The Ethics Committee of the Ghent University Hospital (UZ Gent), Ethics Committee of the North Emilia Wide Area (AVEN), Italy; St. Vincent’s University Hospital Research Ethics Committee, Ireland; Medical Ethics Review Committee Erasmus Medical Centre Rotterdam, the Netherlands; and NHS/HSC Research Ethics

Committee, United Kingdom, approved the study procedure and materials. The Denmark Scientific Ethical Committee system determined that the protocol did not require formal approval. All personal data were processed in accordance with the General Data protection Regulation (GDPR) (EU, 2016/679, in effect since May 25th 2018). All information is gathered confidentially. All data gathered was pseudonymized and accessible to researchers or physicians involved in the study only. Informed consent was obtained from all participants. Participants did not receive any financial compensation for participating in the study.

3. RESULTS

Step 1: Concept design (May 2019 – September 2019)

We identified seven key characteristics as part of the iFOCUS concept design (Table A). iFOCUS is a psychoeducational intervention (1) that addresses the five core components of the FOCUS+ program (2) in four sessions as opposed to three sessions in FOCUS+. The challenge of redistribution of the session content into four sessions was handled by the core development group by iteratively reviewing different renditions of the program structure. The increased number of sessions allows for reduced time per session which might be beneficial for dyads who experience increased symptom burden at the end of life. Dyads can pause and resume at any time. Variation is needed in terms of pedagogic approach and technical functionalities (3) to enhance user engagement. The content of iFOCUS is tailored to the identified needs, priorities, and personal situations of the dyads (4). iFOCUS aims to facilitate communication within the dyad (5) and complement regular care (6). Finally, iFOCUS is accessible to dyads across participating countries on various platforms (desktop, tabletop, or tablet) and in their preferred language (7). A challenge we encountered was effectively convey the idea of the concept design to the web development team, which we resolved by using PowerPoint slides with imagery of the desired program pages and its related functionalities.

Table A. Key characteristics of the iFOCUS program and their operationalization

Key characteristics	Operationalization of key characteristics
1. iFOCUS should be a psycho-educational program	Modus operandi of providing information: To provide information, a logic flow was implemented based on the Stress Coping model from Lazarus and Folkman along with the evidence-based FOCUS program. We aimed to introduce a topic, and assess the needs, priorities, or situation of dyads, followed by providing tailored feedback. For example, as part of the iFOCUS program, in the part ‘Symptom Management’ both patient and caregiver individually get the chance to grade different symptoms. Based on the grading of the symptoms they are referred to pages with information or resources on the symptoms they graded higher. Most exercises and topics end with guiding questions, facilitating reflection or discussion. Long-term learning effect: To allow dyads to reflect in the long term on the information they received and entered into the web program, a reference work in the form of a personal workbook was implemented. This is generated as dyads complete their sessions. The personal workbook functions as a logbook in which the dyads receive standard information based on the content of the sessions and personalized information based on the answers they gave to the exercises and their choices on what additional references (existing information or brochures) they would like to add. The personal workbook can be downloaded in pdf format upon completion of at least one session and can be viewed at any time.
2. iFOCUS should address the five core components of the FOCUS+ program	The different FOCUS+ components are: “Mutuality and engagement in dyad communication” (F), “Resilience and meaning-making” (O), “Coping and Self-efficacy” (C), “Uncertainty reduction” (U), and “Symptom management” (S). These components provide the basis for both FOCUS+ and iFOCUS. Since iFOCUS is based on the face-to-face FOCUS+ program, they are similar both in content and order of presented topics. As part of the “F” component, dyads are encouraged to establish an alliance, assess their roles, analyse their communication patterns, and reflect on how they support one another. In the “O” component, dyads' emotions are normalized and dyads are encouraged to keep a positive outlook while acknowledging difficulties and setting goals. As part of the “O” component, body image and advance care planning are also discussed. The “C” component concerns their coping styles and how they manage their stress levels, body image, and lifestyle. As part of the “U” component, the dyad is

Key characteristics	Operationalization of key characteristics
	stimulated to discuss and map their uncertainties and identify who can assist them with handling these. The “S” component of symptom management covers the side effects of the treatments as well as the effect on intimacy. Dyads are referred to additional resources for all topics covered. All five FOCUS and FOCUS+ core components are addressed across four web-based sessions. Compared to the FOCUS+ program, iFOCUS has four sessions spread over twelve weeks instead of 2 sessions and 1 follow-up call as for the FOCUS+ intervention. In the FOCUS+ intervention duration of the face-to-face sessions was estimated at 1.5h per session, which we reduced to 1h for the iFOCUS intervention. Extra attention was paid to obtaining a good program flow both within and between the different sessions by linking topics to one another and building on previous information.
3. iFOCUS should have a varied pedagogic approach	Didactically varying materials: Various materials such as written text, voice-overs, exercises, tailoring, animated PowerPoints and videos, testimonials, referrals to external sources such as peer support groups and a personal workbook are needed to increase engagement with the program content and to reduce fatigue in patient-caregiver dyads. Relatable content: For the content of the iFOCUS program, the international consortium was instructed to obtain culturally appropriate and contemporary information or resources. To find this information national scientific and grey literature used in healthcare related settings were used. Visually recognizable: Visually, we aimed to increase relatability for different types of dyads by providing diverse images regarding age, sex, ethnicity, and dyad relationship. Furthermore, we included testimonials to increase recognizability for dyads. Testimonial videos are played at the beginning of the session and depict a dyad that completed the session, reflecting on what they learned from it. Number of sessions and session duration: Increasing the number of sessions and the period in which the program is to be completed allowed us to reduce the length of each session. This decision was based on the preliminary assumption that reduced session length would increase the information retention of dyads as it is less exhausting than longer sessions.

Key characteristics	Operationalization of key characteristics
	Program flow within and between sessions: To ensure a positive experience for dyads when going through the iFOCUS program, it was necessary to obtain a good program flow within and between the sessions. All materials gathered for the FOCUS+ intervention on the five FOCUS components were analysed. Firstly, an overarching structure per individual component was created to provide an overview of which topics per component were discussed in which sessions. The overarching content is divided in such a way that each session/topic builds on previous information related to that session or topic. Having a good program flow across sessions meant that information was built upon, but not repeated. Once the topics and components were spread over the four sessions, we examined each session separately, identifying ways to link different topics together. This was achieved by changing the order of topics within a session in such a way that it allowed a coherent story.
4. the content of iFOCUS (information and exercises) should be tailored to identified needs, priorities and situation of the patient-caregiver dyads	Tailoring: Tailoring allows programs to process the information they receive from users into an individualized reply. This means that tailored programs are likely to fit better to the individual context and needs of their end-users, in contrast to default programs in which content remains the same for all users. Although tailoring was well-received in the original web-based FOCUS program, development of tailoring proved to be very time and resource consuming which resulted in only the F-component being translated to a web-component (Northouse et al., 2014). Because of basic tailoring in the iFOCUS intervention, all components have been translated to a web-based format.
5. iFOCUS aims to facilitate dyadic communication between patients and their family caregivers	Guiding questions: During the sessions, dyads are asked to reflect on themselves, one another, or the dyad. In doing so, they are encouraged to think about their strengths, problems and needs related to various topics such as communication, goal setting or disease management. Following the tailored feedback, the dyads are presented with a page containing several guiding questions that encourage discussion amongst themselves. This is intended to steer the conversation in a certain way to allow both patient and family caregivers to develop further insight into the situation.
6. iFOCUS should be complementary to the regular care.	The iFOCUS program provides information to patient-caregiver dyads complementary to information from other resources. During the various sessions we refer to external resources or direct dyads to relevant organizations or peer support groups.

Key characteristics	Operationalization of key characteristics
7. iFOCUS should be accessible to patient-caregiver dyads	Accessibility: The program is accessible through either a laptop, computer, or tablet as we expected most households to have at least one of these options available. The sessions should be completed by patient-family caregiver dyads, sitting side-by-side at a location of their choice. Intelligibility: To increase intelligibility, all content is written at a lower secondary education level (ranging from age 11-14 in accordance with the International Standard Classification of Education, education category ISCED 2) (Statistics, 2012), using principles of plain language, i.e. easy to read and understand. The program is also available in six languages. Program safety and accessibility: As participants share personal data and information throughout the program, we considered protection of user information to be a key priority during development. As such it was important that access to accounts remained limited to the user of the account. On the other hand, based on the assumption that not all participants are knowledgeable about technology, it was also paramount that the program remained easy to access, in a way that wouldn't be threatening to possible participants. To ensure a safe but uncomplicated way to gain access to the program, we implemented authentication by email. When logging in, users enter their email address. On this address they receive a mail which remains viable for a limited duration and which they need to click on to access the program.

Step 2: Development of mock-ups (September 2019 – October 2019)

The digital mock-ups had limited visuals and were based on the initial PowerPoint and the required technical functionalities (Table B). The functionalities included: information icons, written text, voice-overs to read large sections of text aloud, animated text presentations with guidelines, animated explainer videos for more complex topics, testimonials, referrals to external resources or contact information, exercises, and tailoring. Additionally, a personal workbook is created for each dyad as a reference tool for long-term information retention. The workbook can be downloaded and printed for convenience.

Table B. Functionalities of the iFOCUS program

Functionality	Description of functionality
Information icons	Upon encountering a new functionality for the first time, an information icon appears which can be clicked. When clicked on, an explanation of the functionality is presented.
Written text	Much of the information is delivered through written text using a large font to enhance readability.
Voice-overs	A “reading aloud” option was included for sections with a substantial amount of written text. This option allows participants to have the written text read out loud to increase intelligibility.
Exercises and tailoring	Several exercises are included across the sessions. Sometimes these exercises are simply open-ended questions e.g. “Talk about X with your partner” to allow the dyads to gain more insight into the presented topic. Based on the estimated cost in time and resources we included basic tailoring related to names, their position (if they are sitting left or right), patient-caregiver role, and tailoring to dyads’ information needs, e.g. some exercises are tailored so that certain information is only provided if participants completed an exercise indicating a score below or above a pre-defined cut-off. Tailoring was implemented to make the shift from a more generalist support program to a personalized one and to increase the usefulness of the information for the dyad’s specific situation. Pragmatic choices were made to allow us to create a web-based format for all sessions but with reduced tailoring to decrease the time and monetary effort.
Animated text presentations	Certain information, such as guidelines on how the program works is presented using animated text presentations. These are minimalistic videos in which basic guidelines or rules are presented with key messages appearing on screen, as well as spoken text clarifying them. We included these videos to make practical information more engaging.
Animated explainer video’s	Complex concepts, e.g. advance care planning, are explained using animated explainer videos. These videos explain a concept in a story-like manner, with spoken text accompanying the animations. These videos were implemented to make complex concepts more understandable by representing them visually. Within each video, we aimed to represent different people/dyads in relation to age, sex, sexual orientation, and ethnicity to make the videos as inclusive as possible.
Testimonials	Each session begins and ends with a video testimonial of a patient-family caregiver dyad who completed the program. During the sessions, various written testimonials are also presented. These testimonials are intended to create a feeling of recognisability in participating dyads. The video testimonials are performed by actors reading a script developed by the research team.

Functionality	Description of functionality
Referral to external resources or contacts	During different sessions, patient-caregiver dyads are occasionally directed to external resources, peer support groups or contacts for additional information. This is to keep the webtool concise and to the point. These materials have been evaluated by experts involved in the DIAdIC project during the development of the FOCUS+ intervention.
Personal workbook	Since the webtool remains accessible for a limited time (one year after finishing the last session) we wished to include something that registers both the fixed and the dyad-specific tailored information that was entered by or presented to the dyads. The personal workbook functions as a reference and can be downloaded as a pdf file and printed. The personal workbook is considered a tailored result from participating to the iFOCUS program as it can contain additional supplementary materials, chosen by the dyad.

We experienced considerable limitations in available time and effort towards in-depth personalization through tailoring. Given the time and effort required to develop a fully tailored program, we focused on basic tailoring such as customizing the dyad names, patient-caregiver roles, and exercises. The personal workbook logs both general information as well as personalized information, including answers to exercises.

Step 3: Feedback from the international consortium (November 2019)

The international consortium agreed on redistributing information across program sessions but had concerns with the proposed log-in procedure using two-factor authentication and the impact on program accessibility. To ensure data protection and program accessibility, it was agreed to use a log-in procedure linked to email addresses instead of two-factor authentication, as this could decrease accessibility for participants and reduce retention during the trial. No major issues with the proposed functionalities were identified. This feedback was relayed to the web development team for implementation.

Step 4: Technical development of the iFOCUS program (November 2019 – January 2020)

We developed the iFOCUS program into an entirely new platform. The first fully functional English version of iFOCUS (V1.0) was developed featuring all required technical functionalities. The web development team uploaded a limited amount of information to the platform to present a front-end visualization to the international consortium. Table C shows which topics are presented in each session. We have added a few images from the program as Figures D, E, F and G.

Table C. iFOCUS Components

	Mutuality and engagement in dyad communication	Outlook, Resilience and meaning making	Coping and Self-efficacy	Uncertainty reduction	Symptom management
	F	O	C	U	S
Session					
1	Establish alliance Assess roles and teamwork Identify additional needs for support Communication patterns	Normalizing emotions Maintaining a positive outlook	Different coping styles	Different treatments	Side-effects of treatments
2	Reflection on previous session Impact on family and friends	Acknowledging difficulties Setting goals	Communication towards others	Mapping uncertainties Acknowledging uncertainties	Side-effect assessment Information on side-effects
3	Reflection on mutual support	Impact on body image	Managing body changes Tips to cope with stress Encouraging a healthy lifestyle	Talking about uncertainties to a healthcare provider	Intimacy and sexuality Evaluation of symptoms
4	Reflection on previous sessions	Evaluate change in attitude	Coping with stress and energy management	Evaluate capability for managing uncertainty	Evaluate symptom development

	Refer to extra sources	Advance care planning	Refer to extra sources for help	Inform about help for uncertainty	
		Refer to extra sources			

Figure D: Example of single choice item from iFOCUS

Chapters

Introduction

About you

Family involvement

Communication

Emotions

Coping

Treatments and symptoms

Let's recap

Leave Session

Both

Communication

Take a moment to consider how you usually talk to each other about the cancer. Read the descriptions below and choose the one which best matches how you communicate with one another.

☐

Both of us are open about our feelings, we're comfortable talking about the cancer and how it affects our lives.

☐

One of us is more open about our feelings than the other. We are different in how comfortable we feel when talking about cancer.

☐

Neither of us is very comfortable talking about our feelings. We like to keep our feelings about cancer to ourselves.

☐

None of these describe us.

PREVIOUS

NEXT

Figure E: Example of the option to receive additional information from the iFOCUS program

Chapters

Introduction

About you

Family involvement

Communication

Emotions

Coping

Treatments and symptoms

Let's recap

Leave Session

Both

Communication difficulties



Good communication can be put to the test when someone is seriously ill. Emotions that are commonly linked to cancer, such as fear, grief, anger, can lead to problems in communicating clearly with one another.

Below we have listed some common communication issues experienced by families who are dealing with cancer. You can click on any of the boxes for more details.

BEING OVERPROTECTIVE

BEING INSENSITIVE

EXISTING PROBLEMS

AVOIDING TALKING ABOUT SENSITIVE SUBJECTS

Being overprotective

Some people try to hide their feelings, concerns and fears. They do not want to upset or burden others. So, they try to protect their family and friends by not talking about cancer at all or by changing the subject if it happens to come up. Although their intentions are good, this may lead to difficulties in the long term. People with cancer and loved ones who share their feelings openly are in a better position to receive and provide support to one another.

P

NEXT

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Figure F: Example of the videos used during the iFOCUS programs

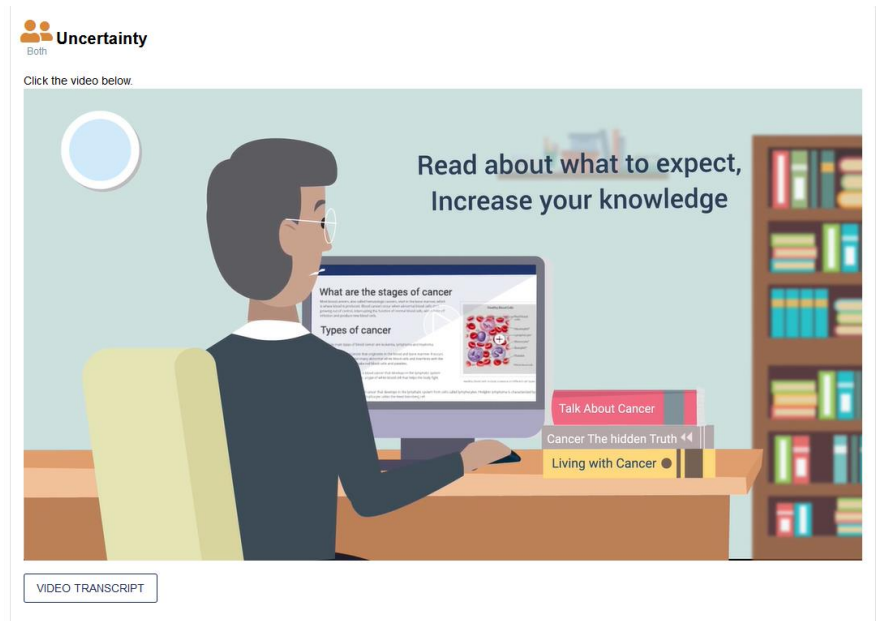


Figure G: Example of exercises for the dyads during the iFOCUS program

Chapters

- Introduction
- Looking back
- Impact of the illness
- Talking With Children
- Uncertainty
- Goals**
- Symptom Management
- Recap
- Leave Session

Goals
Both

An exercise for both of you! Try to think about 3 things that you still want to do (together) and don't want to do anymore, using the tips we've mentioned. This can be anything; certain activities (playing sports, walks...), chores, trips, ... You can write them down together in the scale below.

i

Our Goals

Tip! Download this notepage with both your goals on it, print it out and hang it on your fridge or notice board!

We no longer want to do this

We still want to do this	



Step 5: Creating an iFOCUS version for each of the six participating countries (January 2020 – August 2020)

iFOCUS is available in six languages. As it was developed based on FOCUS+, many materials to be used for iFOCUS had already undergone translation²³. New materials and information were translated by professional translators with input from palliative care experts who spoke the respective native language. All partners provided their translations, which were integrated into the program by the core development team. Since the information was added by non-native speakers, some language errors were expected and were addressed by presenting the program in their respective language to each international partner for feedback. Any linguistic mistakes were reported to the core development team with a clear description, location, and suggested correction. These were addressed by the core development team.

Step 6: Preliminary testing of iFOCUS

A ticketing system was established using an online platform for collaborative project development to manage and track bugs during and after the functional and user testing. Bugs were reported to the core development team with a description and location of the issue. Potential solutions were discussed in weekly meetings with the web development team.

Functional testing

Bugs were classified as either major or minor. Major bugs completely hindered the program's functionality, while minor bugs negatively impacted the user experience. All major bugs were fixed, while minor bugs were evaluated based on their impact versus the effort required to resolve them.

Spelling and grammatical errors, primarily minor, were identified in all sessions and languages. In some exercises, the program logic failed, leading users to irrelevant information. Fixing certain bugs was difficult due to the interconnected nature of the program. Inconsistencies in layout, such as the use of different fonts or colours, were corrected by standardizing the text. Some national teams reported issues with images, such as the depiction of age, sex, or ethnicity, which were replaced. Issues with audio volumes, such as being too loud or soft, were not considered substantial enough to make changes due to the impact on time and budget.

Modifications were made by the responsible partner, research team, or web development team, depending on the situation.

User testing, preliminary acceptability and usability and points of improvement

Twenty dyads and two bereaved family caregivers reviewed the sessions. Patients and family caregivers use the program simultaneously and together behind the same medium (computer or tablet). Participants were mostly female (57.1%) and 55 to 74 years old (72.4%), with most being spouses (81.1%). Breast cancer (25%) and prostate cancer (20%) were the most diagnosed types of cancer among participants. The majority of participants (60%) was in an advanced metastatic stage of cancer (Table D). After participation to the user testing, participants stated that the program structure and content was agreeable and no major issues with program acceptability were mentioned. The program was found to be useful and clear, but some participants felt that some information may not be relevant to them. The session duration was considered appropriate, and participants were satisfied with the variety of videos, text, and exercises. Most comments related to text size and font, spelling errors, and bugs. Videos were well received, although some minor remarks were made about the testimonial videos and their ability to increase the sense of recognition among dyads. Patients with cancer had similar feedback as patients with advanced cancer. No difficulties pertaining to an advanced cancer disease trajectory or its treatment were identified.

“The fact that the videos are supported by text increases the clarity of the information and makes it so that you will remember it longer.” (S, female, Patient, fourth session)

Two major bugs were reported by users: 1) The text was being automatically translated into English and back into their own language while trying to log in, causing the program language to be less than acceptable; 2) Some users were unable to log in due to using outdated software such as Internet Explorer. Most users found the login process to be clear, however, some participants had difficulty navigating the webtool, particularly in starting the videos. Some exercises were also reported to be unclear.

“The exercises – yeah yeah, they could be useful, but we might not need them. Other people might have use for them, but we talk a lot, we have many friends- but there might be people who use them.” (C, Male, Patient, Third session)

Adaptations were made with a pragmatic approach. Time and resource constraints limited the ability to provide additional tailoring, but dyads were given the option to skip certain parts of the program. Major changes to functionalities, content, or form that would have a significant impact

were deemed too costly in terms of time and budget. Instead, minor changes were made to improve the overall quality of the program. We included additional referrals to the “Help” or “Frequently Asked Questions” section to provide better support to dyads. We revised the written text for grammar and clarity and increased font size. Text was also emphasized using italics, bold and underlining to stress important information. The log-in procedure was amended to increase clarity and allow logging in through email. The bug regarding automatic translation was resolved by disabling the translation option provided by web browsers. Participants in the RCT were advised not to use Internet Explorer to access the program.

Table D. Characteristics of participants of user testing (N=42)

Characteristics	Total	Patients	Family caregivers
	N=42	N=20	N=22
	n (%)	n (%)	n (%)
Country*			
Belgium	10 (23,8%)	5 (25,0%)	5 (22,7%)
The Netherlands	8 (19,0%)	4 (20,0%)	4 (18,2%)
The United Kingdom	7 (16,7%)	3 (15,0%)	4 (18,2%)
Ireland	1 (2,4%)	0 (0,0%)	1 (4,5%)
Italy	6 (14,3%)	3 (15,0%)	3 (13,5%)
Denmark	10 (23,8%)	5 (25,0%)	5 (22,7%)
Sex*			
Female	24 (57,1%)	9 (45,0%)	15 (68,2%)
Male	18 (42,9%)	11 (55,0%)	7 (31,8%)
Age*			
18-34	1 (2,7%)	0 (0,0%)	1 (5,3%)
35-54	8 (22,2%)	3 (17,7%)	5 (26,3%)
55-74	26 (72,4%)	13 (76,5%)	13 (68,4%)
75+	1 (2,7%)	1 (5,8%)	0 (0,0%)
Type of cancer patients**			
Breast cancer	5 (25%)		
Prostate cancer	4 (20%)		
Oesophageal cancer	2 (10%)		
Other types of cancer	9 (45%)		

Characteristics	Total	Patients	Family caregivers
Cancer stadium patients**			
Stage IV	12 (60%)		
In Remission	2 (10%)		
Unknown	6 (30%)		
Relationship***			
Spouses	17 (77,3%)		
Parent/child	3 (13,6%)		
Bereaved carers	2 (9,1%)		
Issues logging in?***			
Yes	15 (68,2%)		
No	7 (31,8%)		
Missing values for Age: N=6 (14.3%). Percentages may not add up to 100% because of rounding.			
* Percentages calculated on patient-caregiver individual level			
** Percentages calculated on patient-level, N=20			
** Percentages calculated on dyad-level, N=22			

Step 7: Implementing the final version in an RCT (February 2021)

The final iFOCUS program consists of four sessions that patients and their family caregivers access together and simultaneously using the same device over a 12-weeks period, with a three-week break between sessions. Each session lasts approximately 60 minutes. The program has been implemented in six different languages for six European countries participating in an RCT to evaluate its effectiveness. To implement iFOCUS in the RCT, an onboarding procedure was deemed necessary to introduce participants to the program's timeline and goals and to gather the necessary information for enrolment. This information, including the participants' names and their relationship, will be entered into the system and used to tailor the program. The onboarding procedure was developed by the core development group in collaboration with data collectors and was approved by the international consortium. The process was written down in a guide to be used by data collectors during recruitment. After setting up a profile, both the patient and family caregiver will receive an email inviting them to complete the first session together on the same screen. The program automatically sends emails to participants at a set time for future

sessions. Currently, iFOCUS is being evaluated as part of an international RCT to determine its effectiveness on the quality of life, emotional functioning, self-efficacy, healthcare resource use, and cost-effectiveness among patients with advanced cancer and their family caregivers (ClinicalTrials.gov Identifier: NCT04626349)²². The study will also gather information on participant satisfaction with iFOCUS and aim to uncover its underlying mechanisms.

4. DISCUSSION

4.1. Main findings

The iFOCUS program consists of four sessions over a 12-week period, with a three-week gap between each session. During its development, seven steps were taken: (1) concept design, (2) development of mock-ups, (3) obtaining feedback from the international consortium, (4) technical development of the program, (5) creating country-specific versions for each of the six participating countries, (6) preliminary testing through user and functional testing and (7) implementing the final version for the RCT. Using the Scrum methodology allowed for flexibility and adaptability in the development process, as it included alternating periods of program development and evaluation. Collaboration between different teams and integration of different perspectives helped resolve issues related to program flow, content, language, layout, and bugs, but some pragmatic choices were necessary considering project limitations. User and functional testing showed that the program was acceptable and functional. By building on the philosophy of the FOCUS and FOCUS+ program for patients with advanced cancer and their family caregivers, and by keeping the emphasis on this population during development, no specific remarks pertaining to advanced cancer were identified, indicating the program's successful adaptation to address patients with advanced cancer and their family caregiver. The development process resulted in a self-management psychoeducational eHealth program for people with advanced cancer and their family caregivers that can be used autonomously by the patient-caregiver dyad. Currently, the effectiveness of iFOCUS is being tested in an international RCT. Various challenges were encountered across different steps of development (Table E). The challenges we encountered were related to transferring ideas into working functionalities, spreading of the content, tailoring, determining the log-in procedure, input of translated materials and determining an onboarding procedure.

Table E. Experienced challenges during development

Specific or general challenges	Description of the challenge	Resolved how?
Specific challenges	<i>The amount of information provided in three sessions made the session duration too long:</i> Taking into account the impact of the disease progression on the dyad and related symptom burden the duration of sessions needed to be shorter.	Redistributing the session information across four sessions instead of the initial three was done by the core development group during an iterative process. Different renditions of the program structure were evaluated with attention to program flow within and between sessions. Increasing the amount of sessions allowed the duration of individual sessions to be shorter.
	<i>The amount of tailoring:</i> Tailoring could increase meaningfulness of a program for dyads but in-depth tailoring adds additional complexity to the program code and is a time and resource consuming process.	We focused on basic tailoring such as customizing the dyad names, patient-caregiver roles, and exercises.
	<i>Information input in different languages:</i> Partners provided translations of materials in their respective language. All information was put in by the core development team with knowledge of Dutch and English (limited). Issues in the input of translations was expected mostly in Danish and Italian.	During functional testing programs were presented in the local language to the respective teams. Based on these meetings language errors were filtered out. During user testing further language errors were also removed.
	<i>Onboarding of participants:</i> To provide participants the necessary information on the DIAdIC trial, to introduce them and to reassure them of support, an onboarding procedure needed to be developed to mitigate any challenges related accessing the iFOCUS program.	The onboarding procedure was developed in collaboration with an international consortium and carried out by a data collectors who received a guide with the necessary steps.
General challenges	<i>As researchers conveying the idea of a concept to a web developer:</i> While researchers have	By using a PowerPoint presentation the researchers could use imagery and

Specific or general challenges	Description of the challenge	Resolved how?
	knowledge on topic substance they lack the technical knowledge that web developers have and vice versa. As such their ideas need to be translated to something visual in a way feasibility can be determined.	descriptions on the related functions, which facilitated the online meetings between the two teams.
	<i>Correctly estimating the time and effort for eHealth development:</i> Development of eHealth programs is prone to bugs and at the same time constantly evolving. This makes it difficult to correctly estimate the required time and effort beforehand.	Pragmatic choices were made on how much time and resources were available for the development of the iFOCUS program. During meetings with the web developing team and the international consortium endpoints of development were set.
	<i>Log-in procedure:</i> Developing a log-in procedure which is safe (protects the collected data) as well as easy to use is a balancing act, as safer log-in procedures such as 2-factor authentication often require higher digital skills.	During meetings with the international consortium we brainstormed on the potential safe and easy ways of logging in. Considering that participants needed to register with an email address the consortium assumed that participants could at least work with email and it would be safe and feasible to work with a log-in link being sent to the email address.

4.2. Interpretation and implications of the findings

We encountered challenges common to eHealth development in general as well as specific challenges related to the requirements of the iFOCUS webtool. A general challenge was that despite being functional and usable, there is always room for improvement in eHealth web programs, as they are continually evolving³⁵. Estimating the effort and resources required to develop an eHealth program is challenging, as previous research has shown that eHealth development costs depend on specific program requirements³⁶.

Program-specific challenges during the development of iFOCUS included deciding on the level of tailoring to be implemented. Tailoring can ensure that the program is applicable to the dyad by increasing the perceived program relevance³⁷. Moreover, it increases program engagement and improves outcomes¹⁶, but also adds complexity to the coding and can result in errors³⁸⁻⁴⁰. Additionally, although eHealth interventions might be more cost-effective than face-to-face interventions, designing and developing tailored programs is a very resource-consuming endeavor⁴¹ which explains why we limited the level of tailoring in iFOCUS. Another difficulty encountered during the development of iFOCUS and reported in similar studies is the rapid advancements in technology⁴². Since advanced cancer is more common in older adults⁴³ who often have lower digital competence⁴⁴ it is also critical to be aware of challenges associated with age and the uptake of technological innovations which can be reflected in difficulties with onboarding, logging-in or working with the program in general.

iFOCUS is designed to be used outside of clinical settings, but still requires personal interaction as part of the registration process due to barriers to digital program participation such as limited access to the internet or data, low computer use, and low digital literacy⁴⁵. Interpersonal contact is crucial in overcoming these barriers⁴⁶ and enhancing the user experience and program adherence by improving verbal and non-verbal communication, and building trust between clinicians and participants^{47,48}. Nevertheless, it is essential to be aware of the potential impact of personal interaction as part of the iFOCUS onboarding procedure⁴⁹ without compromising the intended self-sufficient nature of the program.

4.3. Strengths and limitations

Other than the FOCUS program that iFOCUS was based on, there are to our understanding no other dyadic, self-managed, tailored eHealth programs for people with advanced cancer and their family caregivers. The iFOCUS program benefits from being built on the evidence-based face-to-face FOCUS program and its underlying conceptual framework, Lazarus and Folkman's Model of Stress & Coping, and a salutogenic approach. The development of iFOCUS was carried out through an iterative process that involved various teams with different areas of expertise, leading to a wider range of perspectives and access to a broad spectrum of skills. Using the Scrum methodology allowed for multiple feedback loops during development, both within and

between teams, which allowed efficient contributions towards improving the quality of the program and its content.

This study also has some limitations. Due to limited time and resources, it was only possible to receive feedback from end-users in one of the later stages during the development process, i.e. during user testing. Ideally, we would have liked to involve end-users in all stages of the program development as end-users' experiences, insights, and interests are often better incorporated in a co-design process⁵⁰, which can contribute to long-term program availability and implementation⁵¹. Due to limitations in both time and resources, the development team was forced to make pragmatic choices. Furthermore, the COVID-19 pandemic made recruitment for the functional testing challenging. As such we also included bereaved caregivers and people with non-advanced cancer who might have different experiences than those in an advanced stage of the disease^{7,8}.

4.4. Conclusions

Developing a tailored, self-managed eHealth program for dyads is a complex process and involves making pragmatic choices, particularly regarding the level of tailoring. By its nature, an eHealth program requires constant revision and updates. Communication between program developers and end-users is recommended during and after the development of the program, to improve program quality

DECLARATIONS

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VVG, SD, OM, LN, LD, LL, PH, ADV and JC contributed to conception and design of the study. VVG and OM acquired and analysed the data. All authors contributed to the interpretation of the data. VVG, SD, ADV, and JC drafted the manuscript. All authors revised the manuscript critically for important intellectual content and approved of the version of the manuscript to be published.

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Conflicts of interests

Declarations of interest: none

Data availability:

The data sets generated and analysed during the current study are available from the corresponding author upon reasonable request.

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CHAPTER 3

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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Vincent Van Goethem, listed as the FIFTH AUTHOR on this paper, was involved in the data collection of the trial and participated in the review process of this article prior to its submission. This paper is included as part of the PhD dissertation to provide additional background information or to facilitate a discussion on the effectiveness of eHealth.

This paper was included in the PhD dissertation of the first author, Orphé Matthys.

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 multicentre 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.

1. BACKGROUND

Each year, 3.7 million people in Europe are diagnosed with cancer, accounting for 1.9 million deaths¹. The symptoms and burden of cancer patients range from anxiety and depression to pain and fatigue². 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 tasks³. 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 implications⁴. 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 illness⁵⁻⁷. 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 interventions⁸. 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 al⁵ 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 format⁶. 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.

2. 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.

2.1. 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.

2.2. Trial design

This study is an international multicentre 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).

3. METHODS

3.1. 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 systems¹⁰), (3) regional variation across Europe (Northern, Western, Southern) and (4) a relatively advanced level of palliative care development and integration within oncology care.

3.2. 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			

Based on recurrent input from recruitment centres, it was concluded that the use of the surprise question “*the treating physician would not be surprised if the patient died within two years or less*” created a barrier during recruitment. Therefore it was decided to remove this as one of the inclusion criteria.

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 centres

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

3.3. 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 Folkman¹¹. In this model, stress is the result of a dynamic interaction between an individual and their environment. In this model, the individual assesses the stressor (primary appraisal) and the ability to cope with the stressor (secondary appraisal). As a result coping strategies are employed to manage or mitigate the stress, which can either be problem-focused or emotion-focused coping. 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 caregivers¹².

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 intervention⁵ 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.

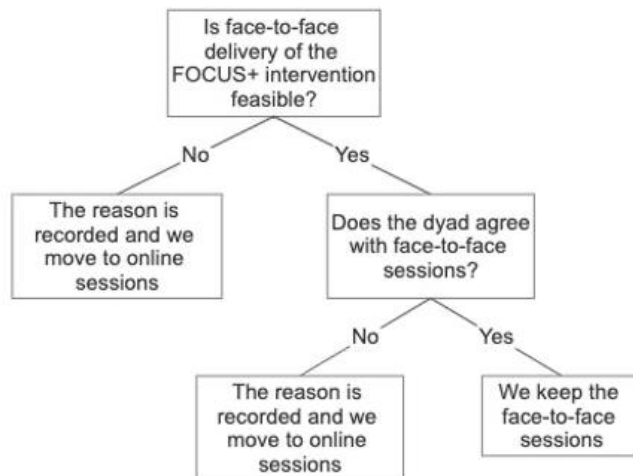
Table 3: Five conceptual core components of the FOCUS+ and iFOCUS interventions

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 analyse 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.

3.4. 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 T₁. The secondary endpoints are QoL of the patient and caregiver, benefits of illness, coping, dyadic communication, ways of giving support at T₁. All listed primary and secondary outcomes are measured at T₂ and formal healthcare use and costs are measured at T₁ and T₂.

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 3 and 4.

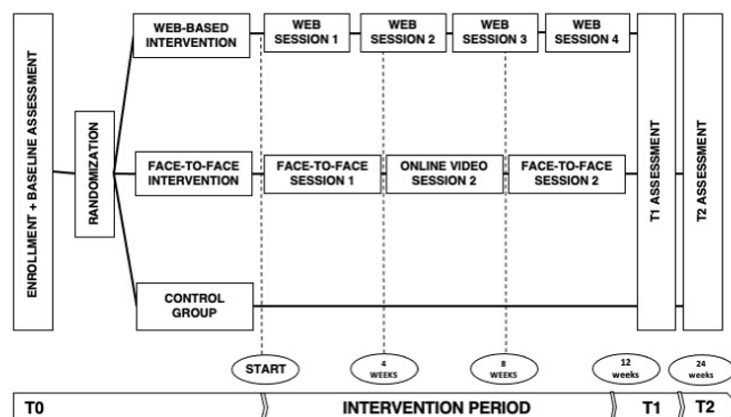
Table 4: Instruments, underlying concepts, and timing

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				

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



3.6. 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 hypotheses¹⁰. 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 interventions⁵⁻⁷ 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 US⁵⁻⁷ 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.

3.7. 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.

3.8. 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 service¹⁴. 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.

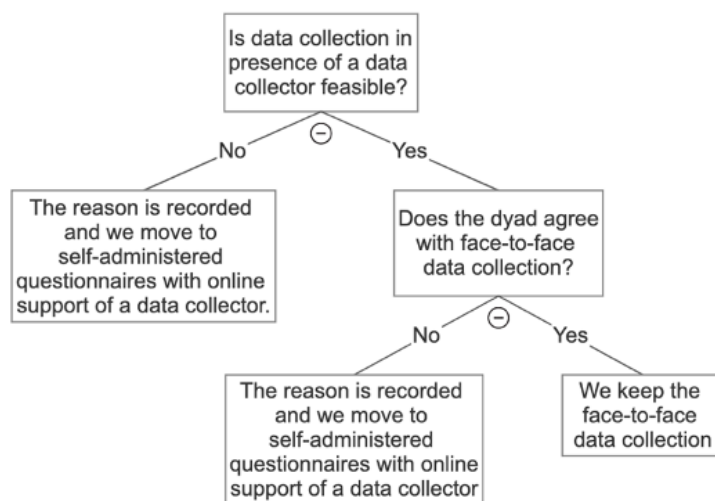
3.9. Data collection, management, and analysis

Data collection methods

The outcomes and outcome measures are described in 2.4. 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 T₂, 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 centre 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 analysing 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, sex, and socioeconomic status. Interaction terms between respectively country, sex, 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 analysed following the framework for evaluating complex interventions¹⁵, integrating normalization process theory (NPT)¹⁶ and the RE-AIM framework¹⁷. 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.

3.10. 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 behavioural 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.

3.11. 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 Middelaers, 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.

4. DISCUSSIONS

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 themselves¹⁸. 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 analysing 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 enrol 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.

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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, PJJ, 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 4

TRIAL RESULTS REGARDING TRIAL RECRUITMENT AND RETENTION, EFFECTIVENESS, IMPLEMENTATION WITHIN THE TRIAL AND SUSTAINABLE IMPLEMENTATION BEYOND THE TRIAL SETTING

CHAPTER 4

Influence of digital competence on participation and retention of patients with advanced cancer and their family caregivers in a randomized controlled trial with an eHealth component: findings from the DIAdIC trial

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ABSTRACT

Background: eHealth programs to empower people with cancer and their family caregivers can improve their quality of life. Successful engagement with eHealth programs requires digital competence. People with lower digital competence might be less likely to participate and complete eHealth trials, affecting trial validity.

Objective: To explore how digital competence differs between individuals according to sociodemographic characteristics and how it influences participation and retention to a trial with an eHealth component.

Methods: We analysed data collected as part of the DIAdIC trial in which a psychoeducational web and face-to-face program for people with advanced cancer and their family caregivers were developed and tested. Recruitment log-files were quantitatively assessed for non-participation reasons. Descriptive statistics outlined sociodemographic factors and digital competence. Multivariable linear regressions assessed digital competence. We reported unstandardized coefficients, 95% confidence intervals and p-values. Logistics regressions examined retention rates. We reported odds ratios and 95% confidence intervals

Results: Among those refusing participation in the trial (N=1752), 2.1% (n=37) cited ICT related factors. Enrolled patients reported lower digital competence than family caregivers (mean 3.07, SD 0.94 vs 3.17, SD 0.090; $p=0.046$). While digital competence varied by sociodemographic characteristics of patients and their family caregivers, digital competence did not significantly predict drop-out.

Conclusion: ICT-related factors were rarely mentioned as a reason for non-participation. Digital competence is associated with sex, age, trial location, educational attainment and perception of income. eHealth related factors or digital competence are no reasons for non-participation to studies with an eHealth component.

1. INTRODUCTION

Rapid digitalization has expanded the use of information and communication technologies (ICT) across society^{1,2}. Although eHealth is defined differently by many authors, it is often conceptualized as the use of ICT in healthcare with the intent to engage, inform, support, and empower patients and/or caregivers^{3,4}.

Patients with advanced cancer and their family caregivers are negatively affected by the disease and can experience increased distress and reduced quality of life⁵⁻⁷. eHealth programs have been shown to improve self-efficacy, informed decision-making and quality of life in people with advanced cancer and their family caregivers while also decreasing their distress^{8,9}. Additionally, eHealth programs could provide cost-effective means of providing care and support through remote patient monitoring, effectively reducing pressure on professional caregivers¹⁰⁻¹².

Digital competence is a set of knowledge, skills, and attitudes that allow confident, critical and responsible use of digital technologies¹³. Lower levels of digital competence may impede patients' access to programs with an eHealth component¹⁴⁻¹⁶. Digital competence can be influenced by various sociodemographic variables such as sex, age, and education level¹⁷. Older people with chronic diseases and lower levels of education, who live in rural areas, are most impeded in their access to eHealth based support programs, while they might benefit the most from additional support¹⁸⁻²¹.

Adults with a lower level of digital competence may be less likely to participate and remain in partly or completely digital trials, introducing selection bias that could threaten the internal validity of RCTs²²⁻²⁴. Furthermore, external validity can also be threatened if people with no or lower digital competence systematically participate less in trials with an eHealth component, resulting in a biased estimation of the potential value and benefits in actual practice²⁵.

Therefore, it is crucial to empirically assess how digital competence affects participation and retention. The DIAdIC trial comprised a three-arm psychoeducational intervention trial for people with advanced cancer and their family caregivers (referred to as dyads) incorporating eHealth in one arm²⁶. Additionally, computer-assisted data collection methods were performed across study arms^{17,23,24}. This trial provides an opportunity to explore the influence of digital competence on the participation and retention of patients with advanced cancer and their family caregivers. We address the following research questions:

1. How often did eligible patients and family caregivers for an international RCT with an eHealth program component explicitly mention ICT as a reason for non-participation?
2. What is the self-reported digital competence among participants enrolled in an RCT with an eHealth program component and what are the associated socio-demographic factors?
3. To what extent does self-reported digital competence predict the retention of participants in an international RCT with an eHealth program component?

2. METHODS

2.1. Study design and setting

We analysed data collected during the DIAdIC trial (“Dyadic psychoeducational Interventions for people with Advanced cancer and their Informal Caregivers”) where we developed and tested a psychoeducational face-to-face program (FOCUS+) and web program (iFOCUS) for people with advanced cancer and their family caregiver. The primary outcomes of the DIAdIC trial were emotional functioning and self-efficacy. The secondary outcomes were quality of life, benefits of illness, coping, dyadic communication, and ways of providing support. The DIAdIC trial spans six European countries (Belgium, The Netherlands, Denmark, Italy, The United Kingdom, and Ireland). Details of the study procedures related to RCT can be found elsewhere²⁶.

2.2. Recruitment and participants

Eligible dyads included patients diagnosed with solid organ cancer who no longer received curative treatment, had a prognosis of at least three months, and were able to identify a family caregiver who was willing to participate. Dyads were excluded if the patient was diagnosed with brain or non-solid cancer, had a prognosis of three months or less, the identified family caregiver was unable to participate or was diagnosed with cancer the past year, individuals were under 18, or were unable to communicate in available languages. Potential participants were required to possess minimum proficiency in using smartphones, computers, or tablets.

Hospital staff screened and referred potential participants. Research staff provided oral introductions to the study. When agreeing to participate, both patient and family caregiver individually provided an informed consent.

2.3. Data collection

The research staff registered information on the screening, recruitment, and participation in an Excel log file. For the RCT, data were collected at three points, but only the baseline (T0) and first follow-up (T1) data were utilized for the research questions presented in this article. The questionnaires were available in the native languages of the participating countries. Data collection methods included self-administered computer-assisted interviews with online support, if needed, or pen and paper surveys. The patients and family caregivers completed the survey independently. Following the completion of the baseline survey, the dyads were randomized into one of the intervention arms or a control group. The data were collected between March 2021 and August 2023.

2.4. Measures

(non-)participation and retention

While a standardized Excel log file for recording participation and non-participation was made available to the partner countries, different regulations among international partners and recruitment centres made it difficult to uphold standardized reporting in these log files. Participants included those who expressed intent, signed an informed consent form, and completed the baseline questionnaire. Eligible individuals declined participation and did not sign an informed consent form were considered non-participating. The participating dyads were randomized to either the intervention arm or the control group. We defined the retention population as participants who completed the T1 follow-up measurements.

Self-reported digital competence

Digital competence was measured by calculating the mean score of two items in the baseline questionnaire: “In general I feel comfortable using a computer, a smartphone or tablet” and “In general I think I am skilled when it comes to using computers, smartphones or tablets” with answers ranging from “Not at all” (1) to “Very much” (4) on a 4-point Likert scale. These items were developed by the researchers of the original FOCUS web-program, predating the development of iFOCUS and FOCUS+²⁷.

Sociodemographic and clinical characteristics

Participants completed sociodemographic items in the baseline questionnaire related to: dyadic relationship, sex, age, household composition, educational attainment, and perception of income. Additionally, research staff registered the trial location and patient's cancer type.

2.5. Data analysis

The recruitment log-files from all participating countries were analysed, identifying ICT-related keywords such as but not limited to 'Computer', 'Tablet', 'Internet', 'Not skilled in using a computer', quantitatively assessing their frequency.

Descriptive statistics were used to summarize sociodemographic variables and self-reported digital competence. Spearman's correlation test assessed whether comfort and skill with computers, tablets, or laptops formed a single factor (digital competence). We performed a Pearson chi-square test to compare responses on feeling comfortable and feeling skilled using a computer, smartphone, or tablet between patients and family caregivers. The variable 'digital competence' was derived from the mean scores of feeling comfortable and skilled using a computer, tablet, or laptop. The difference in digital competence between patients and family caregivers was measured using an independent-sample t-test.

We identified potential predictors of digital competence through the scientific literature and constructed directed acyclic graphs (DAGs) to hypothesize causal relations (Appendix 5, figures 1-6) and guide a deconfounding strategy. Multivariable linear regressions were conducted separately for the patients and caregivers, adjusting for relevant confounders. We reported unstandardized coefficients with 95% confidence intervals and p-values, with significance set at $p \leq 0.05$. We performed a logistic regression for patients and family caregivers individually, analysing retention with digital competence as the predictor, both unadjusted and adjusted for confounders, such as sex, age, and education. We reported the retention rates in absolute numbers and percentages, unadjusted and adjusted odds ratios, and 95% confidence intervals. All statistical analyses were performed using IBM SPSS Statistics (version 29).

2.6. Ethical considerations

All the patients and family caregivers who participated in this study provided written informed consent. The study was approved by the ethics committees of all the participating countries. 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, amended four times (7/09/2021 – 8/02/2022–10/05/2022–06/09/2022); NHS/HSC Research Ethics Committee, United Kingdom, 05/03/2021; Medisch Ethische Toetsings Commissie Erasmus Medisch Centrum Rotterdam, 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 submission of the final protocol.

3. RESULTS

Regarding the first research question on how often eligible patients and family caregivers explicitly mentioned ICT as a reason for non-participation, 37 out of 1752 non-participants (2.1%) explicitly cited ICT-related factors. Within this group, 1.5% expressed not feeling competent enough to engage with a program with an eHealth component, and 0.6% reported the absence of a computer, tablet, or Internet to access online programs (not reported in table). No specific reason for non-participation was reported in 17% of cases, 5.2% were unable to be contacted further, and 10.6% reported “no interest” without elaboration. Disease progression or patient death accounted for 17.2% of the refusals, with the remaining 47.9% citing other unspecified reasons.

In total, 862 participants (431 patients and 431 family caregivers) participated in the DIAdIC trial (Table 1). Most of the participants were enrolled in Belgium (34.1%), Italy (29.2%), and Denmark (24.8%). Patients were most often diagnosed with gastrointestinal (28.8%) or breast cancer (25.5%), and were predominantly spouses or partners or the participating family caregiver (75.6%). Most participants were female (patients: 54.7%, family caregivers: 59.2%), with an average age of 62 years (patients) and 58 years (family caregivers). Approximately 56.3% of the patients and 59.7% of the family caregivers attained secondary education. Approximately half of the patients and family caregivers reported living comfortably on their current income (48.7% and 49.5%, respectively).

Table 1: Sociodemographic and clinical characteristics of patients and family caregivers participating in the DIAdIC trial

	Patients (N=431)	Family caregivers (N=431)
	N (%)	N (%)
<i>Trial location^a</i>		
Belgium	294 (34.1%)	294 (34.1%)
Italy	252 (29.2%)	252 (29.2%)
Denmark	214 (24.8%)	214 (24.8%)
UK	56 (6.5%)	56 (6.5%)
The Netherlands	22 (2.6%)	22 (2.6%)
Ireland	24 (2.8%)	24 (2.8%)
<i>Cancer type^a</i>		
Gastrointestinal	124 (28.8%)	NA
Breast	110 (25.5%)	NA
Other ^b	69 (16.0%)	NA
Lung	47 (10.9%)	NA
Prostate	33 (7.6%)	NA
Gynaecological	27 (6.3%)	NA
Kidney	21 (4.9%)	NA
<i>Dyadic relationship: The family caregiver is my ...^a</i>		
Spouse/partner	326 (75.6%)	NA
Parent	46 (10.8%)	NA
Daughter/son	35 (8.3%)	NA
Friend	13 (3.0%)	NA
Sister/brother	10 (2.3%)	NA
Other relative	1 (0.3%)	NA
<i>Sex</i>		
Female	236 (54.7%)	255 (59.2%)
Male	195 (45.3%)	176 (40.8%)
<i>Age, Mean (SD)</i>	62.61 (10.10)	58.12 (13.73)
<i>Children^c</i>		
I do not have children	62 (14.0%)	87 (19.5%)
I have children under the age of 18	49 (11.0%)	70 (15.7%)
I have adult children age 18 years or older	334 (75.0%)	288 (64.8%)
<i>Educational attainment</i>		

	Patients (N=431)	Family caregivers (N=431)
Primary education	13 (3.1%)	8 (1.9%)
Secondary education	239 (56.3%)	253 (59.7%)
Higher education	172 (40.7%)	167 (39.0%)
<i>Perception of income: Which description comes closest to how you feel about your household income nowadays?</i>		
Very difficult on present income	13 (3.0%)	6 (1.4%)
Difficult on present income	41 (9.5%)	30 (7.0%)
Coping on present income	150 (34.9%)	156 (36.3%)
Living comfortably on present income	210 (48.7%)	213 (49.5%)
Prefer not to answer	16 (3.7%)	23 (5.3%)
Don't know	1 (0.2%)	2 (0.5%)
NA = Not applicable. Missing values in patient sample: age: n=1 (0.23%), Dyadic relationship: n=2 (0.46%), Children: n=6 (1.39%) educational attainment: n=7 (1.6%), Perception of income n=1 (0.23%), Missing values in family caregiver sample: age: n=1 (0.23%), educational attainment: n=3 (0.7%), perception of income n=1 (0.23%), ^a On dyad level ^b Other types of cancer: Head and neck cancer, melanoma, bladder cancer, malignant cancer of other ill-defined sites ^c Percentages may not add up to 100% as participants could indicate more than one option.		

3.1. Self-reported digital competence and its associated factors.

Regarding our second research question on self-reported digital competence among participants enrolled in the trial, patients reported an overall mean digital competence of 3.07 (SD=0.94) (with a maximum score of 4), which was significantly lower than that of family caregivers (mean 3.17, SD 0.90) ($p=0.046$) (Table 2). Patients and family caregivers significantly differed in feeling comfortable, although both most often reported feeling quite a bit comfortable (30.6% of patients, 27.1% of family caregivers) or very comfortable (47.3 and 51.8%, respectively) when using a computer, smartphone, or tablet. Patients significantly more often reported that they were not skilled in using a computer, smartphone, or tablet (11.9%) compared to family caregivers (6.7%), while family caregivers reported being very skilled in using a computer, smartphone, or tablet (43.7%) compared to patients (37.8%) ($p=0.027$).

Table 2: Self-reported digital competence of participants Participating in the DIAdIC trial

	Patients (N=431)	Family caregivers (N=431)	P-value*
	N (%)	N (%)	
Digital competence, Mean (SD)	3.07 (0.94)	3.17 (0.90)	0.046
<i>I feel comfortable using a computer, a smartphone or tablet ^a</i>			0.377
Not at all	29 (6.8%)	21 (4.9%)	
A little	66 (15.3%)	69 (16.0%)	
Quite a bit	132 (30.6%)	117 (27.1%)	
Very much	204 (47.3%)	223 (51.8%)	
<i>I think I am skilled using a computer, a smartphone or tablet ^a</i>			0.027
Not at all	51 (11.9%)	29 (6.7%)	
A little bit	82 (19.0%)	92 (21.4%)	
Quite a bit	135 (31.3%)	121 (28.1%)	
Very much	163 (37.8%)	188 (43.7%)	
* P-value for difference between patient and family caregivers			
^a Missing values: n=1 (0.23%) family caregiver			

In patients, lower digital competence was found among those who were older ($B=-0.02$, $P<0.001$) and those with financial difficulties (difficult on present income $B=-0.25$, $P=0.016$; Very difficult on present income, $B=-0.50$, $P=0.043$). In patients higher digital competence was found among those from Denmark ($B=0.50$, $P<0.001$) and those with higher ($B=1.18$, $P<0.001$) or secondary ($B=0.53$, $P=0.008$) educational attainment (Table 3). Conversely, family caregivers included men ($B=0.24$, $P=0.006$), individuals from Denmark ($B=0.44$, $P<0.001$), and those with higher ($B=1.49$, $P<0.001$) or secondary ($B=0.97$, $P<0.001$) education who reported higher digital competence. Additionally, older family caregivers ($B=-0.02$, $P<0.001$) and those with financial difficulties (Difficult on present income, $B=-0.30$, $P=0.046$) reported lower digital competence.

Table 3: Factors associated with self-reported digital competence in patients and family caregivers participating in the DIAdIC trial

	Patients			Family caregivers		
	Estimate	95% CI	P-value	Estimate	95% CI	P-value
Sex ^a						
Female	Reference			Reference		
Male	0.13	-0.05, 0.31	0.162	0.24	0.07, 0.41	0.006
Age ^{a, b}	-0.02	-0.03, -0.02	<0.001	-0.02	-0.03, -0.02	<0.001
Trial location ^a						
Belgium	Reference			Reference		
Italy	-0.16	-0.38, 0.06	0.149	-0.01	-0.31, 0.11	0.358
Denmark	0.50	0.28, 0.73	<0.001	0.44	0.22, 0.66	<0.001
The Netherlands	0.14	-0.42, 0.70	0.615	0.20	-0.34, 0.74	0.473
Ireland	0.34	-0.20, 0.88	0.214	0.09	-0.43, 0.61	0.729
UK	-0.24	-0.61, 0.13	0.196	0.19	-0.16, 0.55	0.289
Educational attainment ^c						
Primary education	Reference			Reference		
Secondary education	0.53	0.14, 0.90	0.008	0.97	0.50, 1.44	<0.001
Higher education	1.18	0.79, 1.52	<0.001	1.49	1.01, 1.91	<0.001
Children ^d						
I do not have children	Reference			Reference		
I have children under the age of 18	-0.11	-0.39, 0.18	0.466	-0.07	-0.30, 0.16	0.541
I have adult children age 18 years or older	0.04	-0.18, 0.26	0.701	0.03	-0.19, 0.25	0.774
Perception of income ^e						
Living comfortably on present income	Reference			Reference		
Coping on present income	-0.17	-0.35, 0.06	0.058	-0.14	-0.33, 0.01	0.039
Difficult on present income	-0.35	-0.64, -0.07	0.016	-0.30	-0.60, -0.01	0.046
Very difficult on present income	-0.50	-0.98, -0.02	0.043	0.41	-0.21, 1.04	0.195
^a No Confounders						
^b Age as continuous variable						

^c Confounders controlled for: Age, sex, trial location
^d Confounders: Educational attainment, income level and age
^e Confounders: Educational attainment, trial location, age & sex

3.2. Influence of self-reported digital competence on retention

Nearly four in five patients (79.8%, n=344/431) and family caregivers (79.4%, n=342/431) were retained in the study at T1. The retention rates for the patients and caregivers were 71.6% (n=106/148) and 68.9% (n=102/148) in the iFOCUS trial arm, 83.6% (n=117/140) and 86.4% (n=121/140) in the FOCUS+ trial arm, and 84.6% (n=121/143) and 83.2% (n=119/143), in the control group respectively.

High digital competence was associated with a higher likelihood of retention in the trial among patients but not among caregivers across all study arms. When performing separate analyses per study arm, there was no statistically significant association between digital competence and retention. Additionally, after adjusting for age, sex, and educational attainment, self-reported digital competence at the patient and family caregiver levels was not significantly associated with trial retention in either the study arm or the overall trial (Table 4).

Table 4: Association of self-reported digital competence with retention

	<i>Patients</i>		<i>Caregivers</i>	
	Unadjusted OR (95% CI) ^a	Adjusted OR (95% CI) ^b	Unadjusted OR (95% CI) ^a	Adjusted OR (95% CI) ^b
<u>Across all study arms</u>				
Low digital competence	Reference	Reference	Reference	Reference
Medium digital competence	0.92 (0.50, 1.69)	0.81 (0.43, 1.53)	0.78 (0.40, 1.51)	0.71 (0.35, 1.41)
High digital competence	1.88 (1.02, 3.48)	1.53 (0.77, 3.06)	1.14 (0.61, 2.11)	0.93 (0.45, 1.91)
<u>IFOCUS web-program arm</u>				
Low digital competence	Reference	Reference	Reference	Reference
Medium digital competence	1.89 (0.73, 4.89)	1.88 (0.70, 5.08)	0.82 (0.31, 2.16)	0.92 (0.33, 2.57)
High digital competence	2.18 (0.89, 5.37)	1.96 (0.68, 5.63)	1.61 (0.63, 4.09)	1.63 (0.53, 5.02)
<u>FOCUS+ face-to-face arm</u>				
Low digital competence	Reference	Reference	Reference	Reference
Medium digital competence	0.55 (0.18, 1.65)	0.39 (0.11, 1.34)	0.93 (0.24, 3.60)	0.53 (0.10, 2.89)
High digital competence	2.16 (0.61, 7.68)	2.13 (0.47, 9.66)	0.86 (0.24, 3.03)	0.42 (0.08, 2.29)
<u>Control group</u>				
Low digital competence	Reference	Reference	Reference	Reference

Medium digital competence	0.56 (0.16, 1.99)	0.46 (0.12, 1.78)	0.76 (0.18, 3.14)	0.70 (0.17, 2.79)
High digital competence	1.44 (0.39, 5.22)	0.91 (0.22, 3.73)	0.74 (0.19, 2.94)	0.89 (0.27, 2.99)
^a Bivariate analysis ^b Logistic regression analysis in patients and family caregivers with retention as dependent variable and digital competence as independent variable, adjusted for sex, age and educational attainment				

4. DISCUSSION

4.1. Main findings

In this international dyadic RCT in which one of the three arms was an eHealth program, we found no indication that the digital competence of either the patient or the family caregiver plays a substantial role in decisions to participate in the study, nor that it predicts retention. Digital competence is associated with sex, age, trial location, educational attainment, and perception of income.

4.2. Strengths and limitations

Our study investigated the potential impact of digital competence on participation and retention in a trial with an eHealth component using diverse data sources, spanning an extended period including participation or non-participation data, baseline questionnaire data, and data related to dropout at T1. This allowed for a comprehensive description of the influence of digital competence on trial dynamics, such as recruitment trajectory and trial retention.

Although we utilized a standardized form to record document reasons for non-participation, differences in local regulations or agreements with recruitment centres hindered uniform and detailed registration. As 17% of potential participants reported no specific reason for non-participation, it is likely that 2.1% of participants who refused participation in the trial for ICT-related reasons might have been underestimated. Older adults might be reluctant to admit insufficient digital or computer literacy, choosing instead to provide a vague or unspecified reason for nonparticipation. This could possibly have introduced some level of selection bias. Another limitation pertains to our conceptualization of self-reported digital competence, which combines comfort and skills using computers, smartphones, or tablets. The literature suggests that digital competence encompasses other key aspects, such as attitudes towards ICT, critical and responsible use, and engagement across settings, which we did not measure²⁸.

4.3. Interpretation and implications of the findings

Only 2.1% of eligible patients and family caregivers explicitly declined participation due to ICT-related reasons, such as feeling insufficiently competent to engage with an eHealth program or lack of access to a computer, tablet, or the Internet. Research indicates that participation in trials featuring an eHealth component is influenced by ICT-related factors such as Internet and computer access and proficiency, as well as familiarity with and perceived utility of technology^{29, 30}. Nevertheless, it is important to recognize that the impact of ICT-related factors might be minimal and is heavily subject to underlying factors, such as sociodemographic disparities, contributing to persistent digital inequities²⁹⁻³¹. The population that is less likely to use digital technologies overlaps with those who are more inclined to refuse participation in trials in general, namely older individuals with lower education, poorer health, and lower socioeconomic status³¹⁻³⁴.

Other studies corroborate our findings, stating that non-ICT-related reasons for non-participation, such as feeling uninformed about the trial, ongoing participation in other trials, perceiving the trial as overly complex, or simply lacking interest, potentially exert a greater influence on the decision to participate³⁵⁻³⁷. However, detailed reporting of specific non-participation reasons proved challenging in this international RCT, possibly leading to underreporting of ICT-related reasons for non-participation. Despite guidelines, such as the CONSORT statement advocating for standardized recruitment reporting, the recruitment process across diverse sites and countries introduces complexity. Local regulations can impede the registration and sharing of certain information, resulting in recruitment data that varies and lacks clarity. Existing literature echoes these challenges, highlighting difficulties in uniform recruitment registration in international trials due to regional legislative and procedural variations³⁸⁻⁴⁰.

With patient and caregiver retention rates of 79.8% and 79.4%, respectively, the DIAdIC trial demonstrated a relatively high retention. Trials involving eHealth components generally exhibit retention rates ranging from 54% to 95%⁴¹. This may be due to the dyadic nature of participation, as research suggests that trials involving dyads tend to have higher retention rates attributed to the positive influence of family caregivers on patients in adopting and sustaining healthy behaviours⁴².

Compared with the face-to-face FOCUS+ trial arm, retention in the iFOCUS web-program trial arms was over 10 percent lower, suggesting that eHealth interventions may accelerate study

fatigue and increase attrition. However, this effect on attrition may be consistent across digital competence levels, as we found no significant association between digital competence and retention in any of the trial arms. Our findings align with the limited available literature, indicating that while digital competence could influence retention in trials with an eHealth component, other ICT-related factors, such as reluctance to share online information or mistrust in digital trials, may have a more significant impact^{43, 44}.

Similar to enrolment and non-enrolment, participant characteristics such as education level, age, and motivation can directly or indirectly, through digital competence, impact retention in a trial with an eHealth component^{24, 45, 46}. While ICT-related reasons and digital competence do not influence trial participation and retention, future research into which factors do is required.

4.4. Conclusion

Future studies and programs relying on eHealth components should be aware that digital competence might not be equally distributed among populations of interest. Nevertheless, we found no indication that digital competence in patients or family caregivers, or at the level of the dyad, substantially influences participation or retention in trials with a digital component. These findings provide some cautious reassurance regarding the impact of eHealth components on the internal and external validity of the studies.

DECLARATIONS

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Conflicts of interests

None.

Data availability

The data sets generated and analysed during the current study are available from the corresponding author upon reasonable request.

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CHAPTER 5

Impact of nurse-led and web-based psychoeducation for advanced cancer patients and their caregivers on emotional function and self-efficacy: the DIAdIC randomized controlled trial

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Ready for submission

Vincent Van Goethem, listed as the FIFTH AUTHOR on this paper, was involved in the data collection of the trial and participated in the review process of this article prior to its submission. This paper is included as part of the PhD dissertation to provide additional background information or to facilitate a discussion on the effectiveness of eHealth.

This paper was included in the PhD dissertation of the first author, Orphé Matthys.

ABSTRACT

Purpose: Dyadic psychoeducational interventions demonstrate benefits by concurrently addressing challenges for oncology patients and family caregivers. This study evaluates the effects on emotional function and self-efficacy of a face-to-face nurse-led and a web-based psychoeducational intervention for patients with advanced cancer and their family caregivers.

Methods: In this international multicenter parallel-group superiority randomized controlled trial, dyads formed by patients with advanced solid cancer and their primary family caregiver were randomly assigned (1:1:1) without blinding to a web-based psychoeducational intervention (iFOCUS), a face-to-face psychoeducational intervention (FOCUS+), or standard care. The two primary endpoints were emotional functioning (10-item EORTC short form), and self-efficacy (Cancer Self-efficacy Scale) at 12 weeks.

Findings: Between February 2021 and August 2023, 431 dyads were randomized to iFOCUS (148), FOCUS+ (140) or standard care (143). At T1, for patients and family caregivers respectively, iFOCUS did not yield significant improvements compared to control group in both emotional functioning (-0.27; 95%CI -2.11 to 1.57 and 0.30; 95% CI -1.41 to 2.00) and self-efficacy (0.49; 95% CI -6.21 to 7.19 and 3.66; 95% CI -3.36 to 10.68). FOCUS+ did not yield statistically significant improvements in emotional functioning (0.12; 95% CI -1.65 to 1.89 and 0.17; 95% CI -1.45 to 1.79), but significantly improved self-efficacy compared to control group in patients (9.02; 95% CI 2.45 to 15.58), and not family caregivers (3.88; 95% CI -2.84 to 10.61).

Interpretation: Improvement in patient self-efficacy from FOCUS+ supports future use in Europe. The web-based version of the intervention seems less promising. Further process evaluation can clarify why face-to-face but not web-based psychoeducation led to positive findings and why self-efficacy but not emotional function were improved.

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1. INTRODUCTION

Advanced cancer impacts the lives of both patients and their family caregivers^{1,2}. These effects are interrelated; patients' wellbeing and self-efficacy in coping with the illness affect that of the family caregiver and vice versa³. 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 coping⁵.

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}, to result in better outcomes for both, and to be more cost-effective, compared to single target interventions⁸. Psychoeducational dyadic interventions have also increased the quality of mutual communication and support^{9,10}. Among these, the FOCUS intervention, developed in the United States, has demonstrated efficacy in various randomized controlled 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 QOL¹¹. Earlier RCTs of FOCUS also showed positive effects in dyads affected by breast cancer¹² and prostate cancer¹³. A phase 2 feasibility study also demonstrated potential benefit of delivering the FOCUS program as a web-based version¹⁴.

To evaluate the effectiveness of the FOCUS program in a European oncology context, 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, so that it was culturally appropriate to the participating European countries¹⁵. Additionally, a web-based version of the intervention was developed, i.e. the iFOCUS intervention. The rationale for this web-based version was the potential convenience for the dyad and the potential lower resource-intensiveness for its implementation given workforce limitations. Furthermore, there is evidence suggesting that telehealth interventions for patients undergoing cancer treatment have similar effectiveness at improving their quality of life compared to in-person usual care¹⁶.

The overall objective of this study was to evaluate the effectiveness of two psychoeducational interventions (a face-to-face nurse-led intervention called FOCUS+ and a web-based

intervention called iFOCUS) in improving emotional functioning and self-efficacy (primary outcomes) of patients with advanced cancer and their family caregivers at 12 weeks (T1). Both interventions are compared to standard care.

2. METHODS

2.1. Trial design

We conducted 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). Dyads were randomly assigned to one of the three parallel groups in a 1:1:1 allocation ratio. Details on the trial procedures are fully described in the research protocol¹⁷. We report using the Consolidated Standards of Reporting Trials (CONSORT) statement¹⁸.

2.2. Participants

We recruited dyads comprising a cancer patient and their primary family caregiver. Patients were eligible if diagnosed with advanced solid organ cancer (excluding brain cancer). Primary family caregivers were identified as determined by the patient. A detailed overview of the inclusion and exclusion criteria can be found in Box 1.

Box 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
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 *: In August 2022, based on 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 participants who could potentially benefit from the interventions.			

2.3. Setting

The trial took place in Belgium, the Netherlands, Italy, Denmark, Ireland, and the United Kingdom (England and Northern Ireland). The interventions (FOCUS+ and iFOCUS) were administered in the homes of patient-caregiver dyads or in another location of the dyad’s preference.

Participants were recruited from participating hospitals and their respective departments in each country (see Supplemental Appendix 6 for overview of recruiting hospitals and departments).

2.4. Interventions

Both FOCUS+ and iFOCUS interventions were administered in addition to standard care and focused on psychoeducation, aimed at providing dyads with 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 needs and 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 together⁵. A completed TIDieR checklist¹⁹ of both interventions can be found in Supplemental Appendix 7.

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 (see 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 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. 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, content of the sessions was tailored to 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. More details on the development and content of the FOCUS+ intervention are reported elsewhere¹⁵.

Web-based intervention (iFOCUS)

The iFOCUS web-based intervention was a self-managed online program designed for autonomous completion by patient-caregiver dyads. Spanning four sessions spread evenly over a 12-week period, 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, tablet, or smartphone, 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 ensure the adaptation of the intervention according to dyad's characteristics. Further information regarding the development of the iFOCUS intervention is reported elsewhere²⁰.

Control group (standard care as usual)

Similarly to patients in the intervention arms, dyads in the control group received 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)

2.5. 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 bank²¹. Self-efficacy was measured with 17 items from the Lewis Cancer self-efficacy scale²², validated by Northouse.¹¹ The scale assessed the confidence patients and family caregivers had to manage cancer. For both scales, a higher score reflects higher emotional functioning or self-efficacy.

Several secondary endpoints were assessed (see protocol¹⁷), 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 two primary outcome variables measured at T2. Only primary outcomes are reported in this paper.

Socio-demographic and clinical characteristics of patients and family caregivers were collected during enrolment or at baseline through a questionnaire.

2.6. Sample size

To detect a 0.375 SD difference between the control group and the intervention arms at T1 (12 weeks) in both primary outcomes with power at 90% (see detail in study protocol¹⁷), we anticipated that 203 dyads were needed in each arm across all countries (i.e. 609 in total). Based on the previous studies by Northouse^{11–13}, we anticipated a 65% retention rate at T1, requiring 938 dyads to be enrolled across the 6 countries (313 per group).

2.7. Randomization

Randomization was performed with a computer randomization schedule (Mersenne Twister Random Number Generator²³) with a 1:1:1 allocation ratio to one of the two intervention arms or the standard care arm. 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 patients, family caregivers or intervention nurses involved in the face-to-face FOCUS+ intervention.

2.8. Statistical methods

We performed ‘intention-to-treat’ (ITT) as primary analysis and per-protocol (PP) as a sensitivity analysis. For the ITT analysis, we performed multiple imputations (n=50) for missing outcome data using the Fully Conditional Specification (FCS) method in R. 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. 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]). A pre-determined strict fixed sequence procedure defined a hierarchical ordering of the primary endpoints as emotional functioning (1) and self-efficacy (2).

We examined the missing data percentages at the T1 measurement for our primary outcomes, emotional functioning, and self-efficacy. Missing data were imputed based on the assumption that they were missing at random without considering why the data was not collected. A multiple imputation model that included the reason why the data were missing as predictor was developed and analysed as sensitivity analysis (Supplemental appendix 4). The model differentiated between deceased patient, worsening of patient clinical condition, withdrawal for unknown reason/no information.

The ITT population consisted of all dyads randomized to one of the intervention groups. The PP population consisted of all those who completed the T1 measurement (or T2 measurement for the T2 analysis) and, for those in the intervention groups, completed all FOCUS+ or iFOCUS sessions. No imputations for missing data 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.

2.9. Registration, protocol, and funding

The trial is registered on ClinicalTrials.gov, identifier NCT04626349. The protocol of the DIAdIC trial was published in 2021.¹⁷ The DIAdIC project received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 825722.

2.10. Ethics

All patients and family caregivers participating in this study gave written informed consent. The study was approved by the relevant ethics committees in all participating countries.

3. RESULTS

3.1. Baseline characteristics

Recruitment took place between February 2021 and August 2023. In total, 431 dyads were enrolled and randomized to iFOCUS (n=148), FOCUS+ (n=140) or the control group (n=143). Figure 1 shows the participant flowchart with a progression of participants throughout the study. Enrolment results in each country and baseline characteristics of participating patients and family caregivers are shown in Table 1.

Figure 1: Participant flowchart

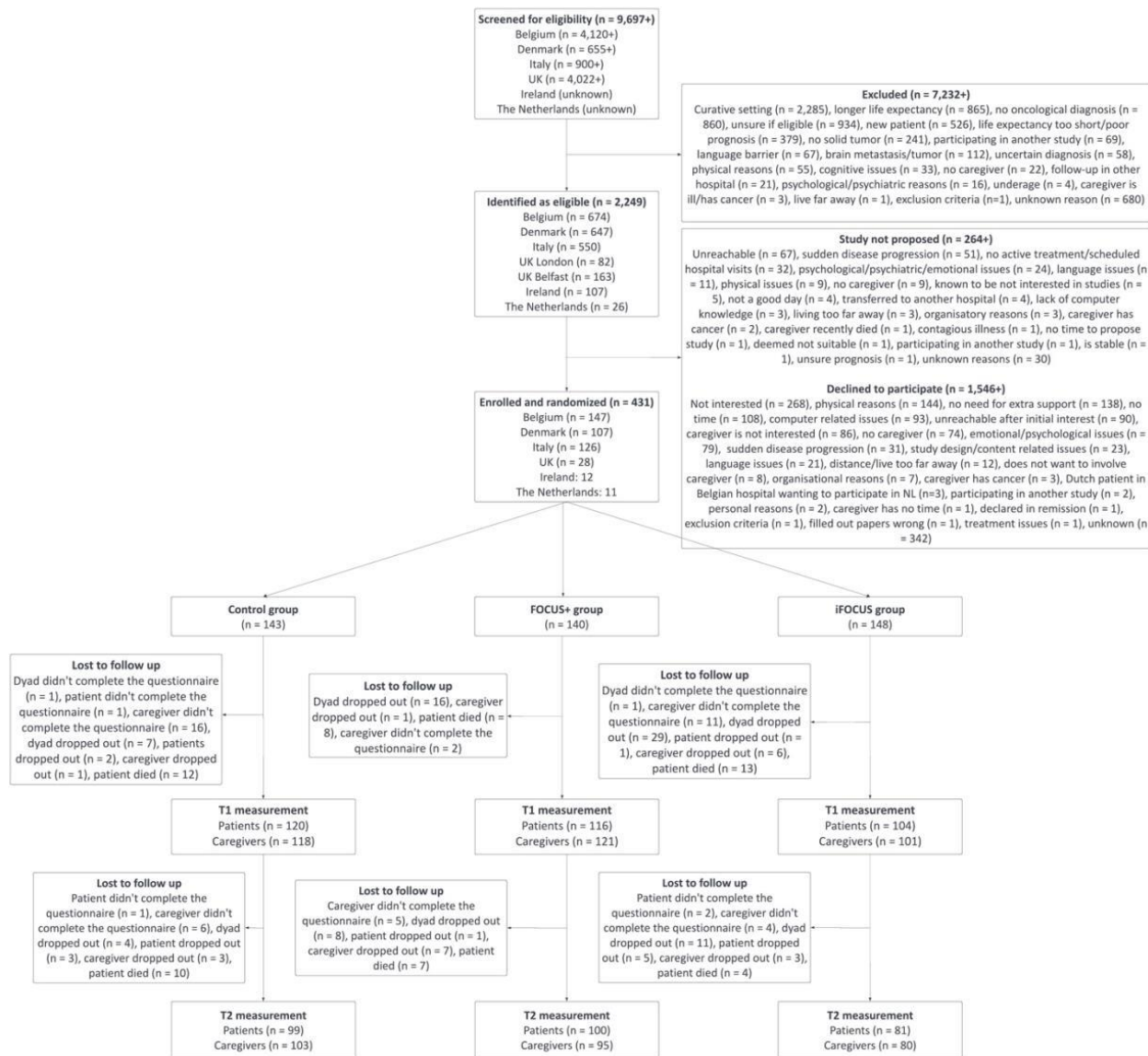


Table 1: baseline characteristics

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
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

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
Cancer Type								
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
Gynaecological	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

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
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
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

Intervention group compliance was 52% in iFOCUS and 76% in FOCUS+. Missing data at T1, for patients and caregivers respectively, was 28% and 21% for emotional function and 28% and 26% for self-efficacy (Appendix 8).

3.2. Primary Analysis (ITT)

The mean scores at baseline for emotional functioning and self-efficacy can be found in Appendix 9.

iFOCUS vs control

Emotional functioning scores did not differ significantly between the iFOCUS intervention group and control group at T1 in patients (baseline-adjusted mean difference [MD], -0.27; 95% CI, -2.11 to 1.57; $p = 0.774$) and family caregivers (MD, 0.30; 95% CI, -1.41 to 2.00; $p = 0.732$) (Table 2). Similarly self-efficacy, did not differ significantly between those in the iFOCUS and control group at T1 in patients (MD, 0.49; 95% CI, -6.21 to 7.19; $p = 0.887$) and family caregivers (MD, 3.66; 95% CI, -3.36 to 10.68; $p = 0.306$).

No significant differences were observed at T2. Effect sizes (Cohen's d) were negligible at both T1 and T2.

FOCUS+ vs control

For emotional functioning, no significant difference was found between those in the FOCUS+ intervention group and control group at T1 in patients (MD, 0.12; 95% CI, -1.65 to 1.89; $p = 0.897$) and family caregivers (MD, 0.17; 95% CI, -1.45 to 1.79; $p = 0.834$). For self-efficacy a statistically significant difference was found between those in the FOCUS+ intervention group and control group at T1 in patients (MD, 9.02; 95% CI, 2.45 to 15.58; $P = 0.007$), but not in family caregivers (MD, 3.88; 95% CI, -2.84 to 10.61; $p = 0.258$). Effect size of the significant difference for patients was small (Cohen's $d = 0.36$; 95% CI, 0.13, 0.60).

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		
		<i>iFOCUS vs control group</i>	<i>FOCUS+ vs control group</i>	<i>iFOCUS vs control group</i>	<i>FOCUS+ vs control group</i>	<i>iFOCUS vs control group</i>	<i>FOCUS+ vs control group</i>	<i>iFOCUS vs control group</i>	<i>FOCUS+ vs control group</i>	<i>iFOCUS vs control group</i>	<i>FOCUS+ vs control group</i>	<i>iFOCUS vs control group</i>	<i>FOCUS+ vs control group</i>
Emotional functioning	Patient	-0.27 (- 2.11 to 1.57)	0.12 (- 1.65 to 1.89)	1.68 (- 0.20 to 3.56)	0.00 (- 1.87 to 1.86)	-0.05 (- 0.28 to 0.18)	0.02 (- 0.21 to 0.25)	0.19 (- 0.03 to 0.43)	0.00 (- 0.23 to 0.23)	0.774	0.897	0.080	0.997
	Family caregiver	0.30 (- 1.41 to 2.00)	0.17 (- 1.45 to 1.79)	0.89 (- 1.25 to 3.02)	-0.66 (- 2.67 to 1.34)	0.04 (- 0.19 to 0.27)	0.02 (- 0.21 to 0.26)	0.10 (- 0.13 to 0.33)	-0.08 (- 0.31 to 0.16)	0.732	0.834	0.414	0.516
Self-efficacy	Patient	0.49 (- 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)	0.02 (- 0.21 to 0.25)	0.36 (0.13 to 0.60)	0.05 (- 0.18 to 0.28)	0.04 (- 0.19 to 0.28)	0.887	0.007	0.671	0.697
	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)	0.14 (- 0.09 to 0.37)	0.14 (- 0.09 to 0.38)	0.09 (- 0.14 to 0.32)	0.11 (- 0.13 to 0.34)	0.306	0.258	0.448	0.357

3.3. Sensitivity analysis

An intention-to-treat analysis with a missing imputation considering reasons for missingness and the per-protocol analysis confirmed the overall findings, with both confirming the significant difference for self-efficacy between FOCUS+ and control group in patients. The per protocol analysis found a larger effect size ($d = .47$; 95% CI, .21 to .74).

Conditional power analysis

To account for our study being underpowered, 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) the observed effect size. These analyses show a 10% to 63% likelihood of significant impact from iFOCUS and an 11% to 67% likelihood of significant impact from FOCUS+ on family caregiver self-efficacy.

4. DISCUSSION

This randomized controlled trial across six European countries evaluated the effects of two dyadic psychoeducational interventions for patients with advanced cancer and their family caregiver on two primary endpoints: emotional function and self-efficacy. The nurse-delivered FOCUS+ intervention did not improve emotional function in patients or family caregivers but did significantly improve patients' self-efficacy at 12 weeks (T1) compared with the control group. No significant improvements in either endpoint were observed from the web-based iFOCUS intervention. The consistent results from the different sensitivity analyses suggest robustness of our findings.

We implemented a 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. A first issue relates to sample size. Enrollment to the study was lower than anticipated most likely due to the COVID-19 pandemic and its

consequences (hospital staff being overwhelmed and patients more hesitant to join a study)²⁴. As time and resources of the project ran out due to limited funding, enrollment was terminated before the target numbers were reached. This resulted in our study being underpowered with an unbalance between countries in recruitment, hence decreasing the probability of finding statistically significant differences. A second 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 may have resulted in conversations about coping with the illness or the pandemic and this may have inadvertently resulted in a supportive effect for participants in such interactions, which might have affected the standard care group. Another limitation is the relatively low program adherence with only 52.0% of dyads completing all sessions of iFOCUS as intended and 76.4% in those of FOCUS+.

The FOCUS+ intervention significantly improved self-efficacy to manage cancer in patients at 12 weeks. However, given the neutral finding for emotional functioning, as per the pre-defined strict fixed sequence procedure, this finding may need to be considered as exploratory rather than confirmatory. On the other hand, the finding does confirm previous findings of an effect of the FOCUS intervention in the USA on self-efficacy to manage cancer. Given the mutual burden in dyads, this observed improvement in patients may have also positively impacted family caregivers across various domains. A longitudinal study found that a higher self-efficacy in patients with advanced cancer was associated with better mental health and better physical health in family caregivers²⁵. Examining the impact on secondary outcomes for patients and family caregivers could provide additional support for this assertion.

The lack of impact on emotional functioning in 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. Dyads face continual changes across various domains, including physical symptoms, and the emotional impact of negative news regarding illness progression, all of which significantly affect emotional functioning and pose challenges to intervention effectiveness in this area. Process evaluation data will be able to shed more light on this.

The interventions evaluated in this trial were based on the FOCUS program²⁶, which has shown effectiveness in multiple randomized controlled trials.^{11–13} Our study partially corroborates previous findings from trials conducted by Northouse et al, as we found a significant improvement for self-efficacy in managing cancer in patients in the FOCUS+ intervention arm at 12 weeks (T1). The trial by Northouse et al., with advanced cancer patients and their spouses also found a significant improvement in dyads' self-efficacy at 3 months, and the effect was not sustained at 6 months.¹¹ However, notable differences in outcomes were observed. The 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 was sustained at 12 months.¹³

Several possible reasons may explain why the effectiveness of our interventions was only partially demonstrated for primary outcomes. First, our trial had insufficient power, which limited the possibility of finding significant effects. Second, perhaps the effects of the FOCUS intervention were larger in the studies in the USA than in our European replication study because the healthcare and cultural contexts are different. Our study also was conducted in different circumstances than the original study. The original FOCUS interventions were developed in the USA, so even though thorough cultural adaptations and translations of the original FOCUS interventions were carried out¹⁵, the adapted content of the interventions might still not offer an added value to patients and family caregivers in Europe comparable to that in the USA. Standard care in Europe during the study period may have included different levels of psychoeducation and support for patients and family caregivers compared to the period when the FOCUS studies were conducted in the USA (i.e., 1996 to 2009), potentially limiting the additional contribution of the intervention. Third, our study was conducted during the COVID-19 pandemic, which posed additional challenges for the cancer population and study conduct. These circumstances also 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 an RCT. In our trial, iFOCUS did not yield statistically significant improvements 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 benefits²⁷. 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 QOL²⁸. Second, we observed lower intervention adherence in the iFOCUS intervention arm which suggests that participants facing advanced cancer 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 suitably 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. Finally, it should be acknowledged that the iFOCUS intervention represented a first version of the web-based program, which could still be improved in both content and design.

The current study shows some promising results for the FOCUS+ intervention that can inform guidelines for implementation in clinical practice. The potential effectiveness of the FOCUS+ interventions, especially with adequate sample size, suggests that healthcare professionals may want to consider its incorporation in oncology settings.

5. CONCLUSION

The nurse-delivered FOCUS+ intervention, which provides psychoeducation to patient-family caregiver dyads, did not improve emotional functioning but did show a positive effect on self-efficacy in patients at 12 weeks, and as such shows promise for future use in Europe. The lack of improvements from the web-based iFOCUS intervention suggest that expectations about the promise of eHealth for interpersonal psychoeducation may need to be tempered, or that it can benefit from design enhancements.

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CHAPTER 6

Developing and implementing a nurse-delivered and a web-based dyadic psychoeducational program for people with advanced cancer and their family caregivers: sharing experiences from a three-arm international randomized controlled trial (DIAdIC)

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**‘Evaluation of Dyadic Psychosocial Interventions for People with Advanced Cancer and their Informal Caregivers (DIAdIC): An international randomized controlled trial’ – ‘DIAdIC’ (EU grant agreement No 825722)

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[Submitted]

ABSTRACT

Background: In the EU, millions are diagnosed with cancer annually. A diagnosis of advanced cancer impacts the quality of life of both the person diagnosed and the caregiver. Despite the interrelated experiences of patients and caregivers, few interventions target both together (i.e., are dyadic interventions).

Objectives: To present our experiences with the development and implementation of two dyadic psychoeducational home-based programs, FOCUS+ and iFOCUS in the context of a RCT in six European countries.

Methods: A chronological narrative describing experiences with development and implementation of iFOCUS and FOCUS+.

Results: The FOCUS+ and iFOCUS programs were successfully developed for the European context through rigorous translation and adaptation processes. Despite recruitment challenges including COVID-19 restrictions and administrative hurdles, 431 patient-caregiver dyads were enrolled across six European countries. Quantitative and qualitative data assessed outcomes of FOCUS+ and iFOCUS interventions, including the primary endpoints emotional functioning and self-efficacy. Fidelity was evaluated using audio recordings, checklists, and user data. Challenges in trial management were addressed with flexible timelines and technical support.

Conclusion: The international DIAdIC trial developed and implemented two psychoeducational dyadic programs for patients with advanced cancer and their family caregivers. Based on our experiences we share several insights for future similar studies. These relate to the attention needed for context-specific adaptations when using existing interventions or programs, the translation of human-facilitated programs to standalone eHealth versions, the challenges of adopting a dyadic focus in the study, the pragmatic challenges of conducting an RCT and evaluating implementation and effects, and the technology used for study management.

1. INTRODUCTION

In the EU, a total of 3.7 million people are newly diagnosed with cancer each year and about 33.9 million people are estimated to be living with cancer¹. Advancements in cancer treatments such as early detection and new therapies change the illness trajectory and prognosis of patients with cancer, enabling patients diagnosed with advanced cancer to experience extended periods of survival^{2, 3}. Nonetheless, a large body of evidence has demonstrated the negative effects of advanced cancer on the quality of life of patients. Besides the symptom burden, patients with advanced cancer also report emotional and spiritual suffering, challenges in their daily functioning and a decline in their overall quality of life, resulting in serious psychosocial care needs⁴⁻⁶. Although patients with cancer often receive state-of-the-art medical care for their physical symptoms, they seldom have access to care which addresses the detrimental effects of the illness on their quality of life. The impact of advanced cancer extends beyond the patient, as family caregivers report similar levels of role adjustment problems and emotional distress as patients do, with anxiety and depression being present in up to 40% of family caregivers.⁷ This reflects the family caregivers' pivotal role in care provision, often providing complex care at home; sometimes with little support from others^{8,9}. Moreover, the sustainability of family caregiving is challenged by a demographic shifts towards an aging the population, increased chronic health conditions among the elderly and the impending shortfall of family caregivers relative to the number of potential care recipients^{10, 11}.

Despite many studies showing that the responses to the illness of patients with advanced cancer and their family caregivers are interrelated¹², there are surprisingly few psychosocial or educational intervention programs to help the patient-family caregiver dyad as a unit of care to manage the effects of illness and maintain their quality of life. Reviews of psychosocial interventions in chronic life-limiting illnesses indicate that dyadic interventions which target patient and family caregiver together, are more likely to result in better outcomes for both parties than single target interventions, and are potentially more cost-effective. At the same time, there is a substantial body of evidence that demonstrates the benefits of early integrated palliative care to patients and family caregivers, even when provided alongside disease-modifying treatments¹³. The World Health Organization (WHO), European Society of Medical Oncology (ESMO) and standards of practice in numerous countries are advocating that palliative care can be offered from the point of diagnosis of advanced cancer. However, present-day practice and research are encouraged to consider new alternatives instead of solely relying on additional healthcare staff to cope with the current healthcare context, characterized by shortages of trained staff, time,

and resources¹⁴. To address these challenges, new dyadic models of care that embrace the philosophy and principles of early palliative care that are accessible, affordable, scalable and sustainable are needed.

For the H2020 DIAdIC project, we developed and evaluated the face-to-face FOCUS+ program and the web-based iFOCUS program, which are both based the US FOCUS interventions. As part of the DIAdIC trial, large-scale international three-arm superiority trial we researched the effectiveness, cost-effectiveness, and mechanisms of change of iFOCUS and FOCUS+. The two interventions aimed to improve the emotional functioning and self-efficacy (primary outcomes) and other secondary outcomes of patients with advanced cancer and their family caregiver. Full details related to the research protocol for the trial can be found elsewhere¹⁵. Results of the effectiveness of the trial are forthcoming.

In this reflexive paper, we present our experiences with (1) the development process of FOCUS+ and iFOCUS for European application and (2) the implementation of FOCUS+ and iFOCUS in the context of a RCT in 6 European countries (Belgium, Denmark, Italy, the Netherlands, Ireland, United Kingdom) aimed at improving the emotional functioning, self-efficacy and various other aspects of health and wellbeing of patients with advanced cancer and their family caregiver.

2. METHODS AND RESULTS

In this ‘methods and results’ section, we use a narrative chronological structure which first outlines the intended development process of FOCUS+ and iFOCUS alongside our experiences, followed by a description of the implementation of these programs in an international RCT and our reflections.

2.1. Experiences during development of the FOCUS+ and the iFOCUS programs

Developing FOCUS+: Participatory and Iterative Process Framework for Language Adaptation (PIPFLA)

The US FOCUS program, developed in 2002 has been tested for dyads with different types of cancer across the USA^{16,17}. Nevertheless, the effectiveness of a program may vary greatly depending on the national and cultural context in which it was developed and implemented¹⁸⁻²⁰. It is likely that there are numerous differences in health-related norms, societal values and the organization of healthcare between the USA twenty years ago and Europe nowadays. Therefore, in order to create a contemporary suitable version of the FOCUS program, fitting to a European context it was essential to conduct a comprehensive process of translation and content adaptation²¹.

The US FOCUS program functioned as a base for the development of the FOCUS+ program. In order to achieve fit to Belgian, Danish, Irish, Italian, Dutch and English contexts, the Participatory and Iterative Process Framework for Language Adaptation (PIPFLA) method was used²². The PIPFLA method consists of multiple steps: 1) preparation, 2) forward translation, 3) backward translation, 4) review of backward translation, 5) harmonizing, 6) review by reference group, 7) harmonizing, 8) review by reference group, 9) harmonizing, 10) Proofreading and 11) final language adaptation^{21, 22}.

In contrast to the original PIPFLA method, our approach involved a preliminary evaluation of the program's appropriateness in each country. We also expanded the involvement of the reference groups, deviating from PIPFLA's guidance where these groups (which provide an emic and etic perspective) are less involved. Additionally, program stakeholders such as nurses, clinicians,

patients, family caregivers from all six countries reviewed the program materials on multiple occasions. Using a template, we collected the feedback from these stakeholders. In order to not deviate too much from the theory underlying the original FOCUS intervention, professor Laurel Northouse (the developer of the original FOCUS intervention), was involved in the analysis of stakeholder feedback. A 'TIDieR checklist (Template for Intervention Description and Replication)', was used to give a detailed description of the resulting FOCUS+ program (Appendix 7). The translation and adaptation process was undertaken from May 2019 to December 2020. More information about the FOCUS+ development process can be found elsewhere²².

Following the slightly adjusted PIPFLA process with greater involvement of reference groups resulted in an adapted version of the original US FOCUS program: the FOCUS+ program. This also included a FOCUS+ conversation manual for use by the nurses implementing the FOCUS+ program. This manual was developed to allow for uniformity across all countries whilst incorporating country-specific language nuances. Modifications to the wording of the original US FOCUS program were permitted for sensitive subjects such as the end of life and sexuality if they were more culturally appropriate and likely to be better accepted by participants. Adaptations to the original FOCUS manual target six topics and are summarized in Box 1:

Box 1: Summary of adaptations in FOCUS+ conversation manual for nurses

- 1. Needs and wishes of the family caregiver:** FOCUS+ addresses both individuals in the dyad equally, incorporating family concerns and redirecting questions initially focused on the patient.
- 2. Self-management:** Recognizing cultural differences, FOCUS+ broadens the concept of self-management beyond normative views, focusing on the comprehensive aspects of living with advanced cancer. The program aims to support open communication between the nurse and the dyad and to explicitly support self-management strategies of the dyad.
- 3. The concept of optimism:** The term "optimism" is replaced with "outlook" to allow for discussions about both positive and negative feelings, acknowledging the diverse emotional experiences of patients and family caregivers.
- 4. The supportive and educational character of the program:** FOCUS+ emphasizes a supportive and educational role for nurses, distancing from therapeutic or psychological care, aligning with the formal responsibilities of nurses in European countries.
- 5. The order of topics:** The sequence of topics was adjusted, with a focus on prioritizing concerns about children and discussing sensitive topics like intimacy and sexuality in face-to-face meetings rather than over the phone.

6. Referral to health care professionals: FOCUS+ refers dyads to their attending health care professionals for questions about diagnosis and treatment options, acknowledging the complexity of individualized oncology therapies that may exceed the knowledge of intervention nurses.

The original US FOCUS program also provided diverse information resources to dyads such as leaflets, booklets, and websites on cancer therapies, consequences of cancer, and referrals. Recognizing the impracticality of translating all US materials and the need for adaptation to diverse European healthcare services, each country selected national equivalents of the materials. These materials were compared and evaluated, leading to the decision from the coordination team to integrate them into a booklet. This booklet aligned with the structure of the FOCUS+ session and served as a reference for dyads throughout the intervention, featuring content, including exercises on dyadic communication.

The development process of FOCUS+ resulted in a homebased face-to-face intervention consisting of two home visits of 90-min and one online video session of 30-min, conducted by a trained nurse, with four weeks between each session. The nurses had access to a conversation manual to provide guidance and support during the sessions.

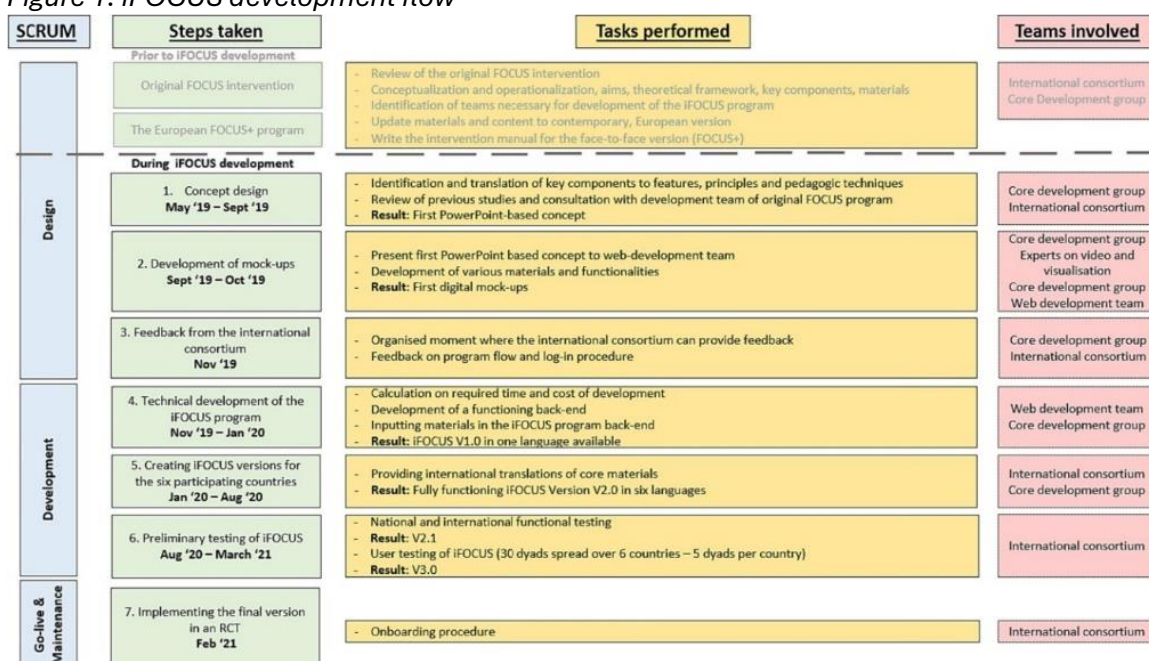
Developing iFOCUS: using the Scrum methodology

The FOCUS+ program served as the foundation for the development of the web-based iFOCUS program. An extensive development process was essential for iFOCUS to become a self-managed, user-friendly psychoeducational web-based program for patients with advanced cancer and their family caregivers, while retaining the essence of FOCUS+.

The development of iFOCUS adhered to the four phases of the agile Scrum methodology namely: design (1), development (2), go-live (3) and maintenance and support (4). In line with the Scrum methodology we applied timeframes of rapid program development and evaluation, also called “sprints”²³. For the development of iFOCUS we developed a seven-step development process (Figure 1), which could be fully integrated in the four-phased Scrum methodology. The seven steps of development were (1) concept design, (2) development of mock-ups, (3) obtaining feedback from the international consortium, (4) technical development of the program, (5) creating country-specific versions for each of the six participating countries, (6) preliminary testing through user and functional testing and (7) implementing the final version for the RCT.

Five teams were involved in the development of iFOCUS: 1) a core development group consisting of academics, clinicians, and healthcare professionals who were actively involved in the daily development of program content and flow, 2) a web development team, 3) the DIAdIC international consortium, 4) audio-visual experts, and 5) potential end-users from each participating country (i.e. patients with advanced cancer and family caregivers)²³.

Figure 1: iFOCUS development flow²³



Each of the seven development steps followed sequentially from the previous one, but flexibility was allowed to enable continuous refinement and correction. The collaborative efforts of different teams and the integration of diverse perspectives enabled the identification and resolution of errors and bugs throughout the development process of iFOCUS.

The primary challenges we faced during the development of iFOCUS included converting the FOCUS/FOCUS+ “identity” (theoretical program background) into functional features, the spreading of content within and between sessions, program tailoring, ensuring both program safety and a user-friendly login procedure, incorporating materials in the iFOCUS program and establishing an onboarding procedure. Based on our experiences and review of available literature, the challenges we faced were either specific to the conceptualization of iFOCUS (program specific challenges) or general to the development of eHealth programs (general challenges). The user testing (step 6) included 42 participants (20 patient-family caregiver dyads and 2 bereaved family caregivers) who reviewed the iFOCUS program. While potential end-users

found the iFOCUS program to be acceptable and usable, minor content, tailoring and program flow adaptations were required.

The development process of iFOCUS resulted in a self-management psychoeducational eHealth program, consisting of four sessions of approximately 60 minutes each, over a 12-week period – with a three-week gap between each session, that could be used autonomously by the patient-caregiver dyad together. More details about the development process are described in CHAPTER 2 of this dissertation²³.

2.2. Experiences during the implementation of the FOCUS+ and iFOCUS programs in an international RCT

Information on the DIAdIC trial study design, setting, and participants can be found in CHAPTER 3 of this dissertation, which encompasses the DIAdIC trial protocol¹⁵.

Recruitment and sample size

Patients were recruited and enrolled via participating hospitals. Hospital staff screened patients for the inclusion and exclusion criteria. Eligible patients received a first oral introduction to the trial, preferably in attendance of the family caregiver. If the dyad agreed to participate, a data collector made an appointment with the dyad to obtain their informed consent. Patients and family caregivers were invited to complete the baseline (T0) measurement independently from each other. Only those who completed the baseline measurement were randomized and considered as enrolled in the study. The recruitment period started in February 2021 and was foreseen to last 12 months.

Inclusion of patient-caregiver dyads within this trial also made recruitment more complex. There were cases in which the patient was interested to participate but was unable to identify a family caregiver. Another challenge pertained to the motivation of the patient or family caregiver to join and how they could influence one another. In most cases, if the patient wanted to participate, then the family caregiver followed and vice versa, but there were also cases where they deterred one another from participation. As a result, recruitment of dyads may make the participating partner a de facto gatekeeper.

While we intended to recruit 156 dyads in each participating country, recruitment went considerably slower than anticipated. The following reasons for this delay were identified:

1. The trial took place during the protective measures taken by governments and healthcare organizations in view of the COVID-19 pandemic. One of the measures implied limited access to hospitals for external staff such as data collectors but also for family caregivers, often making it impossible for family caregivers to accompany patients to consultations. This led to challenges in presenting the study orally to the dyad. COVID-19 also led to increased pressure on healthcare organizations, limiting the available time and means to support recruitment. Research directly aimed at COVID-19 was prioritized, effectively halting other research.
2. Stricter regulations, an excessive administrative burden to obtain approvals for the study, and stricter rules for the screening and invitation of patients to studies caused delays and fewer study referrals in certain countries.
3. Variable recruitment strategies in hospitals played a significant role, with some achieving targets through active data collector involvement in the screening and identification of eligible patients, while other hospitals imposed barriers, leading to lower-than-expected recruitment.
4. Acquiring the informed consent from both patients and their family caregivers for dyadic participation posed an extra challenge, particularly in cases where one party was unwilling to participate.
5. The requirement for computer access and internet familiarity posed a challenge, reducing willingness to participate among those unfamiliar with computer-administered interventions.
6. Various other issues such as the consequences of Brexit, regional healthcare reorganization, and staff shortages increased pressure on time and resources, resulting in a lower priority for psycho-educational research.

Mitigating strategies

To address recruitment delays, the consortium implemented several strategies:

1. The recruitment period was originally foreseen to last a total of 12 months and the data collection period 18 months (to complete T2 for all dyads). However, the slower than anticipated progress in recruitment led the DIAdIC consortium to extend the recruitment period to 24 months and the data collection period to 30 months, providing more time for

countries with lower rates (see Figure 2). The overall project period was also extended by 6 months without affecting deliverables.

2. Additional recruitment sites (hospitals) were included in some countries (see Table 1).
3. If patients were unaccompanied to the hospital, recruitment staff tried to obtain family caregiver contact details and personally introduce the study via phone.
4. Monthly bilateral meetings were organized between the coordinator and all the RCT partners to enhance local screening strategies and reduce gatekeeping in some hospitals. Successful strategies, such as oncology nurses conducting screenings instead of physicians, were shared within the consortium.
5. Monthly online gatherings for data collectors and recruitment staff were established to exchange knowledge and best practices, promoting successful recruitment strategies.

Figure 2: Initial and extended recruitment period

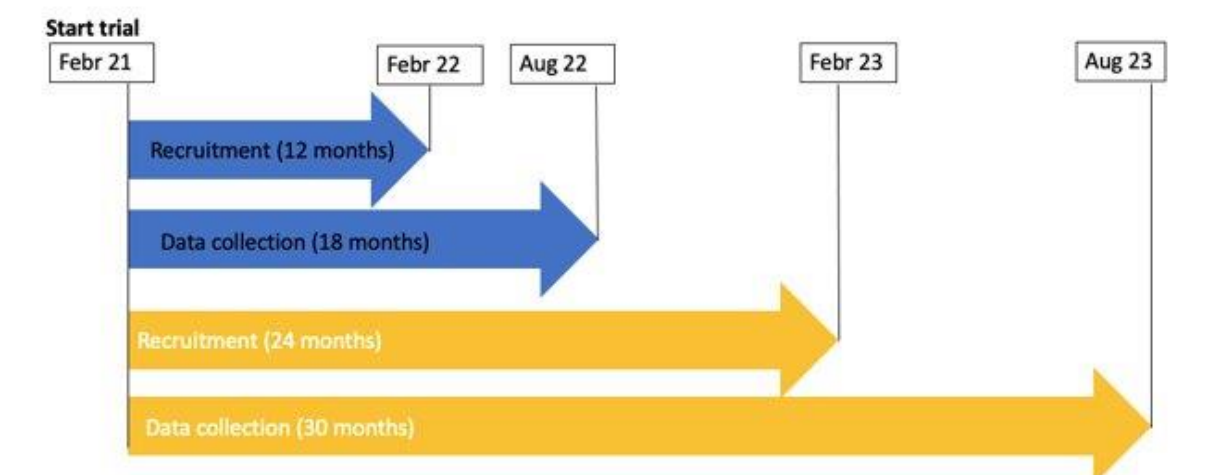


Table 1: Recruitment sites per country and recruitment starting dates

Recruitment site	Belgium	Denmark	Ireland	Italy	The Netherlands	UK-England	UK-Northern Ireland
AZ Maria Middelaes	Feb. 21						
UZ Gent	Feb. 21						
AZ Sint Lucas*	March 22						
AZ Damiaan*	Oct. 22						
Herlev Gentofte University Hospital		March 21					
Rigshospitalet		Aug. 21					
St. Vincent's University Hospital			Nov. 21				
St Francis Hospice			Nov. 21				

Recruitment site	Belgium	Denmark	Ireland	Italy	The Netherlands	UK-England	UK-Northern Ireland
Azienda AUSL-IRCCS Reggio Emilia - Oncologia Provinciale				Sept. 21			
Amphia Hospital					Sept. 21		
Reinier de Graaf Hospital					Sept. 21		
Maasstad Hospital*					Aug. 22		
King's College Hospital NHS Foundation						Aug. 22	
Guys and St Thomas' Trust						Apr. 22	
Belfast Trust, City Hospital							July 21
* Additional recruitment sites							

Even when applying different strategies to mitigate the lower-than-anticipated recruitment numbers, we did not reach the anticipated number of recruited dyads in all countries. At the end of the recruitment period (end of February 2023), a total number of 431 dyads were enrolled in the DIAdIC trial (see Table 2).

Table 2: Recruitment numbers per country

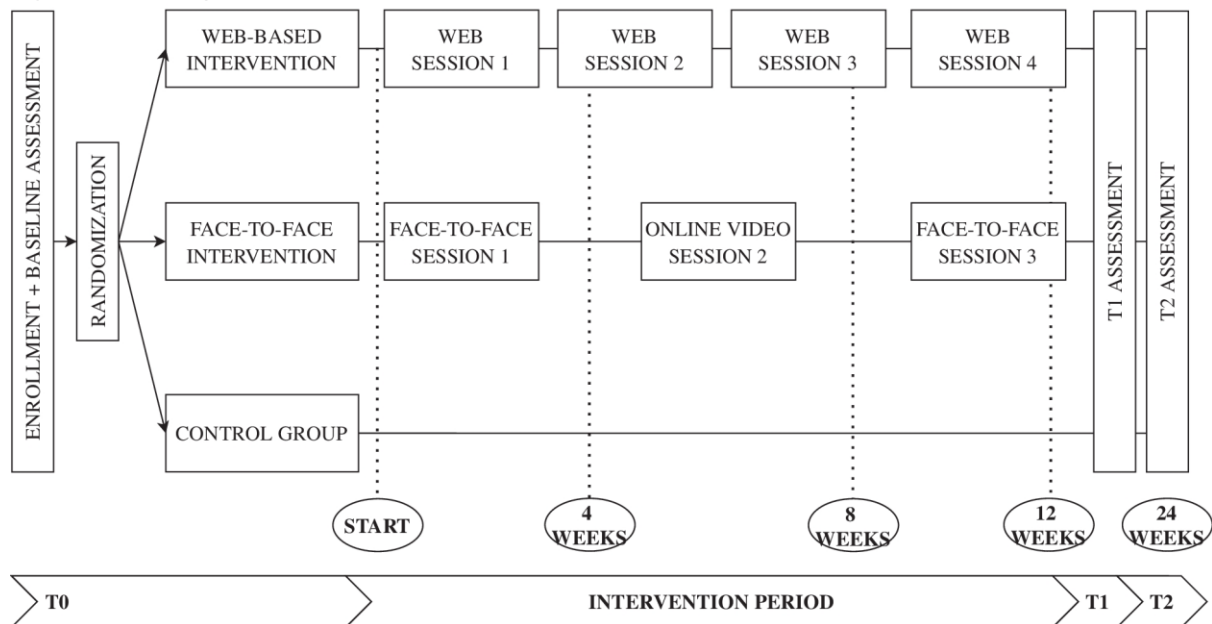
Country	Total	FOCUS+	iFOCUS	Control
Belgium	147	50	46	51
Denmark	107	35	35	37
Ireland	12	5	3	4
Italy	126	37	52	37
Netherlands	11	5	5	1
UK	28	8	7	13
TOTAL	431	140	148	143

Outcomes, measurements and data collection procedures

During the DIAdIC trial both qualitative and quantitative data was collected. Quantitative data was collected at three times from patient-caregiver dyads; T0, the baseline measure before randomization, T1 or first follow-up (T0+12 weeks) and T2 or second follow-up (T0 + 24 weeks). Emotional functioning and self-efficacy in managing the impact of cancer of patients and family caregivers at T1 were the primary endpoints. The secondary endpoints were the primary

outcomes at T2, and other outcomes such as quality of life, benefits of illness, coping, dyadic communication and ways of giving support at T1 and T2. At T1 both the patient and the family caregiver filled in questions to evaluate the effectiveness and satisfaction with the programs. Figure 3 shows the participant timeline and the data collection. An overview of the instruments, underlying measured concepts and their timing is added as a supplementary file (Appendix 12).

Figure 3: Participant timeline¹⁵



Additionally, a process evaluation was conducted to assess program fidelity and to identify and understand the influence of possible mechanisms of change within the interventions. Process evaluation data that were collected included:

1. Audio recording of the FOCUS+ (face-to-face) sessions to measure FOCUS+ fidelity: an objective assessment (1) where a research team member used a checklist on 20% of randomly selected dyads every three months, and a reflective self-assessment (2), where intervention nurses used a checklist on a small sample of dyads they worked with in the initial three months of the trial.
2. Logging of iFOCUS (web-based) sessions to measure iFOCUS fidelity: The following information was recorded: number of logins per session (dyads may complete a session over multiple occasions), time between login and logout, number of clicks in each session (giving an indication of how interactive/participating dyads are in the sessions), time spent per slide, number of clicks on the personal workbook, which videos were watched and, how many times the audio files (voice-overs) were listened to. This

information could be drawn from the iFOCUS platform in an Excel format and reflects important aspects of program fidelity.

3. To explore participants' perceptions of the interventions, their user experiences, core elements central to their experiences, and the mechanisms of change, we conducted interviews: In each country we conducted 6 interviews with intervention nurses, 6 interviews with research staff and 10 dyads who received the intervention and one dyad non-completer

Both quantitative and qualitative findings will be integrated as part of a mixed-method evaluation of the FOCUS+ and iFOCUS programs. This integration will offer deeper insights into the effectiveness of these programs and help in formulating recommendations for future program development and implementation.

While the involvement of a third party with expertise on technical development and maintenance of digital platforms was necessary, this created reliance on the web-development team during development and during the trial implementation of iFOCUS and FOCUS+. Considering the significant role of the iFOCUS platform in the DIAdIC RCT, serving as both one of the intervention programs and as a platform for management and data collection, we became dependant on the web-development team when encountering issues and bugs related to the registration of data such as enrolment, allocation, questionnaires and process evaluation data. To cope with this challenge a ticketing system was established using an online platform for collaborative project development. Errors or bugs were reported in this system with a clear description of the bug and its location. Potential solutions were discussed in weekly meetings.

Adhering to the trial timeline presented challenges, requiring flexibility in the delivery of FOCUS+, iFOCUS and when conducting data collection. These challenges could be attributed to various factors such as the disease progression of participating dyads, their treatment trajectory, and the availability of both patients with advanced cancer and their family caregivers for sessions or questionnaires. Although adherence to the timeline was strongly encouraged, some flexibility was permitted, allowing dyads to deviate from the intended 12 weeks after T0 if needed, prioritizing the completion of all program sessions.

3. DISCUSSION

As part of the international DIAdIC trial we developed and implemented two psychoeducational programs for patients with advanced cancer and their family caregivers: a face-to-face program (FOCUS+) and a web-based program (iFOCUS). We encountered various challenges in relation to development of the digital program, recruitment of dyads, and adhering to the project as described in the protocol, not least due to the wide ranging impacts of the COVID-19 pandemic. Various mitigating strategies were implemented during the development and implementation of FOCUS+ and iFOCUS as part of the DIAdIC trial.

Our experiences with the development and implementation of the two programs in an international RCT, as described in this article, provide some insights that are likely generalizable to other contexts and therefore can provide useful considerations for future similar studies.

First, starting from existing (in our case American) interventions or programs with proven effectiveness provides advantages, but also has its challenges. We started the development process not from zero, but rather opted to take a proven effective psychoeducational program as foundation for the development of FOCUS+ and iFOCUS and make adaptations. Given the accumulating evidence on effective interventions, starting a development process from proven effective programs can increase the likeliness of achieving a positive effect in a new setting or population and might be a more cost-effective and efficient approach to program development²⁴⁻²⁷. Nevertheless, when starting a development process, other factors than potential effectiveness such as the cultural fit and program fit to the population need to be taken into consideration^{28,29}. Considering that interventions hold a degree of context specificity, transferability from interventions to a new location or to a new setting and expecting the same positive outcomes is often uncertain¹⁸⁻²⁰. More so, research indicates that unadapted interventions and programs are likely to be less effective than contextually adapted or locally developed interventions³⁰. Hence for our development, which translated the program to a new context, we used the PIPFLA framework which took into account the contextual differences in cancer care of the USA around 2002 and Europe in 2021²².

Second, translating programs that build on interpersonal interaction and dyadic coping and discussion to an eHealth format is challenging. Our experience has been that the development of a digital psychoeducational program has its own specific challenges in relation to the program requirements or eHealth development in general²³. While described as possibly more cost-

effective than face-to-face interventions³¹ we found the development of a digital psychoeducational program to be a time and resource intensive process, even if based on previously developed programs. Due to limited resources and time we had to make pragmatic choices such as involving potential end-users in a consultancy role as part of user-testing rather than as part of a co-development trajectory. We would have ideally actively involved end-users in all stages of development, as this is likely to create a web program which fits better to their context^{32,33}. However, this creates a conundrum between the ideal development trajectory, which actively involves end-users across all phases of development, and project limitations concerning available time and resources. Therefore, pragmatic choices need to be made during the development of eHealth programs. Nevertheless, our experience is that, while pragmatic, a thorough development process from a face-to-face to a web-based format is necessary if we assume that the mode of delivery and the prerequisites differ greatly between face-to-face and web programs³⁴. One example of this is that while web-based programs are often evaluated on accessibility, user-friendliness, and data safety, these prerequisites are less or not applicable in face-to-face programs^{23,35,36}. Drawing from our experience, when developing a web-based program, it may be better to pragmatically explore the psychoeducational potential of existing technologies rather than attempting to mimic human-facilitated interaction. That said, rapid advancements in technology also introduce a temporal dimension to development and implementation of digital programs^{37,38}. It is reasonable to assume that the technological possibilities will have changed by the time a digital program gets implemented, creating a potential lag between the development and implementation phases³⁹.

Third, deliberately adopting a dyadic focus was important but also came with challenges. Other research has suggested that many aspects of stress and coping in relation to cancer and its treatment have an interdependent impact on patient and family caregivers and that dyadic programs are more aligned to that reality and are therefore more likely to have positive outcomes for both patients and family caregivers^{40,41}. However, this comes with a particular challenges as recruitment of dyads involves specific additional challenges compared to recruitment of individual patients or individual family caregivers separately. Moreover, the exclusion of dyads who can not identify a family caregiver is a concern in dyadic trials.

Fourth, considering the challenges during recruitment, our experiences reiterate the question whether the RCT paradigm, assuming rigidity and strict control, matches well with the real-world contexts in which people deal and cope with the illness, treatments and the complex

consequences on all aspects of life. Pragmatic trial designs have been put forward as more fit approaches to these contexts^{42,43}. However, even when adopting a pragmatic trial design, questions about permitting flexibility in aspects not initially identified will inevitably arise. Therefore, to gain insights in these processes and mechanisms of change we conducted a process evaluation using both qualitative and quantitative data as part of the DIAdIC trial.

Fifth, the potential challenges of the IT technology that is relied on for the study need to be considered. Because of the complexity and different components of our study we decided, together with an eHealth-specialised company, to develop a web-platform that integrated the different aspects of the study, including study management aspects such as enrolment, questionnaire administration, randomization, reminders but also including the iFOCUS program. However, this created a dependence on the web-development team to resolve bugs, errors and issues before starting the data collection (and to a lesser extent resolvable minor ones during the data collection). Separating the eHealth intervention (in our case iFOCUS) from study management technology may be a better option. For instance, programs like REDCap (Research Electronic Data Capture), that are specifically designed for data collection in research studies, are widely used and have proven to be reliable and secure and can offer a less concerning basis for the study management⁴⁴.

4. CONCLUSION

The international DIAdIC trial developed and implemented two psychoeducational dyadic programs for patients with advanced cancer and their family caregivers: a face-to-face version (FOCUS+) and a web-based version (iFOCUS). Based on our experiences we share several insights for future similar studies. These relate to the attention needed for context-specific adaptations when using existing interventions or program, the translation of human-facilitated programs to standalone eHealth versions, the challenges of adopting a dyadic focus in the study, the pragmatic challenges of conducting an RCT and evaluating implementation and effects, and the technology used for the study management.

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Ethics approval

All the patients and family caregivers who participated in this study provided written informed consent. The study was approved by the ethics committees of all the participating countries. Commissie Medische Ethiek UZ Gent, Belgium, 22/10/2020; Ethisch Comité AZ Maria Middelaers, 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, amended four times (7/09/2021 – 8/02/2022–10/05/2022–06/09/2022); NHS/HSC Research Ethics Committee, United Kingdom, 05/03/2021; Medisch Ethische Toetsings Commissie Erasmus Medisch Centrum Rotterdam, 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 submission of the final protocol.

Author contributions

ADV and VVG are the main authors and drafted the manuscript with input from the other authors. All authors received the possibility to provide additional feedback and approved for submission. All authors consented with publication.

Conflicts of interests

None.

Data availability:

The data sets generated and analysed during the current study are available from the corresponding author upon reasonable request.

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CHAPTER 7

Implementation of dyadic psychoeducational support programs at home for people with advanced cancer and their family caregivers: Stakeholder perspectives on barriers, facilitators, risks and opportunities

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[Submitted]

ABSTRACT

Purpose: To identify barriers, facilitators, risks or opportunities for the sustainable implementation of psychoeducational home-based programs for patients with advanced cancer and their family caregivers similar to the web-based iFOCUS program and the face-to-face FOCUS+ program.

Methods: We conducted online semi-structured in-depth interviews in Flanders, Belgium with external stakeholders identified as potential contributors to implementing psychoeducational home-based programs for patients with advanced cancer and their family caregivers. Our interview guide was based on the Medical Research Council, RE-AIM, and Normalization Process Theory frameworks. Data analysis happened inductively following a thematic analysis approach and based on the Bronfenbrenner Ecological model.

Results: We interviewed 13 stakeholders from hospital and home settings. We identified themes which could act as barriers, facilitators, risks, and opportunities for sustainable implementation of psychoeducational home-based programs across micro, meso, and macro levels. Four themes emerged: Intervention Characteristics, Reaching the target population, Program Embedding in Healthcare Organizations, and Policy and Societal Factors. Across levels stakeholders emphasized the need for clarity on psychoeducational programs. Achieving effective implementation requires organizational integration, training of personnel, leadership support, and policy changes across levels.

Conclusion: Various inherently connected themes which could act as a barrier, facilitator, risk or opportunity for sustainable implementation of psychoeducational home-based programs for patients with advanced cancer and their family caregivers emerged across levels. To cope with the challenges across levels our findings suggest a need for transmutal collaboration, reorganized healthcare, lobbying and multidisciplinary involvement to facilitate sustainable implementation of these programs.

1. INTRODUCTION

Both patients with advanced cancer and their family caregivers experience a multitude of physical, psychological, spiritual, and economic concerns as well as an increased burden and lower quality of life^{1,2}. Psychoeducational interventions focusing on both the patient and their family caregivers as a dyad have been shown to effectively and efficiently promote their well-being, lessen their burden and reduce the economic impact of cancer on their lives^{3,4}. Despite increasing evidence supporting the positive effects of psychoeducational interventions only a small portion are implemented into routine care⁵⁻⁷.

The FOCUS program as developed by Northouse in the United States is a dyadic home-based program for patients with advanced cancer and their family caregivers which provides psychoeducational support complementary to regular care and which effectively improves the quality of life and well-being in dyads⁸⁻¹⁰. As part of the DIAdIC trial (“Dyadic psychoeducational Interventions for patients with advanced cancer and their Informal Caregivers”)¹¹ two dyadic psychoeducational home-based programs were developed and tested in an international multicentre parallel-group three-arm superiority trial across six European countries (Belgium, the Netherlands, Denmark, Italy, The United Kingdom and Ireland)¹². Both psychoeducational programs were based on the original FOCUS program, the first being a nurse-led face-to-face program called FOCUS+, the second one being iFOCUS, a self-managed web-based program¹². The DIAdIC trial investigated whether FOCUS+ and iFOCUS generate favourable outcomes on emotional function and self-efficacy (primary outcomes) in dyads. Results regarding these findings are forthcoming elsewhere. While FOCUS has been evaluated in multiple studies among different populations, implementation of the program has only occurred on a small scale in the USA and has not been the case yet for iFOCUS and FOCUS+^{9,13}.

To increase the likeliness of sustainable program implementation, insights of healthcare professionals and other relevant stakeholders into the process of implementation of psychoeducational home-based programs such as iFOCUS and FOCUS+ is needed. Therefore, this study aimed to identify barriers, facilitators, risks or opportunities for sustainable implementation of psychoeducational home-based programs like iFOCUS and FOCUS+.

2. METHODS

2.1. Study design

Parallel to the ongoing DIAdIC trial¹², we conducted a process evaluation. Process evaluations in Randomized Controlled Trials (RCTs) aim to understand interventions by examining implementations, agents of change, and contextual factors¹⁴. The DIAdIC process evaluation is based on the MRC Framework with additional elements reflecting normalization process theory (NPT) and the RE-AIM framework¹².

As a part of the DIAdIC process evaluation, we conducted online semi-structured in-depth interviews with external stakeholders not affiliated with the trial to gain insights on the topics of context (Medical Research Council, MRC Framework), maintenance (RE-AIM framework) and cognitive participation, collective action and reflexive monitoring (Normalization Process Theory, NPT). We used the Consolidated criteria for Reporting Qualitative Research (COREQ)(Appendix 13)¹⁵. The online semi-structured in-depth interviews were conducted between November 2022 and March 2023.

2.2. Setting & Participants

We conducted online semi-structured in-depth interviews in Flanders, Belgium with external stakeholders identified as potential contributors to implementing psychoeducational home-based programs for patients with advanced cancer and their family caregivers. The aim was to explore the hypothetical implementation of psychoeducational home-based programs for patients with advanced cancer and their family caregivers like iFOCUS and FOCUS+, addressing barriers, facilitators, risks, and opportunities. Participants qualified for inclusion if they potentially contributed to the implementation of these types of programs. Individuals were excluded if actively involved in the development and implementation of iFOCUS and FOCUS+ as part of the DIAdIC trial to reduce insider bias.

Recognizing the roles of policy makers, medical clinicians, and paramedical clinicians in the care and support for patients with advanced cancer and/or their family caregivers^{16,17}, we designed a framework outlining these roles and settings (home and hospital). Stratified sampling was employed to construct a representative list of healthcare professionals and stakeholders

involved in delivering psychoeducational support. Through purposive sampling, representation was ensured across each segment of the framework. Participants were contacted via email or telephone to explain the interview's purpose and provide information on the programs and trial

2.3. Data collection

We developed an interview guide based on context (MRC Framework), maintenance (RE-AIM framework), and cognitive participation, collective action, and reflexive monitoring (NPT) to explore barriers, facilitators, risks, and opportunities for sustainable implementation of home-based psychoeducational programs for patients with cancer and their family caregivers (see Appendix 14). Estimating participant numbers for qualitative studies is challenging, particularly considering the ongoing debate on data saturation¹⁸. Therefore, we aimed for 10-15 participants to ensure adequate data for analysis given the study's scope and pragmatic considerations. After six interviews, we refined the guide based on insights and participant feedback (see Appendix 15), clarifying concepts, eliminating irrelevant questions on psychoeducational support knowledge, and introducing additional inquiries on the integration of psychoeducational programs for deeper insights. Interviews were conducted by VVG, a trained, male PhD student experienced in qualitative research, via online video conferencing, recorded, and pseudonymized for data richness. Fieldnotes were taken in the local language to ensure thick description of the data.

2.4. Data analysis

All interviews and field notes were thoroughly analysed using a thematic analysis approach¹⁹, which facilitated the inductive identification, analysis, and reporting of themes and patterns from the data¹⁹. Through iterative coding, codes were generated inductively and organized into themes and subthemes, while continuously comparing existing data and patterns with new data. Based on the Bronfenbrenner Ecological model²⁰ themes and subthemes with their respective codes were placed in micro, meso, and macro levels to gain insights into how these codes interacted across levels²¹. A two-step iterative coding process was employed, initially coding five interviews using NVivo 1.7, with three interviews independently coded by another researcher for cross-checking. Subsequent adjustments were made, and codes were integrated into the initial code tree. A multidisciplinary team reviewed and refined the code tree, leading to further adaptations based on their reflections. Remaining interviews were coded both deductively and inductively. In

the final phase, all codes were integrated into themes and subthemes corresponding to different levels. These findings underwent additional review by a local multidisciplinary team involved in the DIAdIC trial, incorporating their insights for further refinement.

2.5. Ethical considerations

This study was approved by the ethics committee of the University Hospital Ghent (B.U.N. B6702022000355, 11/08/2022).

3. RESULTS

3.1. Description of Participants

We contacted 33 potential participants of whom 7 refused and 13 did not reply. Between November '22 and March '23 we conducted 13 interviews which lasted 56 minutes on average (min=38, max=81). Most participants were policy makers (n=6), working in hospitals (n=7), and had more than 10 years of experience (n=6). (Table 1).

Table 1. Characteristics of participants (N=13)	
Sex	
Male	2
Female	11
Age	
<30	1
30-49	8
50+	4
Discipline	
Clinician, medical	2
Clinician, paramedical	5
Policy maker	6
Years of experience in oncology	
<5	5
5-9	2
10+	6
Setting	
Hospital	7
Home	6

3.2. Findings

Many of our findings can function as either barriers, facilitators, risks, or opportunities, depending on how they are addressed, and while categorizable within the micro, meso, and macro levels of the Bronfenbrenner ecological model²⁰, they are inherently interconnected and mutually influential. At micro level, we examined interactions between individual patients and healthcare providers, while the meso level addressed organizational dynamics. The macro level encompassed the healthcare system or government level^{21,22}. Within these levels, we identified four themes: (1) Intervention Characteristics (micro-level), (2) Reaching the target population (micro-level), (3) Program Embedding in Healthcare Organizations (meso level), and (4) Policy and societal factors (macro-level). Table 2 outlines these levels, their corresponding themes, and subthemes, specifying which type of participants made statements in regard to the subcategory.

Table 3: <i>Identified themes and subthemes per level, per stakeholder group</i>						
	Hospital (N=7)			Home (N=6)		
	Policy maker n=2	Medical n=1	Paramedical n=4	Policy maker n=4	Medical n=1	Paramedical n=1
<i>Micro level</i>						
<u>Intervention Characteristics</u>						
Perceived benefits and evaluation of psychoeducational programs	X*		X	X	X	X
Delivery methods and resource considerations	X	X	X	X	X	
Places of introduction to the program			X	X		X
<u>Reaching the target population</u>						
Motivation to participate and perception of the program			X	X		X
Introduction to reach potential participants		X	X	X		X
Role of care providers	X	X	X	X		
<i>Meso level</i>						
<u>Program Embedding in Healthcare Organizations</u>						
Fit within the organization	X			X		X
Evaluation of benefits and drawback	X	X	X	X	X	X
Leadership and executive support	X		X	X		
<i>Macro level</i>						
<u>Policy and societal factors</u>						
Healthcare reorganization			X	X		X

Policymakers' engagement				X		X
Taboo and stigma surrounding psychological topics	X	X	X	X		
Pressure on society and formal healthcare	X		X	X	X	X
* 'X' indicates which profiles made statements in relation to the identified subcategory						

Intervention Characteristics

In the subcategory of perceived benefits and evaluation of psychoeducational programs, a large majority of stakeholders argued that achieving sustainable program implementation requires clarity on the benefits of psychoeducational programs. Three stakeholders highlighted the challenge of quantifying benefits in psychological care compared to biomedical advancements such as treatments and medicines.

Regarding the subcategory delivery methods and resource considerations most stakeholders favoured face-to-face psychoeducational programs over digital psychoeducational programs, finding it better fitted to provide this type of support to this population, but also argued that face-to-face psychological support is expensive. Stakeholders acknowledge the potential cost-effectiveness of computer-based programs, highlighting their minimal impact on organizational resources. However, digital psychoeducational programs require a computer, tablet, laptop or phone with access to the internet and digital competence.

In the subcategory concerning the place of introduction to the program, five stakeholders state that psychoeducational home-based programs could benefit from being integrated in some form of transmural care pathway, since the place of program introduction (likely a secondary care setting) is not the place of program provision (likely home). Integrating these types of programs into transmural care pathways guarantees care continuity and communication between the involved care providers.

“Transmural care pathways in oncology are finding more and more entry, which is logic, hospitals are stuffed. And if you truly focus on the patient and their world then it’s only logical that you end up at their home eventually” (Staff member, male, 38 years)

Reaching the target population

In the subcategory of motivation to participate and perception of the program, four stakeholders emphasized the significance of patient motivation as a key determinant influencing participation in psychoeducational programs such as iFOCUS and FOCUS+. Seven stakeholders agreed that

potential participants might have low motivation to participate due to difficulties in perceiving the benefits of psychological support compared to the perceived burdens of participation, specifically related to the required effort and time. One stakeholder noted that patient motivation to participate in programs like iFOCUS or FOCUS+ could be influenced by the higher motivation of the family caregiver, and this influence could work reciprocally.

In the subcategory titled introduction to reach potential participants six of the 13 stakeholders highlighted the importance of the program introduction in reaching and engaging participants. Most participants do not immediately recognize the benefits of psychological care. Therefore four stakeholders emphasized the need for informative and motivating introductions to psychoeducational programs. These introductions should be led by healthcare professionals with expertise in psychological care and trusted by recipients. Involving various professionals (e.g., nurses, psychologists, physicians) at different points of contact during the introduction phase allows dyads to ask questions, positively influencing program credibility.

In the subcategory regarding the role of care providers in psychoeducational home-based programs, seven stakeholders emphasized psychologists' crucial role in delivering psychological care. However, three stakeholders argued against the outdated belief that only psychologists can provide such support, advocating instead for integrating psychoeducation into the practices of diverse healthcare professionals like nurses, general practitioners (GPs), and psychologists. Regardless of the healthcare professional's background, adequate training was identified as necessary before providing psychoeducational programs, with six stakeholders highlighting its importance in enhancing program effectiveness.

Program Embedding in Healthcare Organizations

Almost all stakeholders agreed that for successful, sustainable implementation of psychoeducational programs like iFOCUS and FOCUS+, these programs need to be integrated into existing healthcare organizations to allocate resources, personnel, and efforts to their program-related processes.

“When financing stops, the intervention is over and out because then there are no more people available who can introduce or execute the program!” (GP, female, 49 years)

Across interviews stakeholders found it challenging to identify one “ideal” healthcare organization or professional which should be the sole responsible for the embedding of psychoeducational home-based programs for patients with advanced cancer and/or their family caregivers. Consequently we refrain from appointing ideal partners and opted for broad terms like "healthcare organizations" or "healthcare professionals" in the Results and Discussion settings.

Challenges impeding Program Embedding in Healthcare Organizations include: the absence or incompleteness of a legal framework which regulates this type of care, its reimbursement ..., lack of mandate to provide home care, and inadequate availability of resources, time, and personnel. While eight stakeholders stated that transmural collaboration could help navigate this challenge, collaboration between primary and secondary care is currently limited and predominantly aimed at biomedical care.

“Who will provide medical guidance, who will provide care at home, who will administer the injection. Primary and secondary care collaborate on these matters because that is the common language they share...(Coordinator caregiver representative organization, female, 33 years)

In the subcategory concerning fit within the organization, three stakeholders emphasized the importance of aligning programs with the goals, processes, and target population of healthcare organizations. They asserted such alignment as crucial because organizations secure funding based on statutory mandates, obligating them to provide specific types of care. This funding allows healthcare providers to allocate resources to different care programs.

In the subcategory on evaluation of benefits and drawbacks, almost all stakeholders agreed on the necessity of assessing program impact before deciding on embedding within an organization. Eleven stakeholders emphasized potential benefits to organizations including cost reduction, a competitive advantage over other healthcare organizations or providers and improved outcomes for patients and family caregivers. When benefits are perceived to outweigh the drawbacks, program embedding within the organization is more likely.

In the leadership and executive support subcategory, four stakeholders stressed the importance of support from both leadership and executive personnel for successful program embedding.

They highlighted factors influencing leadership decisions, such as evidence-based information, cost-benefit analyses, and organizational advantages. In contrast, executive personnel are influenced by workload impact, feedback from the target population, and potential costs or benefits for patients and family caregivers, as observed by four stakeholders.

Policy and societal factors

In the healthcare reorganization subcategory, most stakeholders agreed that healthcare remains primarily biomedical in structure, lacking defined frameworks and legislation for transmurals psychological care. This absence results in less or no reimbursement for such care, making it costly and less accessible. Consequently, fewer patients access transmurals psychological care, making it less known and harder for patients to identify its benefits. Six stakeholders advocated for healthcare reorganization to include transmurals psychoeducational care and support as part of a care pathway to enable sustainable program implementation.

Regarding policymakers' engagement, three stakeholders stressed the importance of persuading policymakers to establish an integrated psychoeducational care framework. They suggested using evidence-based information, economic arguments, anecdotal experiences, and Patient Reported Outcome Measures (PROMs) to sway policymakers. Five stakeholders noted a positive trend in recognizing PROMs as a measure of psychoeducational program impact, facilitating engagement with policymakers and healthcare management in decision-making and policy development. One stakeholder recommended influencing policymakers through lobbying efforts, utilizing input from various sources to advocate for expanded policy on psychoeducational home-based support.

“Well, lobbying started a debate on palliative care at policy level, which in turn resulted in more research towards palliative care being performed.” (GP, female, 49 years)

In the taboo and stigma subcategory, two stakeholders noted reduced stigma surrounding psychological topics. However, stigma persists on specific issues like end-of-life care, death, and coping with illness, particularly relevant for patients with advanced cancer and their family caregivers. This ongoing stigma hinders this population from accurately assessing the necessity for psychological support, cultivates feelings of shame, and causes potential participants to disregard these topics. Consequently, beliefs such as "I don't need this care" or "I should handle this alone" hinder uptake of psychoeducational programs by this population.

In the subcategory titled "Pressure on Society and Formal Healthcare," almost all stakeholders recognized significant challenges stemming from the need for cost-saving measures. These measures have become necessary due to heightened pressure on formal care systems for various reasons, such as an aging population and an increased psychological burden at the societal level. Simultaneously, the stakeholders recognized a growing demand for psychological care and support which leads to extensive waiting lists and inaccessible psychological care. Therefore, the need for concise psychoeducational support could be a way to prevent worsening psychological burden.

"I think in general, there is just such a shortage in care professionals, medical and paramedical, which influences the waiting lists. And that just hinders people who want to participate."

(Adjunct head nurse, female, 26 years)

4. DISCUSSION

4.1. Main findings

This study aimed to identify factors influencing the sustainable implementation of psychoeducational home-based programs like iFOCUS and FOCUS+. Our findings are inherently interconnected and mutually influential and many factors can act as either barriers, facilitators, risks, or opportunities, depending how they are addressed (e.g. perceiving the benefits of psychoeducation is a facilitator, not perceiving the benefits is a barrier). Four key themes emerged: intervention characteristics, reaching the target population (micro level), Program Embedding in Healthcare Organizations (meso level), and influencing the outer setting (macro level).

4.2. Strengths and limitations

The strength of this study lies in conducting stakeholder interviews as part of a comprehensive process evaluation, grounded in frameworks like MRC, RE-AIM, and Normalization Process Theory^{14,23}. These frameworks guided data collection, with patterns, themes and relationships

emerging inductively through a thematic analysis approach and based on the Bronfenbrenner Ecological model. Data analysis involved an iterative process, constant comparison, and multidisciplinary team involvement to ensure robustness. Purposive sampling of clinical and policy stakeholders facilitated comprehensive identification of implementation factors across micro, meso, and macro levels, ensuring diverse perspectives were considered.

Acknowledging limitations, our participant sample lacked diversity, notably in medical clinicians (2/13), despite their pivotal role in hospital decision-making²⁴. Therefore, our findings may be more aligned with policymakers and paramedical professionals. Our pragmatic approach of conducting 10-15 interviews may have limited thorough exploration of key themes due to time and resource constraints. Additionally, while targeting policymakers and clinicians across hospital and home settings is reasonable, other stakeholders like social workers or community health workers, whose perspectives could be valuable, were not included. Moreover, exploring hypothetical scenarios may lead to responses based on conjecture rather than real experiences, potentially resulting in over or underestimation of the actual situation²⁵.

4.3. Interpretation and implications of the findings

In relation to Intervention Characteristics and Program Embedding in Healthcare Organizations, specific challenges were expensiveness of home-based face-to-face psychoeducation, determining the place of program contact and determining the healthcare organization or healthcare providers responsible for this type of care. Other research also identified program cost, availability of trained professionals and lack of patient screening, management and follow-up as factors hindering sustainable implementation of home-based programs^{26,27}. While our findings suggest transmurall collaboration as a way to cope with this challenge, our findings suggest that this is more common in biomedical care but rare in the provision of psychosocial care. Nevertheless, transmurall oncology care has shown to increase motivation, self-management, and quality of care for advanced cancer patients and their caregivers while also reducing burden on oncology centres, promoting communication between care providers, and offering insights into patients' living conditions, social environment, and medical history^{28,29}. An explanation for the suboptimal integration of psychological care into transmurall care pathways could be the 'wait-and-see' attitude of some healthcare professionals and a lack of policy on this topic²⁹. Transmurall collaboration on psychosocial topics can be stimulated by identifying and involving actors throughout the care trajectory of patients with advanced cancer and their family caregivers and fostering shared leadership of the care trajectory across settings^{29,30}.

Identifying the potential benefits of psychoeducational programs poses a recurring challenge across various levels, hindering the sustainable implementation of home-based programs. Individuals may struggle to perceive the benefits of psychological support; organizations may hesitate to embed such programs; and legislative decisions may overlook their positive impact. Nevertheless, in healthcare systems facing pressure to balance quality of care with economic constraints, further understanding the potential benefits of psychoeducational programs alongside their challenges and drawbacks could facilitate sustainable implementation^{4,31,32}. The challenge in identifying the potential benefits or gains of psychoeducational programs could be attributed to its delayed effects and the subtle application of newly learned skills or coping styles^{5,33,34}. Other factors which could contribute to the challenges with identifying the benefits of psychoeducational programs are the lack of open public discussion of acquired help on taboo topics such as end-of life care and support and the biomedical view on healthcare, neglecting psychosocial and existential needs^{5,35,36}.

The influence of the biomedical organization of care across levels becomes evident when considering how a substantial portion of the public, healthcare providers, organizations, and funding structures still prioritize medically oriented clinical care, overlooking the holistic needs of patients and neglecting vital social, economic, and psychological aspects of care³⁷⁻⁴⁰. A biopsychosocial-holistic approach, recognizing interconnected physical, psychological, social, and behavioural factors, could support sustainable implementation of psychoeducational programs^{38,41}. While palliative care aligns with this approach, funding policies inadvertently favor certain types of care over others and palliative care is not always adequately funded, hampering the sustainable implementation of psychoeducational home-based programs⁴²⁻⁴⁴. Therefore, our findings suggest that lobbying efforts should be employed to engage policymakers, reform healthcare, and allocate more resources towards biopsychosocial-holistic and/or palliative care to better integrate psychoeducational home-based initiatives³⁷. PROMs emerge as a promising tool to demonstrate the impact of these programs, being of influence on policymakers and healthcare management⁴⁵.

5. Conclusion

We identified various factors which could act as a barrier, facilitator, risk and opportunity for the sustainable implementation of psychoeducational home-based programs for cancer patients and their caregivers across micro, meso, and macro levels. Within the themes of intervention characteristics, reaching the target population, embedding programs into healthcare

organizations, and policy and societal factors influencing factors were identified. Our findings highlighted challenges in determining program contact points and responsible healthcare providers, recognizing the benefits of psychoeducational home-based programs and the biomedical organization of care. However, transitioning to a biopsychosocial care approach, continued lobbying efforts, multidisciplinary involvement, and the adoption of new impact measures like PROMs can support the sustainable implementation of these programs.

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Conflicts of interests

None.

Data availability

The data sets generated and analysed during the current study are available from the corresponding author upon reasonable request.

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PART 5

GENERAL DISCUSSION AND CONCLUSIONS

GENERAL DISCUSSION AND CONCLUSIONS

1. INTRODUCTION

The main objective of this dissertation was to develop and evaluate a home-based psychoeducational eHealth program for patient-caregiver dyads in an advanced cancer trajectory. In **Chapter 1**, we described that a considerable part of the adult population provides family care for someone with a serious illness and that these family caregivers may experience increased burden. In **Chapter 2**, we outlined the seven-step development process of the home-based psychoeducational eHealth program (iFOCUS) for people with advanced cancer and their family caregivers. **Chapter 3** included the protocol for the DIAdIC trial, an international, multicentre, three-arm randomized controlled trial evaluating the effectiveness and cost-effectiveness of the iFOCUS program and a nurse-delivered psychoeducational program FOCUS+, for patients with advanced cancer and their family caregivers. Our findings in **Chapter 4** indicated showed that ICT-related factors were rarely explicitly cited as a reason for non-participation in the trial. Although the level of digital competence varied between sociodemographic groups, it did not significantly predict dropout. The results in **Chapter 5** showed that the psychoeducational eHealth program called iFOCUS did not have a significant effect on the self-efficacy and emotional functioning of patients with advanced cancer and their family caregivers. **Chapter 6** describes experiences, challenges, and solutions during the development and implementation of two psychoeducational dyadic programs for patients with advanced cancer and their family caregivers in the DIAdIC trial. Based on stakeholder interviews, presented in **Chapter 7**, various barriers, facilitators, risks or opportunities for sustainable implementation of home-based psychoeducational programs for patients with advanced cancer and their family caregivers were identified at the micro, meso and macro levels.

This discussion section begins with a brief summary of our main findings. We then address methodological considerations, strengths, and limitations. Next, we discuss the relevance of our findings in the context of current knowledge about psychoeducational eHealth support for patients with advanced cancer and their family caregivers. Finally, we will provide recommendations for future research, clinical practice and policy.

2. SUMMARY OF THE MAIN FINDINGS

The **first aim** of this doctoral dissertation was to delineate the number, characteristics and experiences of family caregivers of people with serious illness.

In **Chapter 1**, we present a secondary analysis of data from the 19th Social-Cultural Changes (SCC) Survey in Flanders, conducted from March to July 2014 by the Study Service of the Flemish Government. A random sample of 2,581 Dutch-speaking individuals between the ages of 18 and 95 residing in Flanders or Brussels was selected from the national population register using a stratified two-step sample. The results indicated that a considerable part of the adult population in Flanders and Brussels (7.6%, equivalent to approximately 494.000 individuals) provided family care to someone with serious illness in the last 12 months. The majority of family caregivers of individuals with a serious illness were female (57.9%), between the ages of 35 and 74 (70.2%) and married (67.5%). Nearly half of the family caregivers of someone with a serious illness provided care to a parent (47.8%). While 42.3% of family caregivers of someone with a serious illness worked full-time, nearly one in three (31.8%) provided at least 10 hours of family care each week. In comparison to other family caregivers, family caregivers of people with a serious illness provided care to care recipients who were male significantly more often (46.5% vs 29.5%, $P=0.001$). Additionally, family caregivers of someone with a serious illness more often provided care to care recipients who were aged 35-74 (49.5% vs 25.8%, $p<0.001$), and to care recipients who lived with relatives other than the participating family caregiver (48.2% vs 28.7%, $p<0.001$). Family caregivers of people with serious illness, compared to other family caregivers, provided more medical and nursing care (33.3% vs 22.5%, $p=0.027$). Additionally, when providing medical and nursing care, both groups of family caregivers experience elevated burden, which is higher for family caregivers of people with other conditions but not significantly different (mean=0.261, 95%CI=-0.211 – 0.733 vs mean= 0.400, 95%CI 0.008 – 0.793). When not providing medical and nursing care, only family caregivers of people with other conditions experience elevated burden (mean=0.116, 95%CI=-0.283 - 0.516 vs mean =-0.290, 95%CI =-0.620 - 0.039) which is significantly different from the burden experienced by other family caregivers.

The **second aim** of this PhD dissertation was to describe the development of a psychoeducational eHealth program (iFOCUS) to support patients with advanced cancer and their family caregivers and its implementation in an international RCT.

In **Chapter 2** we describe our experiences and our challenges during the development of iFOCUS, a psychoeducational eHealth program for people with advanced cancer and their family

caregivers. Additionally we describe the evaluation of the initial acceptability and usability of the iFOCUS program. The psychoeducational, home-based eHealth program named iFOCUS was developed in seven steps, guided by the Scrum methodology. The development process involved seven steps: (1) Concept design, (2) Development of mock-ups, (3) Obtaining feedback from the international consortium, (4) Technical development of the program, (5) Creating country-specific versions for each of the six participating countries, (6) Preliminary testing through user and functional testing and (7) Implementing the final version for the RCT. The development of the iFOCUS program involved the collaboration of several teams, including a core development group (1), a web development team (2), an international consortium (3), audio-visual experts (4), and potential end-users (5). The resulting web-based psychoeducational program for patients with advanced cancer and their family caregivers is accessible from home. The program comprises four sessions spread over a 12-week period with three weeks between each session. The challenges encountered during the development of iFOCUS were related to the transfer of ideas into functional components, the spreading of the content, tailoring, determining the log-in procedure, input of translated materials and determining an onboarding procedure. Using the Scrum methodology facilitated a flexible and adaptable development process. Collaboration between different teams and integration of different perspectives helped resolve issues related to program flow, content, language, layout, and bugs, but some pragmatic choices were necessary considering project limitations. The program was described as both acceptable and usable by other researchers and potential end-users during the user and functional testing. Feedback mainly focused on text size and fonts. Minor changes to the content, tailoring, and program flow were required.

Chapter 3 presents the protocol describing the implementation of the iFOCUS program as part of the DIAdIC trial, an international multicentre three-arm randomized controlled trial conducted 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 were randomized to one of three 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 (web-based iFOCUS and face-to-face FOCUS+) offer tailored psychoeducational support for patient-family caregiver dyads which was accessible at home. The face-to-face FOCUS+ program consisted of two 90-minute home visits and one 30-min online video session, conducted by a trained intervention nurse over 12 weeks. The web-based iFOCUS intervention was a self-managed intervention that was completed autonomously by the patient-caregiver

dyads together in their home (or a location of their preference). iFOCUS encompassed four sessions spread over 12 weeks. The overall objective of the DIAdIC trial was to evaluate the effectiveness, cost-effectiveness, and mechanisms of action of iFOCUS and FOCUS+ 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.

The **third aim** was to describe the outcomes of the DIAdIC trial, focusing on recruitment for the trial, the effectiveness of iFOCUS and FOCUS+ on primary outcomes (self-efficacy and emotional functioning), the implementation of these programs within the trial, and the sustainable implementation of iFOCUS and FOCUS+ beyond the trial setting.

In **Chapter 4** we demonstrate how digital competence varies between individuals according to sociodemographic characteristics and how it affects participation and retention to a trial with an eHealth component. We analysed data collected during the DIAdIC trial, specifically data on trial screening, recruitment and participation, as well as baseline and first-follow-up data. Among those refusing participation in the trial, only a minority of eligible patients and family caregivers (37 out of 1752 non participants or 2.1%) explicitly mentioned technology as the reason for non-participation. Enrolled patients reported significantly lower digital competence than their family caregivers (3.07 vs 3.17, $p=0.046$). Digital competence is associated with sex, age, trial location, educational attainment, and perception of income. It can be reasonably inferred that the digital competence of either the patient or the family caregiver predicts trial retention.

Chapter 5 presents the results from the DIAdIC trial, which evaluated the effectiveness of iFOCUS and FOCUS+ on the primary outcomes emotional functioning and self-efficacy. The DIAdIC trial was an international multicentre parallel-group three-arm superiority trial conducted in six countries (Belgium, the Netherlands, Italy, Denmark, Ireland, and the United Kingdom). As part of the DIAdIC trial dyads were randomly assigned to one of the three parallel groups: (1) the FOCUS+ face-to-face intervention, (2) the iFOCUS web-based intervention, or (3) standard care (control group). Between February 2021 and August 2023, 431 dyads were randomized 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 (patients: -0.27; 95%CI -2.11 to 1.57, family caregivers: 0.30; 95%CI -1.41 to 2.00) or self-efficacy (patients: 0.49; 95%CI -6.21 to 7.19, family caregivers: 3.66; 95%CI -3.36 to 10.68). FOCUS+ did not yield statistically significant improvements at T1 for patients or family caregivers in emotional functioning (patients: 0.12; 95% CI -1.65 to 1.89, family caregivers: 0.17; 95% CI -1.45 to 1.79)

but significantly improved self-efficacy in patients, compared to the control group at T1 in patients (9.02; 95% CI 2.45 to 15.58), but not in family caregivers (3.88; 95% CI -2.84 to 10.61).

In **Chapter 6** we present our experiences with the development and implementation of two dyadic psychoeducational home-based programs, FOCUS+ and iFOCUS in the context of a RCT in six European countries. Within this trial we successfully developed and implemented two psychoeducational programs for patients with advanced cancer and their family caregivers. However, we encountered various challenges during this process. These challenges pertain to the attention needed for context-specific adaptations when utilizing an existing intervention or program as a foundation for development, the translation of human-facilitated programs to standalone eHealth versions, the challenges of adopting a dyadic focus in the study, the pragmatic challenges of conducting an RCT and evaluating implementation and effects, and the technology used for the study management.

In **Chapter 7**, we identify barriers, facilitators, risks or opportunities for the sustainable implementation of psychoeducational home-based programs for patients with advanced cancer and their family caregivers. To this end, we conducted online semi-structured in-depth interviews in Flanders, Belgium with relevant stakeholders identified as potential contributors to the implementation process of psychoeducational home-based programs for patients with advanced cancer and their family caregivers. In order to gain insights on the topics of context (Medical Research Council, MRC Framework), maintenance (RE-AIM framework) and cognitive participation, collective action and reflexive monitoring (Normalization Process Theory, NPT). Data analysis was conducted inductively following a thematic analysis approach and was based on the Bronfenbrenner Ecological model. Between November 2022 and March 2023, 13 interviews were conducted with an average duration of 56 minutes. Most participants were policy makers (n=6), working in hospitals (n=7), and had more than 10 years of experience (n=6). Four themes were identified across three levels of the Bronfenbrenner Ecological model (micro, meso and macro level): intervention characteristics (micro level), reaching the target population (micro level), program embedding in healthcare organizations (meso level), and policy and societal factors (macro level). While our findings were categorized within the micro, meso, and macro levels of the Bronfenbrenner ecological model, they are inherently interconnected. In order to address the challenges across these levels, our findings suggest a need for transmurial collaboration, reorganized healthcare, lobbying and multidisciplinary involvement to facilitate sustainable implementation of these programs.

3. METHODOLOGICAL CONSIDERATIONS, STRENGTHS AND LIMITATIONS

To address our research questions, we employed three distinct study designs. In Chapter 1, we conducted a secondary data analysis of cross-sectional survey data. Chapters 2-6 were based on an international multicentre three-arm randomized controlled trial. In Chapter 7, we analysed data from online semi-structured in-depth interviews with relevant stakeholders. The methodological strengths and limitations are discussed below.

3.1. A secondary data analysis of the cross-sectional population-based Social-Cultural Changes survey

We performed a secondary analysis on data from the 19th Social-Cultural changes survey (SCC) in Flanders survey, between March and July 2014 by the Study Service of the Flemish Government¹. A particular strength of this study was that it used a representative sample of the adult population in Flanders by selecting 2,581 participants from the national population register using a stratified two-step sample participants. This approach enhanced the generalizability of our findings on family caregiving in serious illness to the entire adult population. Additionally, the use of computer-assisted personal interviewing (CAPI) by trained interviewers, regular quality checks of interviews and control for interview variance improved the quality of the data. Using a random sampling method for the SCC survey, where family caregivers were not the primary focus, reduced the likelihood of ascertainment bias.

This study also had several limitations. One such limitations was that the analysis was performed on data gathered in 2014. While this data represented the most recent information collected on family caregiving as part of the SCC (at that time) it is possible that our findings regarding the prevalence of family caregiving for people with serious illnesses could be an underestimation compared to the current prevalence. This is particularly plausible given the increased number of patients with chronic or severe conditions, compounded by the effects of the COVID-19 pandemic^{2,3}. Other limitations included possible issues of measurement bias. For instance, in the questionnaire family caregiving for someone with a serious illness was separated from other family caregiving, where family caregiving of older people and of people with dementia were put into the "other" category. However, this population also typically exhibits a multitude of chronic

and serious conditions. This could have led to misclassification bias, which would have altered the results. Additionally, excluding family caregivers who were not registered to a private household may have introduced selection bias, as their experiences may differ from those of family caregivers registered to a private household. Nonresponse could also have introduced selection bias, but the Study Service of the Flemish government performed a logistic regression based on living situation, sex, marital status, age, and nationality to generate a nonresponse weight. Finally, it is possible that participants may have provided socially desirable responses influenced by societal expectations associated with caregiving for a partner, parent, or family member.

3.2. An international multicentre three-arm randomized controlled trial

We analysed data from the DIAdIC trial to describe the digital competence of participants and how it influenced retention in the DIAdIC trial. In particular, the data from the screening, recruitment and participation processes, as well as the baseline and first follow-up data, were analysed. Utilizing multiple data sources, collected over an extended period facilitated a thorough examination of how digital aspects and digital competence influenced various aspects of the trial dynamics such as recruitment and trial retention. Moreover, drawing on data collected from an international multicentre trial spanning six countries resulted in a substantial sample size.

Due to variations in local regulations and agreements with recruitment centres uniform and standardized registration was challenging. These local regulations may have hindered comprehensive data collection, potentially introducing reporting bias. Therefore it is suspected that the 2.1% of non-participants who explicitly declined participation due to ICT-related reasons could be an underestimation, given that 17% of non-respondents reported no specific reason and 47.9% reported no interest (without elaboration). Furthermore, measurement bias may have occurred, given that digital competence was operationalized as a combination of skills and comfort using computers, smartphones or tablets. Nevertheless, literature suggests that digital competence encompasses additional key aspects, including attitudes towards ICT, critical and responsible use, and engagement across settings⁴.

We also used data from the DIAdIC trial to assess the effectiveness iFOCUS and FOCUS+ on emotional functioning and self-efficacy in patients with advanced cancer and their family

caregivers. By including a heterogeneous group of patients with advanced cancer and their family caregivers in terms of cancer diagnoses, age, sex and the relationship between the patient and family caregiver across six European countries, the external validity of our findings was enhanced. Additionally, the primary outcomes were measured using validated instruments⁵.

There are however several limitations. First, difficulties were experienced in implementing the trial, which were compounded by the ongoing COVID-19 pandemic and the protective measures implemented by governments and healthcare institutions. Obtaining informed consent from both the patient and the family caregiver was a prerequisite, but since family caregivers and external personnel had restricted or no access to hospital wards, trial recruitment was hindered. Furthermore, the COVID-19 pandemic increased the pressure on formal healthcare, limiting the available time and resources to support trial recruitment and COVID-19 related research was prioritized over other research. In addition to this, regulations and administrative requirements for study approvals, coupled with varying recruitment strategies across hospitals, contributed to delays and reduced referrals in certain countries. Consequently, despite the implementation of mitigating strategies, including the extension of the recruitment period and the inclusion of additional recruitment sites, the targeted sample size of 609 dyads could not be attained. This resulted in our study being underpowered, thereby reducing the probability of identifying statistically significant differences. To address this issue, a conditional power analysis was performed, which revealed that if the trial had proceeded as initially intended, there would have been a 10% to 63% likelihood of a 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. While selection bias might have been introduced by informing participants about the psychoeducational or eHealth aspect of the trial, the different adherence rates, being 52% for the iFOCUS program and 76.4% for the FOCUS+ program, suggested that participants may have had other motivations for participating. Finally, since datacollectors were often present when completing questionnaires, reflection and communication with the datacollectors could have introduced placebo effects.

3.3. Online semi-structured in-depth interviews with external stakeholders

A strength of this study is that the interview guides were developed using constructs from implementation frameworks such as the MRC framework ref, RE-AIM ref, and the Normalization Process Theory⁶⁻⁸. By using these frameworks to inform the development of the interview guides, we ensured a comprehensive exploration of relevant constructs. Additionally, the adoption of a thematic analysis approach⁹ and the incorporation of the Bronfenbrenner Ecological Model¹⁰ facilitated the identification of patterns, themes, and relationships to be identified, enhancing the depth and richness of the analysis. Constantly comparing existing findings with new data, involvement of a multidisciplinary team and the purposive sample strategy further contributed to the credibility, robustness and validity of the findings.

Acknowledging limitations of this design, purposefully sampling may have resulted in the overrepresentation or underrepresentation of specific populations. In particular, our efforts to include medical clinicians (2/13) were less successful. Consequently, the insights gained may be incomplete, as the sample in this design may not fully represent the diverse perspectives of stakeholders involved in the implementation process of psychoeducational home-based programs for patients with advanced cancer and their family caregivers. However, our efforts to diversify the sample were effective in the inclusion of paramedical clinicians and policymakers from hospital and home settings, which are also important stakeholders in the sustainable implementation of psychoeducational programs^{11,12}. Asking stakeholders about hypothetical situations may introduce both hypothetical bias, where respondents provide insights based on hypothetical rather than real scenarios, and social desirable answers, where respondents provide answers they believe the interviewer wants to hear. However, our findings retain their scientific merit, offering insights into stakeholders' perceptions, attitudes, and ideas, thereby enriching our understanding of the contextual factors influencing the implementation of psychoeducational home-based programs for patients with advanced cancer and their family caregivers.

4. DISCUSSION OF THE FINDINGS IN LIGHT OF THE CURRENT STATE OF KNOWLEDGE IN RELATION TO EHEALTH PSYCHOEDUCATIONAL SUPPORT FOR PATIENTS WITH SERIOUS ILLNESS AND THEIR FAMILY CAREGIVERS.

The interpretation of our findings in light of current state of knowledge and challenges, happens in four major topics 1) the prevalence and burden of family caregivers, 2) the neutral findings for the effectiveness of the iFOCUS program, 3) challenges of a rigorous eHealth development process and potential solutions; 4) integration of eHealth support programs into regular care.

4.1. The prevalence and burden of family caregivers

- *The prevalence of family caregiving*

In **Chapter 1**, we described that over the past year more than a quarter (25.7%) of respondents provided family care. This is lower than the proportion providing informal caregiving in Belgium as estimated by the European Social Survey (38.7%)¹³. However, substantial variability exists both nationally (in Belgium) and internationally in family caregiving prevalence rates, potentially reflecting differing perceptions of what constitutes family caregiving¹⁴⁻¹⁶. While a considerable proportion of the population currently provides family care, the sustainability of family caregiving is challenged by demographic shifts towards an aging population¹⁷, increased chronic health conditions among the elderly^{18,19}, and the impending shortfall of family caregivers relative to the number of older individuals requiring care^{20,21}.

- *Exploring the burden in family caregivers of someone with a serious illness*

In **Chapter 1**, our findings indicate that family caregivers of someone with a serious illness significantly more often report that the care they provide is psychologically demanding (45.6% vs 28.7%, $p=0.001$). This finding is supported by other research, which demonstrated that depression rates are higher among family caregivers of patients in the terminal or palliative stages of cancer compared to those caring for individuals with non-advanced cancer²². Considering how psychological burden has been identified as the most frequent and most taxing form of burden in family caregivers^{23,24}, this could explain why our results indicate that the overall

burden in family caregivers of people with serious illness is higher than in other family caregivers (mean score of 0.187 vs -0.039, $p=0.038$)^{23,24}.

Family caregivers of people with serious illnesses are more likely to provide medical and nursing care compared to other caregivers (33.3% vs 22.5%, $p=0.027$), which other research has identified as a demanding task²⁵⁻²⁷. Our results also show that when family caregivers provide medical and nursing care there is no significantly higher experienced burden for the caregivers of people with serious illnesses compared to those of people with other conditions (and rather, the latter have a slightly, albeit not statistically significant, burden: mean=0.261, 95%CI=-0.211 – 0.733 vs mean=0.400, 95%CI 0.008 – 0.793). In contrast, when other than medical and nursing care tasks are provided, caregivers for people with serious illness report a significantly higher burden (mean=0.116, 95%CI=-0.283 - 0.516 vs mean =-0.290, 95%CI =-0.620 - 0.039). Therefore, further research is warranted to identify the influence of caregiving tasks on the experienced burden in family caregivers of people with serious illness. Additionally, other factors can contribute to the experienced burden in family caregivers of people with serious illness. Research has indicated that family caregivers of someone with a serious illness experience increased distress due to co-suffering, wherein family caregivers experience heightened distress due to the diminished physical, psychological, and emotional well-being of the patient²⁸⁻³⁰. Furthermore, patients with serious illness and their family caregivers may have unmet care needs (e.g., need for information, need for coping strategies...) which increase their burden³¹⁻³⁴. Additionally, fear of death of the loved one, which is more likely in patients with serious illness, has also been shown to increase the distress of the family caregiver^{35,36}.

Our results showed no evidence of any sociodemographic characteristics, such as sex, being significantly associated with burden in family caregivers (except for providing medical or nursing care). Additionally, the results did not indicate that a greater proportion of family caregivers for individuals with serious illnesses were female (57.9% women vs. 50.4% men, $p = 0.177$). This runs counter to other research which often suggests family caregiving to be predominantly provided by women and suggests an influence of sex on burden. Other research, for instance, shows that female family caregivers often experience higher burden³⁵⁻³⁷. The reason for this are complex and not fully understood^{14,38,39}. Higher burden in female family caregivers may be due to the extensiveness and demanding nature of the caregiving tasks, with hands-on care being more often provided by female family caregivers^{14,28,39}. Furthermore, the burden could be compounded by the fact that prolonged and intensive family caregiving disproportionately falls on middle-aged

women, who are frequently managing multiple roles, including employment⁴⁶⁻⁴⁸. Therefore further research is necessary to explore the impact of sociodemographic variables on the burden experienced by family caregivers of individuals with serious illness.

4.2. The neutral findings for effectiveness of iFOCUS on emotional functioning and self-efficacy in managing the impact of cancer in patients with advanced cancer and their family caregivers

In **Chapter 5** we present the results of the DIAdIC trial, which was a multicentre RCT across six European countries. Results from this trial indicate that the psychoeducational **face-to-face FOCUS+** intervention significantly improved patients' self efficacy at 12 weeks compared to a control group (9.02; 95% CI 2.45 to 15.58). No significant effects were found for the second primary outcome emotional functioning. With the focus of this PhD thesis particularly on the **eHealth** equivalent of the program (**iFOCUS**) the neutral findings compared to FOCUS+ warrant deeper exploration and interpretation. We found no significant results for self-efficacy (patients: 0.49; 95% CI -6.21 to 7.19, family caregivers: 3.66; 95%CI -3.36 to 10.68) and emotional functioning (patients: -0.27; 95%CI -2.11 to 1.57, family caregivers: 0.30; 95%CI -1.41 to 2.00) at T1. Northouse's and colleagues' one-group pretest-post-test of a tailored web-based psychoeducational intervention (only the F-component) for patients with cancer and their family caregivers indicated positive effects on the emotional distress of dyads and improved self-efficacy in family caregivers, which would be comparable to the effects observed in the nurse-facilitated FOCUS intervention. The absence of a control group in their study, however, was a serious threat to internal validity and limited causal inference⁴⁰. Additionally, there are a number of remarkable difference between our trial with iFOCUS and their web FOCUS one-group pretest-post-test. Their study found low enrolment (51%) but high retention (86%) rates, with participating dyads rating the program as less useful (4.4/7) and satisfactory (4.8/7) compared to its usability (6/7)⁴¹. In contrast, **the iFOCUS intervention arm in our study** had lower retention rates specifically with 71.6% retention in patients and 68.9% in family caregivers at T1.

In summary, it seems that the eHealth delivery of the program (iFOCUS) appears to be less effective in influencing relevant outcomes than a nurse-facilitated program (FOCUS+), and our iFOCUS seems to have been implemented less effectively within the study. These differences

warrant further investigation into three key areas: 1) the theoretical background and the implementation of the program theory, 2) program content (usefulness and program satisfaction) and 3) mode of delivery (digital aspect). While the forthcoming DIAdIC process evaluation will likely provide insights into aspects of implementation, engagement and mechanisms of action (or lack thereof) we can formulate some preliminary hypotheses.

- *Reflecting on the theoretical background of iFOCUS*

Reflecting on the theoretical background of iFOCUS, table 1 shows theoretical methods for behaviour change techniques, which are grounded in the Transactional Model of Stress and Coping by Lazarus and Folkman⁴³. Theoretical methods refer to systematic approaches which are based on established theories that guide the development and implementation of strategies to modify behaviour. Each theoretical method is linked to program components and is brought in relationship to one or both primary outcomes. Considering the absence of significant effects on the primary outcomes (self-efficacy in managing the impact of the disease and emotional functioning in patients and family caregivers), it is possible that while these theoretical methods served as a basis for developing practical applications, their practical implementation was insufficient, suggesting a potential gap between the theoretical foundations of the iFOCUS program and the practical execution. However, since process evaluation data is still being analyzed, definitive conclusions about this potential gap have yet to be made.

The Transactional Model of Stress and Coping by Lazarus and Folkman and Northouse's empirical work provided a solid theoretical foundation for the iFOCUS program^{41,42,44,45}. Using behavioural change frameworks such as the Theory of Planned Behavior⁴⁶ or other conceptual models, such as Brandstadter's Dual Process Model⁴⁷ or Skinner's Functional Approach⁴⁸ could have provided different conceptual views on outcomes such as stress and coping, and underlying mechanisms such as attitudes, subjective norms, and perceived behavioral control. While these theories might have highlighted different aspects of the iFOCUS program, there is limited and inconsistent evidence on the use of behavioural change frameworks such as the Theory of Planned behavior during the development and evaluation of eHealth programs. Additionally, while other theories might have highlighted different aspects of the iFOCUS program, elements from the Theory of Planned Behavior, Brandstadter's Dual Process Model, and Skinner's Functional Approach are implicitly integrated into the iFOCUS program, as there are shared common elements. Even if these models were more explicitly applied, it is not certain that the iFOCUS program or the outcomes would be significantly different.

Reflecting on the method used for the development of iFOCUS we used the Scrum method because of its flexibility, adaptability, and the technical teams' familiarity with this approach^{49,50}. However, alternative methods or development frameworks such as Intervention Mapping could have highlighted different aspects of program development, potentially more explicitly identifying and addressing critical program components such as dyadic elements^{51,52}. Our choice to use the Scrum method, rather than a different development framework, was informed by the existing evidence from the FOCUS program, ensuring the continuity and integrity of the original program while adapting it to an eHealth context.

Table 1: theoretical methods & behavior change techniques applied in the iFOCUS program

Family involvement	Outlook	Coping	Uncertainty reduction	Symptom management
Theoretical methods: <u>Social support seeking:</u> Establishing an alliance and reflecting on mutual support. <u>Communication skill training:</u> Improving communication patterns and addressing roles and teamwork	Theoretical methods: <u>Positive Reappraisal:</u> Acknowledging difficulties and setting goals enhance <u>Cognitive Reframing:</u> Normalizing emotions and maintaining a positive outlook	Theoretical methods: <u>Coping Skill Training:</u> Educating on different coping styles and providing tips to cope.	Theoretical methods: <u>Information Provision:</u> Providing information on different topics to alleviate uncertainties.	Theoretical methods: <u>Self-Monitoring:</u> Regular evaluation of symptoms and side-effects.
Program components: Assessing roles and teamwork, identifying strengths in each other, identifying additional needs for support from each other, reflecting on existing communication patterns and how to improve them...	Program components: Normalizing emotions, maintaining a positive outlook, acknowledging difficulties and setting goals, evaluating changes in attitudes, advance care planning...	Program components: Informing and educating them about different coping styles, providing tips and tricks on both problem and emotion-focused coping, providing energy management techniques...	Program components: Offering detailed and relevant information about cancer progression, treatment options, caregiving strategies and additional help and support	Program components: Teaching caregivers and patients to monitor symptoms regularly and providing feedback to help manage and respond to these symptoms effectively.

Relation to the primary outcomes: <u>Self-Efficacy in managing the impact of cancer:</u> By improving dyadic communication individuals can voice concerns and learn from each other's perspectives, gaining more confidence in their ability to navigate cancer-related challenges. <u>Emotional functioning:</u> Improved communication skills and social support help facilitate a supportive environment, which can alleviate stress and emotional burden.	Relation to the primary outcomes: <u>Emotional functioning:</u> Reducing feelings of helplessness and promoting a more positive mindset.	Relation to the primary outcomes: <u>Self-Efficacy in managing the impact of cancer:</u> Educating individuals on diverse coping strategies and enhancing their self-efficacy directly contributes to their ability to manage the impact of cancer. <u>Emotional functioning:</u> Effectively coping with challenges is likely to reduce the emotional burden on individuals.	Relation to the primary outcomes: <u>Self-Efficacy in managing the impact of cancer:</u> Providing information to reduce uncertainty increases the individuals' confidence in managing cancer-related uncertainties, thereby improving self-efficacy. <u>Emotional functioning:</u> Reducing uncertainty alleviates anxiety and stress.	Relation to the primary outcomes: <u>Self-Efficacy in managing the impact of cancer:</u> empowering individuals to take proactive steps in managing cancer symptoms.
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- *Reflecting on the program content of iFOCUS*

Other research indicates that the perceived relevance and usefulness of program content may influence both program adherence and effectiveness in eHealth programs, with irrelevant or less usable programs having higher attrition rates and lower overall effectiveness^{51,52}. As discussed in **Chapter 2**, user testing involving twenty dyads and two bereaved family caregivers revealed that the program was usable and its content was generally acceptable, yet concerns regarding content usefulness were raised. Northouse suggested two potential explanations contributing the moderate usefulness of the web-based program: the program's narrow focus and patients' existing access to comprehensive support^{42,53}. However, these arguments may be less applicable to iFOCUS, given our translation of all FOCUS components into digital modules and our finding of no significant effects on self-efficacy and emotional functioning in both patients and family caregivers.

The absence of significant effects on self-efficacy and emotional functioning may not be due to the amount of iFOCUS content or the support dyads do or do not receive. Rather, it may be due to concerns regarding content relevance. As described in **chapter 2** topics such as symptom management, family involvement, coping,... are an integral part of the iFOCUS program and are relevant topics to patients with cancer and their family caregivers^{33,54-57}. However in prolonged illnesses like advanced cancer, needs could be more multifaceted and shift more towards managing worsening symptoms, functioning, and financial strain^{58,59}. Therefore, patients with advanced cancer and their family caregivers might benefit more from practical information and support^{33,34}. Reflecting on our description of the iFOCUS program in **Chapter 2**, it is possible that the program may have primarily focused on coping with the emotional aspects of the disease, possibly neglecting the explicit integration of practical strategies for managing daily tasks or financial challenges. Instead, this practical information was integrated in the references throughout the program, which had to be interacted with by the dyad. Furthermore, given the increased 5-year survival rate and the recurrence of advanced cancer as a second diagnosis, patients and their family caregivers often have extensive diagnosing and treatment experience^{60,61}. Consequently, this population is likely to have managed the disease for extended periods, potentially encountering multiple professionals, treatments, and information sources⁶²⁻⁶⁵. This exposure may have reduced the perceived usefulness of the iFOCUS program, thereby impacting program engagement and effectiveness. This could explain why patients and family caregivers in the user-testing found the program usable, but less useful.

While the above perceives iFOCUS primarily as a program focused on delivering information to dyads, identifying what could contribute to the program's (i)relevance, it is essential to underscore that the program's core or goals extends beyond mere dissemination of information. In addition to providing information, iFOCUS is also designed to facilitate dyadic communication, foster mutual appreciation of needs and strengths, and enhance coping mechanisms. While results on these topics are forthcoming, it's noteworthy that eHealth support is predominantly perceived as a tool for information dissemination⁶⁶. Therefore, uncertainty persists about whether the eHealth iFOCUS program can fully encapsulate the essence of the FOCUS program and move beyond the perception of being solely an information-providing program.

- *Reflecting on the delivery mode of iFOCUS*

While the digital nature of the iFOCUS program did not influence trial participation and retention (as demonstrated in **Chapter 4**), certain digital attributes may influence the effectiveness of eHealth programs, which is reflected in our results.

Firstly, successfully accessing and using eHealth programs requires a level of digital skills or affinity^{67,68}. Therefore, efforts may need to be made to enhance the accessibility of eHealth programs. Additionally, both care recipients and care providers value face-to-face contact and the opportunity to establish connections with others^{69,70}. This underscores one of the reasons why eHealth cannot fully replace face-to-face programs. Nevertheless, eHealth could serve as a supplementary tool to face-to-face care, allowing for relationships to be established and maintained while still providing continuous and ongoing support^{67,71}. Consequently, adopting a blended approach, which combines both face-to-face and eHealth elements could be an interesting way to provide support⁷²⁻⁷⁴.

Additionally, potential program users expect eHealth programs, to be up-to-date and aligned with their standards and expectations, which are informed by their experiences with current digital programs and tools⁷⁵. As discussed in **Chapter 6**, it can be questioned how feasible this is approach is as rapid technological progress often results in a temporal gap between program development, testing, and implementation, particularly within the context of a clinical trial. This gap may lead to programs being out of sync with users' expectations by the time they are broadly implemented^{76,77}. Furthermore, the importance of keeping a program up-to-date extends beyond meeting the perceived standards and expectations of potential end-users. Up-to-date eHealth

programs also tend to be safer, addressing concerns that potential end-users may have, which could otherwise deter them from accessing and using eHealth programs^{78,79}.

Digital programs may benefit from being simple, brief and to the point, which would enable participants to better manage their illness^{80,81}. However, as previously stated, it is possible that the effect of a program is not influenced by its briefness or extensiveness, but rather by its relevance, which can be influenced by digital modalities such as tailoring. As described in **chapters 2 and 4** we made pragmatic choices during the development of iFOCUS, which were influenced by limited available time and resources. Consequently, we tailored to the dyad names, patient-caregiver roles, and exercises. However, other research indicates that more profound tailoring such as content matching to demographic, behavioral and psychological profiles could be more engaging, increase information retention, be perceived as more useful and be more satisfactory and effective⁸²⁻⁸⁶. Nevertheless, further empirical research on the topic of tailoring is required, as the mechanisms and effects of these types of tailoring might be fundamentally different⁸⁷.

4.3. The challenges of a rigorous eHealth development process and potential solutions.

In **Chapter 2** we describe the seven-step development process of the psychoeducational eHealth iFOCUS program. Our experience with the development of the iFOCUS program underscore the considerable time and resources required for the development of a psychoeducational eHealth program, even when building upon an existing framework. While we had an extensive, agile development process with input from various teams, we must also acknowledge that the development process happened in a relatively short time, pushed by trial limitations. Nevertheless, a rigorous development process based on relevant theory, available evidence and the involvement of users is recommended as this could increase program feasibility, acceptability and potentially effectiveness⁸⁹⁻⁹¹.

- *Rigorous development, a role for user-centered designs*

As described in **Chapter 2**, we made the pragmatic decision to only include potential end-users in a consultancy role during user-testing rather than having them involved in all stages of development. Nevertheless, for the development of eHealth programs it is recommended that

stakeholders be involved in a more extensive and early manner, beyond a consultancy role^{89,91-93}. Therefore several designs based on the similar principle of user-involvement have been proposed such as a user-centered design (UCD), human-centered design (HCD), and a co-design^{89,94,95}. While all three designs are based on the same principle of user-involvement, they operationalize users and user-involvement in different ways. These designs have been proposed as feasible approaches for the development of eHealth as they could increase program relevance, user-satisfaction and sustainable implementation^{89,92,96,97}. Depending on the program objectives and the goal of the user-involvement either design can be a feasible approach to eHealth development.

- *Reflecting on user-involvement during the development of iFOCUS*

While user involvement is recommended to enhance program satisfaction and effectiveness⁹⁸, it also presents challenges that must be managed with care⁹². A first challenge is that user-involvement could be influenced by sampling bias⁹⁹. User-centered designs in eHealth development tend to rely on a relatively small sample with certain populations often being over or underrepresented (e.g. older vs younger)^{99,100}. Additionally input from end-users input may also be inherently biased, considering how user insights are based on personal experiences, internalized routines and assumptions⁹⁹. To address this challenge, we included a sizable sample of 42 participants (20 dyads, 2 bereaved caregivers) internationally to participate in the user-testing of iFOCUS, as detailed in **Chapter 2**. While we included a diverse group of participants internationally, the participants involved in the user-testing were predominantly older. Nevertheless, this demographic aligns with our target population, with advanced cancer being more prevalent in older adults¹⁰¹. Additionally, it's important to consider that the user-testing participants were spread across six countries, therefore we cannot exclude recruitment bias on a national level. To address the potential selection bias that may arise during user involvement, it is crucial to thoroughly document which populations are under or overrepresented⁸⁰. Based on the scope of the research it could be decided to evaluate the developed eHealth program specifically for the overrepresented subpopulation or to conduct additional development activities that involve the formerly excluded populations^{99,102}.

Secondly, designs based on user-involvement tend to over-rely on end-user input, potentially diminishing the significance of the knowledge, creativity, and skills of design and development teams^{99,103}. This challenge likely had minimal impact on the development of iFOCUS, as we engaged end-users at a later stage, after the majority of the technical development had been

completed. Another potential pitfall related to the aforementioned is the over-reliance on end-user stakeholders, which may overlook input from stakeholders at meso and macrolevels⁹⁹. While insights from stakeholders at these levels were gathered regarding the sustainable implementation of psychoeducational home-based programs (as discussed in **Chapter 7**), they were not involved in the user-testing of the eHealth iFOCUS program. Consequently, their insights were not integrated into the development process. However, engaging stakeholders at micro, meso, and macro levels early in the development process, rather than afterward, could facilitate sustainable program implementation⁹⁹. However, determining the extent and depth of user-involvement is challenging, and further research is needed to understand how user involvement enhances the development of eHealth programs^{99,104}.

A final challenge is that user-centered designs also tend to experience practical challenges such as correctly estimating the cost of the development process and delays due to conflicting interests, agenda's, communication styles ...¹⁰⁵⁻¹⁰⁸. One way to cope with this challenge is to account for extra means and time for development, which is straightforward but effective¹⁰⁸. However, as described in **Chapter 6** for the development of iFOCUS we also need to consider that the COVID-19 pandemic was an unforeseeable circumstance which severely impacted program development and implementation. Consequently, this approach would have been inadequate in addressing the challenges posed by the pandemic.

4.4. Implementing eHealth support into regular care

While numerous studies claim a widespread implementation of eHealth programs¹⁰⁹⁻¹¹¹ this mostly pertains to electronic health records, social alarms, and online client portals¹¹¹. However the sustainable implementation of psychoeducational eHealth programs such as iFOCUS, which is the scope of this dissertation, is scarce¹¹¹.

- Barriers and solutions for sustainable implementation of eHealth programs

While we identified barriers, facilitators, risks, and opportunities that could impact the sustainable implementation of home-based psychoeducational support programs for patients with advanced cancer and their family caregivers in **Chapter 7**, our research did not explicitly focus on the sustainable implementation of eHealth programs. Therefore we will compare our identified implementation challenges for psychoeducational programs in general, with

implementation challenges specific to the implementation of eHealth programs, as identified by other research.

At the macro-level, we identified “policy and societal factors” that influence the sustainable implementation of psychoeducational programs. These factors include: the need for healthcare reorganization, policymakers' engagement, taboo and stigma surrounding psychological topics, and pressure on society and formal healthcare. Other research has also identified delayed legislation as having an impact on the sustainable implementation of eHealth programs, with a lack of uniform agreements resulting in a complex eHealth landscape with many non-interoperable eHealth programs^{112,113}. Additionally, there is also ambiguity in laws regarding data safety, security, and sharing, which hinders the sustainable implementation of eHealth programs¹¹³⁻¹¹⁵. While we identified a lack of funding to support the sustainable implementation of eHealth programs as a challenge at the meso-level, this issue could originate from the macro-level, where insufficient funding structures may hinder healthcare organizations in implementing eHealth programs sustainably^{109,116}. However, other research suggests that most of these issues could be resolved by developing centralized macro-level regulations (on technical modalities, program interoperability, data security and sharing ...) and funding structures, but with a decentralized operationalization, giving executive power to local organizations^{1091,112,115}.

At the meso level we identified factors related to the ‘program embedding in healthcare organizations’ which influence the sustainable implementation of psychoeducational programs. Our results indicated that achieving organizational fit encompassed both cultural aspects (alignment with goals) and operational aspects (alignment with organizational processes). Other research on the sustainable implementation of eHealth programs underscores the significance of achieving alignment in operational aspects such as workflow, organizational structures, system language...^{109,117}. While we identified the importance of engaging executive personnel and organizational leadership to embed psychoeducational programs into healthcare organizations in **Chapter 7**, this also applies for the sustainable implementation of eHealth programs^{90,95}.

Additionally, engaging with executive personnel (professional care providers) could also be viewed as a micro-level influence. While we identified ‘characteristics of the intervention’ and ‘reaching the target population’ as influencing the sustainable implementation of psychoeducational programs, other research underscores the characteristics of professional care providers as influential on the sustainable implementation of eHealth programs¹¹⁵. Care

providers play a substantial role in reaching the target population, which we also identified as being of influence on the sustainable implementation of psychoeducational programs¹¹⁸. On micro level, professional caregiver characteristics, such as skepticism toward programs, could hinder sustainable eHealth program implementation by limiting program introduction to potential end-users^{119,120}. Involving these stakeholders in the development process could enhance their understanding and engagement which could positively affect the embedding of eHealth programs in healthcare organizations^{109,115}. Additionally, these stakeholders can be engaged and familiarized with newly developed eHealth support through workshops or success stories^{111,114,116}.

- *Can eHealth psychoeducation replace face-to-face psychoeducation?*

The iFOCUS program was never intended to replace face-to-face psychoeducation. While eHealth could offer an innovative approach to alleviating some of the burden on formal healthcare, there are drawbacks and ethical discussions to consider.

In addition to the aforementioned drawbacks (as discussed previously,) completely self-managed eHealth programs, like iFOCUS, may feel distant, and impersonal, even if properly tailored^{80,63}. Additionally, interpersonal contact is often more nuanced than digital communication, which is crucial when discussing challenging topics such as advanced disease and treatment or care^{121,122}. Finally, completely self-managed digital eHealth programs might be more challenging for healthcare providers to follow up on (e.g., session timing, discussion content), potentially widening the gap between care recipients and professional care providers⁷³.

Additionally, on the ethical aspects of eHealth the systematic review from Jokinen, Stolt and Suhonen (2020) identified four ethical themes in relation to eHealth being: (1) privacy in eHealth, (2) beneficence and nonmaleficence in eHealth, (3) justice in eHealth and (4) trust in eHealth¹²³. With regard to the matter of privacy in the context of eHealth, it has been proposed that tailoring should be employed in order to enhance the relevance and effectiveness of eHealth programmes⁸²⁴⁻⁸⁴. However, the process of tailoring necessitates that participants should disclose varying degrees of information, with deeper tailoring (matching demographic, behavioural and psychological profiles) requiring more extensive input from the participants^{83,84}. While individuals typically prefer autonomy when sharing information, those with poorer health or long-term illness may be more inclined to share information if they believe it will facilitate their

access to healthcare services^{68,124}. Consequently, within the DIAdIC trial, our data collectors introduced the trial to potential participants before obtaining informed consent, clearly outlining the program's expectations. In considering the principles of beneficence and nonmaleficence in eHealth, research suggests that eHealth support has the potential to enhance the availability of health information, thereby empowering care recipients^{123,125}. However, it is crucial to ensure the protection of sensitive information and privacy rights to prevent unwarranted access or misuse¹²⁶. Therefore, while eHealth initiatives offer significant benefits in promoting patient autonomy and empowerment, measures must be in place to safeguard patient privacy and confidentiality. Justice in eHealth encompasses the principles of equity and equality, presenting notable challenges. As previously discussed in **Chapter 4**, while only a minority of eligible patients and family caregivers explicitly mentioned technology as the reason for non-participation, it is important to consider the vulnerability of certain populations in regards to digital aspects. In our trial, many participants fell into the older adult demographic, potentially facing difficulties in effectively accessing and utilizing eHealth programs or fostering more distrust towards the digital programs⁶⁸. Despite these challenges, efforts were made to enhance the accessibility and usability of the iFOCUS program for all participants. Additionally, while the iFOCUS program targeted dyads, patients with advanced cancer who lacked a designated family caregiver were excluded, thus limiting program access for this subgroup. In discussing trust in eHealth, transparency regarding the potential benefits and drawbacks of using eHealth is crucial¹²⁷. People should have access to comprehensive information to make well-informed decisions about whether to utilize eHealth support or not¹²³. It's noteworthy that many individuals prefer eHealth to complement rather than replace personal contact¹²⁸ indicating the importance of maintaining a balance between technology-based support and traditional interpersonal interactions.

- *Towards a blended approach, a feasible approach*

Both eHealth and face-to-face programs have their respective strengths and challenges. However, adopting a blended approach, which combines the potential of both face-to-face and eHealth methods could be an interesting way to provide support⁷²⁻⁷⁴. By adopting a blended approach, participants are able to reflect on the content of the digital programs with a healthcare provider, which has been demonstrated to not only increase program adherence, but also to be associated with better program outcomes^{73,129}. Furthermore, integrating eHealth and face-to-face support allows professionals to address program challenges and provide additional guidance, effectively promoting program adherence^{96,130}.

Nevertheless, there has been minimal research conducted on the factors influencing the integration of blended care, particularly with regard to patients dealing with advanced cancer and their family caregivers. However, research in other settings indicates that many of the challenges encountered by eHealth and face-to-face care, are also applicable in a blended approach¹³¹⁻¹³³.

5. RECOMMENDATIONS FOR RESEARCH, POLICY AND PRACTICE

Based on our experiences during the development and implementation of a psychoeducational eHealth program (iFOCUS) to support and empower patients with advanced cancer and their family caregivers we propose a series of recommendations. These recommendations for research, clinical practice and policy, aim to address the complexities inherent in developing, evaluating and implementing effective and impactful eHealth interventions, particularly for populations facing serious illnesses like advanced cancer.

5.1. Recommendations for research

Developing an eHealth psychoeducational program could benefit from early and extensive involvement of various stakeholders.

The development of an eHealth psychoeducational program for patients and their family caregivers presents a number of intriguing challenges. There is much to consider regarding the thoroughness of the development process and its rigor, as well as project limitations and pragmatism. A thorough development process is recommended, with user-involvement being suggested as a way to stimulate the development of a relevant, effective and sustainable eHealth programs⁸⁸⁻⁹¹. Moreover, user-involvement should aim to extend beyond a design that solely engages end-users (potential participants) in a consultancy role at the project's conclusion but should involve many different stakeholders early and extensively⁹²⁻⁹⁴. Addressing potential recruitment bias is essential, necessitating thorough documentation of underrepresented and overrepresented populations in the program's development⁸⁰. It may be worthwhile to consider either tailoring the program specifically for the overrepresented populations or conducting further development involving the underrepresented populations^{99,102}. Designs based on user-involvement also tend to over-rely on end-user input, potentially diminishing the significance of the knowledge, creativity, and skills of design and development teams^{99,103}. Therefore, it could be interesting to elicit some power or 'votes' to other parties involved in the development process such as those responsible for the technical development⁹⁹. User-involvement can also result in practical constraints such as available time and resources, and conflicts among those involved in the development process. Therefore while an extensive design with user-involvement is recommended, project leads should still be able to take decisive action to protect the project goals and timeline^{95,134}.

Be aware of the explicit or subliminal influence of digital aspects on trial recruitment and retention.

Although our findings indicated that only a minority (2.1%) of potential participants explicitly cited eHealth as a reason for non-participation, a considerable proportion of the population reported no specific reason (17%) or no interest (no further elaboration) (47.9%). Consequently, it is plausible that the population who refrain from participating in a trial with an eHealth component due to its digital aspects is considerably larger. Furthermore, it is important to consider that underlying sociodemographic disparities could contribute to persistent digital inequities, leading to the systematic exclusion of certain subpopulations from these types of trials⁶⁸. However, the systematic exclusion of certain subpopulations from these trials can introduce significant bias to the results and the conclusions, potentially leading to the development of eHealth programs that are applicable to certain subpopulations. Consequently, it is imperative to not only investigate the underlying reasons for non-participation in these types of trials but also to ascertain which populations are more or less likely to participate in these trials and the implications of this for the results of these trials.

Efforts to improve retention rates in eHealth trials are essential.

Overall, retention rates of the DIAdIC trial were satisfactory. However, disparities may exist among trial arms, as observed in the lower retention rates in the eHealth iFOCUS intervention group. This suggests that there were factors which led to accelerated study fatigue and attrition. While we did not associate digital competence with trial retention (which in turn could be biased by mostly including digitally competent participants), other program or participant factors could influence trial retention. Consequently, further research is required to ascertain the factors that influence retention in eHealth trials, and whether these factors are associated with the program or with demographic factors.

Further exploration of the mechanisms of change which influence the effectiveness of eHealth programs

Our results indicated that the psychoeducational eHealth iFOCUS program had no significant effect on the self-efficacy and emotional functioning of patients with advanced cancer and their family caregivers. However, according to other research, digital support could significantly improve the psychosocial wellbeing of both patients with advanced cancer and their family caregivers^{86,135}. Therefore further research in the mechanisms of change of eHealth interventions is needed, which are important insights from the forthcoming DIAdIC process evaluation.

In our discussion, we identified both user and program characteristics as potential influences on the effectiveness of eHealth programs. These factors were for example the absence of relevant information for the population of patients with advanced cancer and their family caregivers, specifically considering their 'expertise', built through their prolonged trajectory and their potential need for more practical information^{58,59}. It is therefore possible to hypothesize that the eHealth iFOCUS program could be more effective in other populations, such as patients and family caregivers who have received a first diagnosis. This is typically characterized by a severe psychological burden^{56,57}, which may be more aligned with the content covered by the iFOCUS program. Additionally, content relevance may be influenced by program characteristics such as tailoring. While other research suggests that more profoundly tailored programs could be perceived as more useful⁸⁴⁻⁸⁶ more research towards the effectiveness of surface or deep-level tailoring is required, considering the potential implications on eHealth program relevance, engagement, and effectiveness.

Nevertheless, it is worth considering whether eHealth programs could or should replace face-to-face contact. During the discussion, we highlighted potential factors influencing the effectiveness of iFOCUS. However, digital programs can still be seen as distant and impersonal, particularly when addressing challenging topics related to advanced cancer interpersonal contact and connection could be important^{80,121,122}. Additionally there are some ethical considerations such as privacy in eHealth, beneficence and nonmaleficence in eHealth, justice in eHealth and trust in eHealth. To counter some of the limitations of eHealth a blended-approach could be explored, which combines face-to-face and digital elements and leverages the strengths of both modalities^{86,88}.

5.2. Recommendations for clinical practice

Provide support to family caregivers of someone with a serious illness

A considerable part of the adult population provides prolonged and intensive family caregiving to someone with a serious illness. Often these family caregivers provide care in combination with other obligations such as employment. While family caregivers of someone with a serious illness find their family care meaningful, they do experience significantly higher burden compared to other family caregivers. However, family caregivers play a substantial role in the provision of long term care and support and their role might become increasingly important due to an ageing population^{21,136}. The pressure on family caregivers is however expected to continuously rise,

raising questions on sustainability of this model^{26,27}. While the experienced burden between patients and family caregivers shows signs of interconnectedness, this applies for their shared resilience^{137,138}. Therefore, it could be interesting to provide care and support not only to patients but also to their family caregivers. Not only are dyadic programs more aligned with the reality of patients and family caregivers, research also suggests that they could result in positive outcomes¹³⁹⁻¹⁴¹.

Stimulate the adoption and integration of eHealth programs with consideration for a blended approach

This dissertation never suggested that eHealth could or should replace face-to-face psychoeducational support to patients with advanced cancer and their family caregivers. However eHealth as a tool is worthy of consideration for its potential to provide additional remote care and support^{142,143}. By integrating eHealth into care pathways, these types of programs are more likely to become accessible to both patients and their family caregivers^{80,96}. To facilitate the integration of eHealth programs into existing care pathways, support from management and executive personnel is necessary. By involving these stakeholders during the development process of eHealth programs, their skepticism could be alleviated and sustainable program integration could be facilitated, thereby requiring less reorganization^{114,144}.

Furthermore, it may be beneficial to consider a blended approach to psychoeducational support for patients with advanced cancer and their family caregivers, integrating both digital and face-to-face elements. A blended approach could leverage the strengths of both the face-to-face and the digital modalities, contributing to program adherence and effectiveness^{80,96,145}.

5.3. Recommendations for policy

Stimulate initiatives which support both patients with advanced cancer and their family caregivers.

As this dissertation demonstrates, both patients with advanced cancer and their family caregivers experience significant intrinsically connected burden which is likely to increase as the disease progresses. Due to demographic changes both the population with advanced cancer and the population of family caregivers is expected to rise^{21,146}. Consequently, further research into innovative support programs (such as eHealth or a blended approach) is recommended for this population, not only to safeguard their quality of life but also to alleviate some of the future burden on formal care. While no significant effects of iFOCUS on self-efficacy and emotional

functioning were found, we must also consider that due to recruitment challenges the trial was underpowered and that the conditional power analysis suggested potentially significant effects had we achieved our target number of participants. Therefore to stimulate research towards these topics, but also to allow for sufficient recruitment time additional funding is required.

There is a need for clear and structured policy regarding psychoeducational eHealth support.

The lack of clarity regarding the optimal level of organization and coordination for eHealth has led to a lack of uniform agreements on the interoperability of eHealth programs, which has resulted in a complex eHealth landscape^{112,113}. Additionally, there is also ambiguity in laws regarding data safety, security, and sharing, but also funding structures, deterring organizations from integrating eHealth support¹¹³⁻¹¹⁵. Therefore, policymakers need to be engaged to develop uniform regulation which focus on the technical modalities, interoperability, security and reimbursement^{109,110}. By involving stakeholders across various levels policymakers should be able to develop feasible macro-level regulations, while also stimulate local bottom-up initiatives which are conform the agreements and therefore interoperable and accessible^{109,112,115}.

6. CONCLUSION

Patients with advanced cancer and their family caregivers experience interlinked burden and resilience. As the disease progresses, the burden in both is expected to continuously rise. Due to demographic shifts, it is anticipated that the population of patients with advanced cancer and their family caregivers increase. However, the availability and sustainability of a care model where family caregiving is a cornerstone is questionable. Therefore, new and innovative approaches to support both patients with advanced cancer and their family caregivers as one unit of care are required. While eHealth support cannot and should not replace in-person care and support, it is important to acknowledge its potential. Although our results show no impact of eHealth on the self-efficacy in managing the impact of the disease and emotional functioning of dyads, there are signs that appropriate eHealth support can provide benefits to both dyads with advanced cancer and healthcare organizations. For the sustainable implementation of eHealth psychoeducational programs, a comprehensive approach is crucial, addressing policy, organizational, and stakeholder factors. In light of the multifaceted considerations surrounding the implementation of eHealth, adopting a blended approach that integrates face-to-face and digital methods emerges as a promising strategy.

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ENGLISH AND DUTCH SUMMARY

1. INTRODUCTION

A significant portion of the adult population lives with a serious life-limiting illness which severely impacts the life-expectancy, functioning and quality of life of patients and family caregivers. Advanced cancer is considered serious impact because of the impact of the diagnosis, treatment and disease trajectory.. While many people still die from cancer, early diagnosis and novel treatments have led to longer survival for patients with advanced cancer, which is why it is increasingly being described as a chronic rather than an acute disease. The disease trajectory of people with advanced cancer is characterised by a prolonged period of relative comfort and wellbeing, followed by a rapid decline. People with advanced cancer may experience high levels of physical, psychological and existential or spiritual distress that severely impair their functioning, increase their distress and reduce their quality of life. However, the impact of advanced cancer goes beyond the patient and also affects family caregivers. Research shows that caregivers experience similar levels of adjustment problems and emotional distress as patients, with up to 40% experiencing anxiety and depression. In addition, a positive correlation has been found between the distress experienced by the cancer patient and the caregiver, a phenomenon known as co-suffering. However, it's important to recognise not only the interconnectedness of experienced burden and distress, but also the inherent resilience within patients and carers as a unit of care, or dyad. Dyads can provide mutual support that has a positive impact on each other's wellbeing and has been shown to alleviate depressive symptoms.

A dyadic way of coping with the disease

As awareness grew that cancer affects not only the individual patient but also their family caregivers, multiple dyadic coping models emerged in the 1990s. These models have guided research into dyadic coping and each offer an unique perspective on dyadic dynamics. While there is no contradiction between the models, there is serious overlap as they each build upon the theoretical model of Lazarus and Folkman. In developing and implementing the eHealth programme examined in this dissertation, we drew from the theoretical framework of Lazarus and Folkman, while not strictly adhering to any specific model or framework

Palliative care for patients with advanced cancer and their family caregivers and the role of psychoeducation

Palliative care has been recommended to address the non-curative aspects of care related to the physical, psychological, existential, social and practical needs associated with living with and coping with the effects of illness. The 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. It prevents and relieves suffering through the early identification, correct assessment and treatment of pain and other problems, whether physical, psychosocial or spiritual*”. Accumulating evidence shows that a mix of specialist and generalist, early, home-based dyadic palliative care for patients with advanced cancer and their family caregivers could provide positive outcomes for both patients and family caregivers. Psychoeducation, defined as ‘*a brief process of therapy focused on the communication of varied aspects of disease- and/or treatment-related information*’ could be a valid approach to provide additional care and support as part of palliative care.

eHealth for patients with advanced cancer and their family caregivers

Historically, the majority of psychosocial care and psychoeducational interventions for patients with advanced cancer and their family caregivers were delivered face-to-face. Face-to-face programs are typically more expensive since facilitators are needed to systematically provide this type of support. Considering the pressure on formal care, technological advancements and the use telephone or internet should be increasingly considered as valid ways of providing support. eHealth, which can be defined as “*health services and information delivered or enhanced through the Internet and related technologies*.” could be cost-effective additions for the provision of face-to-face psychoeducational support. One of its benefits is that using eHealth programmes to provide psychoeducational support could reduce the pressure on professional caregivers and reduce the feeling of intrusiveness patients and family caregivers can experience linked to face-to-face home-based support. Given the potential benefits of eHealth support for patients with advanced cancer and their family caregivers, which have not been adequately investigated, further research is warranted.

Identifying promising interventions for the development of dyadic psychoeducational programs

As part of the DIAdIC trial we developed the face-to-face FOCUS+ program and the web-based iFOCUS program. In order to select the most promising and innovative early palliative care dyadic interventions for patients with advanced cancer and their family caregivers, the DIAdIC research

consortium reviewed the available evidence about dyadic interventions, and evaluated the potential 'fit' and relevance of these interventions to a European context. Based on the review of the DIAdIC consortium, the FOCUS intervention developed by Northouse was identified as among the most effective and potentially relevant for the European context. The FOCUS intervention is a nurse-led psychoeducational dyadic intervention for patient-caregiver dyads in a cancer trajectory consisting of five modules: Family involvement (F), Optimistic outlook (O), Coping effectiveness (C), Uncertainty reduction (U), and Symptom management (S), and is delivered simultaneously to patients and family caregivers. The F-component (family involvement) of the face-to-face program was translated into a tailored, web-based format and was associated with better patient and family caregiver quality of life, emotional distress, perceived benefits of illness/caregiving, and improved caregiver self-efficacy.

2. RESEARCH AIMS

The primary objective of this dissertation is to develop and evaluate a psychoeducational home-based eHealth program for patient-caregiver dyads in an advanced cancer trajectory. The first aim is to describe the numbers, characteristics and experiences of family caregivers of people with serious illness. The second aim is to describe the development of a psychoeducational eHealth program (iFOCUS) to support patients with advanced cancer and their family caregivers and its implementation in an international RCT. The third aim is to describe the outcomes of the DIAdIC trial, focusing on recruitment for the trial, effectiveness of iFOCUS and FOCUS+ on primary outcomes (self-efficacy and emotional functioning), implementation of these programs within the trial, and sustainable implementation of iFOCUS and FOCUS+ beyond the trial setting.

3. DESIGNS AND METHODS

For the first aim we performed a we performed a secondary analysis of data from the 19th Social-Cultural Changes survey (SCC) in Flanders conducted from March to July 2014 by the Study Service of the Flemish Government. Participants were divided in three groups, family caregivers of people with serious illness (1), family caregivers of people with other conditions (2) and people not providing family care (3). We reported the socio-demographics of the three groups using descriptive statistics. We conducted a Pearson chi-square test to compare the differences on sociodemographic between all groups, and on family caregiving characteristics between family caregiver groups. We used the Mann-Whitney U test to test the differences in experiences of

family caregiving between the family caregiving groups. A principal component analysis was used to reveal underlying structures of family caregiving. To identify differences on these constructs between caregiver groups, a one-way analysis of variance was conducted (ANOVA). Constructs that were significantly associated with the family caregiver group ($p < 0.05$) were included in multivariable ANOVA.

For the second aim we wrote a report delineating our experiences, describing the step-by-step development process of the psychoeducational home-based eHealth program (iFOCUS) using the scrum methodology. Additionally we added the research protocol for the DIAdIC trial where the eHealth iFOCUS program for patients with advanced cancer and their family caregivers was part of an international three-arm superiority RCT. This study was an international multicenter parallel-group three-arm superiority trial in six countries (Belgium, The Netherlands, Denmark, Italy, The United Kingdom and Ireland) 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). This study used both qualitative and quantitative data to measure the outcomes of the intervention. Data was collected three times from patient-caregiver dyads; (1) baseline measure before randomization to the study arms (T0) (2) first follow-up at 12 weeks (T1) and (3) second follow-up at 24 weeks (T2). The primary endpoints were emotional functioning and self-efficacy of both the person with advanced cancer and the family caregiver at T1.

For the third aim we preformed an analysis of recruitment files and data collected during baseline and first follow-up questionnaires. Additionally we analysed results from the DIAdIC trial in relation to self-efficacy and emotional functioning of patients with advanced cancer and their family caregivers at T1 (12 weeks after baseline). We performed 'intention-to-treat' (ITT) as primary analysis and per-protocol (PP) as a sensitivity analysis. In relation to the third aim we also wrote a report reflexive report delineating our experiences during the development and implementation of the dyadic face-to-face FOCUS+ and web-based iFOCUS program. Finally, we performed qualitative interviews with stakeholders involved in the implementation of psychoeducational programs to gain insights on the barriers, facilitators, risks and opportunities for sustainable implementation of psychoeducational home-based programs.

4. FINDINGS

In chapter 1 titled we found that 7.6% of the total population provided family care to someone with serious illness during the last 12 months. More than one third of family caregivers were aged

35 to 54 or 55 to 74. Family caregivers of people with serious illness were more often women compared with people who did not provide family care. More than one out of three family caregivers were full-time employed or self-employed and 62.9% were married or legally cohabiting. Nearly half of the family caregivers of people with serious illness provided care to parents or parent in-law. Compared with care recipients with other illness, those with serious illness were more often men, aged 35-54 or aged 55-74 and more often lived with relatives other than the participating family caregiver. Nearly one in three family caregivers of people with serious illness provided care on a daily basis and 44.7% provided family care one or more times a week; 31.8% provided care for more than ten hours a week. Compared with family caregivers of people with other conditions, family caregivers of people with serious illness more often provided medical and nursing care. Compared with family caregivers of people with other conditions, family caregivers of people with serious illness more often reported that providing care is psychologically demanding and meaningful. Family caregivers of people with serious illness experienced higher burden than family caregivers of people with other conditions but did not differ in experienced meaningfulness and work-life conflict. However, our results indicate that while providing medical and nursing care leads to an elevated burden for both family caregiving groups, when this type of care is not provided, the elevated burden is observed only in family caregivers of people with serious illnesses.

In Chapter 2 we describe the iFOCUS development process across seven steps: (1) concept design, (2) development of mock-ups, (3) obtaining feedback from the international consortium, (4) technical development of the program, (5) creating country-specific versions for each of the six participating countries, (6) preliminary testing through user and functional testing and (7) implementing the final version for the RCT. Using the Scrum methodology allowed for flexibility and adaptability in the development process, as it included alternating periods of program development and evaluation. The development of iFOCUS involved five teams: (1) the core development group consisted of academics, clinicians, and healthcare professionals, (2) the web development team made up of software developers, a user expert/cancer survivor, and the CEO of the IT firm, (3) the international consortium involved in the DIAdIC project, (4) experts on videos and visualization and (5) potential end-users from each participating country. The challenges we encountered were related to transferring ideas into working functionalities, spreading of the content, tailoring, determining the log-in procedure, input of translated materials and determining an onboarding procedure. At the end of the development process Users found the iFOCUS program to be acceptable and usable.

In chapter 3 we describe the protocol for the DIAdIC trial, delineating the international multicentre 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 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.

In Chapter 4 we found that 37 out of 1752 non-participants (2.1%) explicitly cited ICT-related factors as a reason for non-participation. Patients with advanced cancer reported a significantly lower digital competence than family caregivers. Patients and family caregivers significantly differed in feeling comfortable, although both most often reported feeling quite a bit comfortable or very comfortable when using a computer, smartphone, or tablet. Patients significantly more often reported that they were not skilled in using a computer, smartphone, or tablet compared to family caregivers. In patients, lower digital competence was found among those who were older and those with financial difficulties, and higher digital competence was found among those from Denmark and those with higher or secondary educational attainment. Family caregivers reported higher digital competence in men, Danes, and those with secondary or higher education. Older family caregivers and those with financial difficulties reported lower digital competence. After adjusting for age, sex, and educational attainment, self-reported digital competence at the patient and family caregiver levels was not significantly associated with trial retention in either the study arm or the overall trial.

In chapter 5 we describe the results from the face-to-face FOCUS+ and web-based iFOCUS program as part of the DIAdIC trial on the primary outcomes (self-efficacy and emotional functioning in patients with advanced cancer and their family caregivers). iFOCUS did not yield significant improvements compared to control group at T1 for patients or family caregivers in emotional functioning or self-efficacy. FOCUS+ did not yield statistically significant improvements at T1 for patients or family caregivers in emotional functioning, but significantly improved self-efficacy compared to control group among patients, but not family caregivers at T1. No significant T2 improvements were found.

In chapter 6 we share our experiences on the development and implementation of two psychoeducational home-based programs as part of an international multicentre superiority trial. Despite recruitment challenges including COVID-19 restrictions and administrative hurdles, 431 patient-caregiver dyads were enrolled across six European countries. Challenges in trial management were addressed with flexible timelines and technical support.

As part of chapter 7 we interviewed 13 stakeholders in Flanders, Belgium from hospital and home settings. We identified barriers, facilitators, risks, and opportunities for sustainable implementation across micro, meso, and macro levels. Four key themes were identified: intervention characteristics, reaching the target population (micro level), Program Embedding in Healthcare Organizations (meso level), and influencing the outer setting (macro level).

5. GENERAL DISCUSSION

While a considerable population currently provides family care, the sustainability of family caregiving is challenged by demographic shifts towards an aging population. Family caregivers of someone with serious illness experience significant psychological burden. This finding is consistent with existing research indicating higher depression rates among caregivers of terminally ill patients and could explain why the overall burden in this population is higher. While family caregivers of people with serious illnesses are more likely to provide medical and nursing care, they experienced a higher burden compared to caregivers for people with other conditions only when the latter did not provide medical and nursing care tasks. This suggests that additional factors beyond caregiving tasks contribute to caregiver burden, such as distress arising from witnessing the patient's diminished well-being and unmet care needs, including information and coping strategies. Fear of the loved one's death, more common in patients with serious illnesses, further exacerbates caregiver distress. Sociodemographic characteristics like sex did not significantly associate with burden, contrary to common assumptions, suggesting the need for further exploration. Understanding the factors contributing to caregiver burden is critical for developing effective support interventions.

Results from the DIAdIC trial show that while FOCUS+ demonstrated a significant improvement in patients' self-efficacy compared to the control group, iFOCUS yielded neutral results. Therefore, we reflected on three key areas: The theoretical background and the implementation

of the program theory (1), program content (2) and mode of delivery (3). Reflecting on the theoretical background, it is possible that while theoretical methods served as a basis for the development of iFOCUS, their practical implementation was insufficient. However, since process evaluation data is still being analyzed, definitive conclusions about this potential gap have yet to be made. Additionally, while using models such as the Theory of Planned Behavior, Brandstadter's Dual Process Model, or Skinner's Functional Approach might have offered different perspectives on outcomes and underlying mechanisms, it is important to note that these models share some concepts with the Transactional Model of Stress and Coping by Lazarus and Folkman. Consequently, it is not certain that the iFOCUS program or its outcomes would have differed significantly. Reflecting on the content of iFOCUS we can state that while providing emotional support to patients with advanced cancer and their family caregivers is crucial, practical information on symptom management and financial strain may have been overlooked. Additionally, while iFOCUS could be perceived as a program which provides dyads with information, it was also designed to facilitate dyadic communication, foster mutual appreciation of needs and strengths, and enhance coping mechanisms. However uncertainty persists whether an eHealth program such as the iFOCUS program can fully encapsulate the essence of the FOCUS program and move beyond the perception of being solely an information-providing program. Additionally, the digital nature of iFOCUS could also pose challenges which attribute to the neutral findings on effectiveness. Firstly, successfully accessing and using eHealth programs requires a level of digital skills or affinity. Additionally, both care recipients and care providers value face-to-face contact and the opportunity to establish connections with others. Furthermore, it is also important to keep the program novel and up-to-date, not only for the end-user expectations but also to ensure program safety. Finally, tailoring iFOCUS to user profiles and preferences may enhance engagement and effectiveness. While pragmatic choices were made in iFOCUS development, deeper tailoring based on demographic, behavioural, and psychological profiles could improve satisfaction and effectiveness. Further empirical research on tailoring mechanisms is needed to optimize digital interventions. Nevertheless, further empirical research on the topic of tailoring is required, as the mechanisms and effects of these types of tailoring might be fundamentally different.

Our experience with the development of the iFOCUS program underscore the considerable time and resources required for the development of a psychoeducational eHealth program, even when building upon an existing framework. While we had an extensive, agile development process with input from various teams, we must also acknowledge that the development

process happened in a relatively short time, pushed by trial limitations. Nevertheless, a rigorous development process based on relevant theory, available evidence and the involvement of users is recommended as this could increase program feasibility, acceptability and potentially effectiveness. User-involvement is suggested by other research as being a feasible approach to develop eHealth programs. However, user-involvement should be broad and extensive, going beyond a mere consultancy role. Various design approaches, such as user-centered, human-centered, and co-design, are highlighted as potential strategies to boost program relevance, satisfaction, and sustainability. Nevertheless user-involvement also has its challenges including sampling bias and over-reliance on end-user input, which may overshadow the expertise of design and development teams. Additionally user-involvement also has practical challenges, like estimating development costs and navigating unforeseen disruptions such as the COVID-19 pandemic.

Numerous studies emphasize the widespread implementation of eHealth programs, particularly in electronic health records and online client portals. However, the sustainable implementation of psychoeducational eHealth programs, like iFOCUS, remains scarce. We identified barriers and solutions for sustainable implementation, comparing challenges for psychoeducational and eHealth programs. Macro-level factors such as delayed legislation and funding shortages impact both, suggesting centralized regulations and decentralized execution. Meso-level challenges include organizational fit and leadership engagement, crucial for both psychoeducational and eHealth programs. Engaging professional care providers at the micro-level is vital, influencing target population reach and program scepticism.

The iFOCUS program was never intended to replace face-to-face psychoeducation. While eHealth offers innovative approaches, drawbacks like impersonality and follow-up challenges exist. Ethical considerations, including privacy, beneficence, and justice, must be addressed, ensuring patient autonomy and safeguarding sensitive information. However, acknowledging that both eHealth and face-to-face programs have their unique strengths and challenges, a blended approach combining eHealth and face-to-face methods is suggested. Integrating digital programs with professional guidance enhances adherence and outcomes. However, research on blended care, especially for patients with advanced cancer and their caregivers, remains limited, necessitating further exploration of challenges and strategies.

6. RECOMMENDATIONS FOR RESEARCH, CLINICAL PRACTICE AND POLICY

6.1. Recommendations for Research:

- **Developing an eHealth psychoeducational program could benefit from early and extensive involvement of various stakeholders.** A thorough development process, including user involvement, is crucial for ensuring the program's relevance, effectiveness, and sustainability. This involvement should extend beyond end-users and encompass different stakeholders from the outset. Addressing potential recruitment bias and balancing input from various parties are essential considerations. User involvement may present practical challenges, However project leads should be able to take decisive action to protect the project goals and timelines.
- **Be aware of the explicit or subliminal influence of digital aspects on trial recruitment and retention.** While explicit mentions of eHealth as a reason for non-participation were low, a significant portion of the population cited no specific reason or lack of interest, suggesting a broader influence of digital components on participation rates. Sociodemographic disparities may also contribute to digital inequities and systematic exclusion from such trials, leading to biased results and conclusions. Therefore, it is crucial to investigate the reasons for non-participation and understand which populations are more or less likely to participate, informing the interpretation of trial results.
- **Efforts to enhance retention rates in eHealth trials are imperative.** Despite overall satisfactory retention rates, disparities may exist among trial arms, as observed by the lower retention rates in the eHealth iFOCUS intervention group. This highlights the need to identify factors contributing to study fatigue and attrition. While digital competence was not directly linked to trial retention, other program or participant factors could play a role. Further research is warranted to explore these factors and their association with trial retention, including potential demographic influences.
- **Further exploration of the mechanisms of change which influence the effectiveness of eHealth programs.** While our study found no significant impact of the psychoeducational eHealth iFOCUS program on self-efficacy and emotional functioning, other research suggests the potential for digital support to enhance psychosocial well-being in similar populations. Therefore, a deeper understanding of these mechanisms is crucial, with

insights expected from the forthcoming DIAdIC process evaluation. Factors such as the relevance of information and the level of tailoring could play significant roles. Exploring the effectiveness of surface versus deep-level tailoring is essential, considering their implications for program relevance, engagement, and effectiveness.

6.2. Recommendations for practice:

- **Provide support to family caregivers of someone with a serious illness**, given the significant burden they often face. Many adults undertake prolonged and intensive caregiving responsibilities alongside other obligations such as employment. Despite finding their role meaningful, family caregivers experience higher levels of burden compared to others in similar roles. However, their contribution to long-term care and support is invaluable, particularly in the context of an aging population but the sustainability of this model can be questioned. Dyadic support programs, designed to address the needs of both patients and caregivers, not only reflect their shared reality but also have the potential for positive outcomes. Research suggests that such programs could enhance the well-being of both patients and caregivers, offering a holistic approach to support.
- **Stimulate the adoption and integration of eHealth programs with consideration for a blended approach.** While this dissertation did not advocate for the replacement of face-to-face psychoeducational support, it highlighted the potential of eHealth as a valuable tool for providing additional remote care and support. Integrating eHealth into care pathways can enhance accessibility for both patients and their family caregivers. To facilitate the integration of eHealth programs, support from management and executive personnel is crucial. Involving these stakeholders during the development process can alleviate scepticism and promote sustainable program integration without significant reorganization. Moreover, adopting a blended approach to psychoeducational support for patients with advanced cancer and their caregivers could be beneficial by combining digital and face-to-face elements, leveraging the strengths of both modalities to improve program adherence and effectiveness.

6.3. Recommendations for Policy:

- **Stimulate initiatives which support both patients with advanced cancer and their family caregivers.** This dissertation underscores the interconnected burden experienced by both groups, a burden expected to increase with demographic shifts leading to a rise in

these populations. Therefore, further research into innovative support programs, including eHealth or a blended approach, is recommended to improve their quality of life and reduce future burdens on formal care. While the iFOCUS program did not show significant effects on self-efficacy and emotional functioning, recruitment challenges led to underpowering of the trial. Additional funding is needed to stimulate research in these areas and allow for sufficient recruitment time.

- **There is a need for clear and structured policy regarding psychoeducational eHealth support.** The lack of uniform agreements on the interoperability of eHealth programs and ambiguity in laws regarding data safety, security, and funding structures have resulted in a complex eHealth landscape. Policymakers need to be engaged to develop uniform regulations focusing on technical modalities, interoperability, security, and reimbursement. By involving stakeholders across various levels, policymakers can develop feasible macro-level regulations and stimulate local bottom-up initiatives that are interoperable and accessible.

NEDERLANDSTALIGE SAMENVATTING

1. INLEIDING

Een aanzienlijk deel van de volwassen bevolking leeft met een ernstige levensbeperkende ziekte die de levensverwachting, het functioneren en de kwaliteit van leven van patiënten en familieleden ernstig beïnvloedt. Gevorderde kanker wordt als een ernstige ziekte beschouwd vanwege de impact van de diagnose, behandeling en ziekteverloop en heeft een diepgaande invloed op zowel de persoon met kanker als op de mantelzorgers. Dankzij vroegtijdige diagnosestelling en nieuwe behandelingen overleven mensen met kanker gemiddeld langer, waardoor deze ziekte steeds vaker als chronisch wordt beschouwd in plaats van acuut. Het ziekteverloop van mensen met gevorderde kanker wordt gekenmerkt door een langere periode van behoud van comfort en functioneren, gevolgd door een snelle achteruitgang. Mensen met gevorderde kanker kunnen ernstige fysieke, psychologische en existentiële of spirituele nood ervaren die hun functioneren ernstig beïnvloeden, hun stress verhogen en hun kwaliteit van leven verminderen. Desalniettemin heeft de diagnose van gevorderde kanker ook een invloed op de mantelzorgers. Onderzoek toont aan dat mantelzorgers vergelijkbare niveaus van aanpassingsproblemen en emotionele stress ervaren als patiënten, waarbij angst en depressie aanwezig zijn bij tot wel 40%. Bovendien is een positieve correlatie vastgesteld tussen de ervaren last van de patiënt met kanker en hun mantelzorgers, als gevolg van een fenomeen genaamd co-suffering (mede-lijden). Desalniettemin is het cruciaal om niet alleen de onderlinge gelinkte belasting en stress te erkennen, maar ook de inherente veerkracht binnen dyades. Dyades kunnen elkaar onderlinge steun bieden, wat een positieve invloed heeft op elkaars welzijn en de symptomen van depressie kan helpen verminderen.

Een dyadische manier om met de ziekte om te gaan

Naarmate het bewustzijn groeide dat kanker niet alleen de individuele patiënt, maar ook de mantelzorger beïnvloedt, ontstonden er in de jaren 1990 meerdere dyadische coping-modellen. Deze modellen hebben het onderzoek naar dyadische coping geleid en bieden elk een uniek perspectief op dyadische dynamiek. Hoewel er geen tegenstelling is tussen de modellen, is er aanzienlijke overlap omdat ze elk voortbouwen op het theoretische model van Lazarus en Folkman, dat ook gebruikt is bij de ontwikkeling van het eHealth-programma in deze dissertatie.

Palliatieve zorg voor patiënten met gevorderde kanker en mantelzorgers en de rol van psychoeducatie

Om aspecten van zorg aan te pakken die niet als doeleinde hebben het fysiek genezen van de ziekte maar andere fysieke, psychologische, existentiële, sociale en praktische behoeften met betrekking tot het leven en omgaan met de impact van de ziekte, werd palliatieve zorg aanbevolen. Palliatieve zorg wordt door de WHO gedefinieerd als *‘een benadering die de kwaliteit van leven van patiënten (volwassenen en kinderen) en hun families verbetert die worden geconfronteerd met problemen die verband houden met een levensbedreigende ziekte. Het voorkomt en verlicht lijden door vroege identificatie, correcte beoordeling en behandeling van pijn en andere problemen, of deze nu fysiek, psychosociaal of spiritueel zijn’*. Onderzoek toont aan dat een mix van specialistische en algemene, vroegtijdige, thuisgebonden dyadische palliatieve zorg voor patiënten met gevorderde kanker en hun mantelzorgers positieve uitkomsten kan opleveren voor zowel patiënten als mantelzorgers. Psychoeducatie, gedefinieerd als *‘een kort proces van therapie gericht op de communicatie van verschillende aspecten van ziekte- en/of behandeling gerelateerde informatie’*, zou een benadering kunnen zijn om aanvullende zorg en ondersteuning te bieden als onderdeel van palliatieve zorg.

eHealth voor patiënten met gevorderde kanker en hun mantelzorgers

Historisch gezien werden de meeste psychosociale zorg en psychoeducatieve interventies voor patiënten met gevorderde kanker en hun mantelzorger face-to-face geleverd. Face-to-face programma's zijn doorgaans duurder omdat facilitators moeten worden geïdentificeerd die in staat zijn om systematisch dit type ondersteuning te bieden. Gezien de toenemende druk op formele zorg worden technologische ontwikkelingen en het gebruik van telefoon of digitale tools steeds vaker beschouwd als manieren om ondersteuning te bieden. eHealth, dat kan worden gedefinieerd als *"gezondheidsdiensten en informatie die worden geleverd of verbeterd via het internet en gerelateerde technologieën"* zou een kosteneffectieve toevoegingen kunnen zijn voor het verstrekken van psycho-educatieve ondersteuning. Het gebruik van eHealth als een manier om psychoeducatieve ondersteuning te bieden zou de druk op professionele zorgverleners kunnen verminderen en een lagere drempel hebben dan face-to-face psychoeducatieve. Gezien de potentiële voordelen van eHealth-ondersteuning voor patiënten met gevorderde kanker en hun familie verzorgers beperkt onderzocht is, is verder onderzoek gerechtvaardigd.

Identificatie van veelbelovende interventies voor de ontwikkeling van dyadische psycho-educatieve programma's

Als onderdeel van de DIAdIC-studie hebben we het face-to-face FOCUS+ programma en het webgebaseerde iFOCUS programma ontwikkeld. Om de meest veelbelovende en innovatieve vroege palliatieve zorg dyadische interventies voor patiënten met gevorderde kanker en hun familieleden te selecteren, heeft het DIAdIC-onderzoeksconsortium het beschikbare bewijs over dyadische interventies beoordeeld en de potentiële 'fit' en relevantie van deze interventies voor een Europese context geëvalueerd. Op basis van de beoordeling door het DIAdIC-consortium werd de FOCUS-interventie ontwikkeld door Northouse geïdentificeerd als een van de meest effectieve en mogelijk relevante interventies voor de Europese context. De FOCUS-interventie is een door verpleegkundigen geleide psycho-educatieve dyadische interventie voor patiënt-zorgverlener dyades in een kankertraject, bestaande uit vijf modules: Family involvement (F), Optimistic outlook (O), Coping effectiveness (C), Uncertainty reduction (U) en Symptom management (S), en wordt gelijktijdig aangeboden aan patiënten en familieleden. De F-component (family involvement) van het face-to-face programma werd vertaald naar een op maat gemaakt webgebaseerd formaat en was geassocieerd met een betere kwaliteit van leven van patiënten en familieleden, vermindering van emotionele stress, waargenomen voordelen van ziekte/zorgverlening en verbeterde zelf-efficacy van de zorgverleners.

2. ONDERZOEKSDOELEN

Het hoofddoel van dit proefschrift is om een psychoeducatief eHealth programma te ontwikkelen en te evalueren voor patiënt-mantelzorger dyades met gevorderde kanker waar ze thuis toegang toe hebben. Het eerste doel is om de aantallen, kenmerken en ervaringen van mantelzorgers van mensen met ernstige ziekten te beschrijven. Het tweede doel is om het ontwikkelingsproces van een psychoeducatief eHealth programma (iFOCUS) ter ondersteuning van patiënten met gevorderde kanker en hun mantelzorgers te beschrijven, evenals de implementatie van iFOCUS als onderdeel van een internationale RCT. Het derde doel is om de resultaten van de DIAdIC-studie te beschrijven, met een focus op de rekrutering voor de studie, de effectiviteit van iFOCUS en FOCUS+ op primaire uitkomsten (eigen-effectiviteit en emotioneel functioneren), de implementatie van deze programma's binnen de studie, en de duurzame implementatie van iFOCUS en FOCUS+ buiten de context van de studie.

3. DESIGNS EN METHODEN

Voor het eerste doel voerden we een secundaire analyse uit van gegevens uit de 19e Sociaal-Culturele Veranderingen survey (SCV) in Vlaanderen, uitgevoerd van maart tot juli 2014 door de Studiedienst van de Vlaamse Overheid. Deelnemers werden verdeeld in drie groepen: Mantelzorgers van mensen met ernstige ziekten (1), Mantelzorgers van mensen met andere aandoeningen (2) en mensen die geen mantelzorg verlenen (3). We rapporteerden de sociodemografische kenmerken van de drie groepen met behulp van beschrijvende statistieken. We voerden een Pearson chi-kwadraat test uit om de verschillen in sociodemografische gegevens

tussen alle groepen en op mantelzorg kenmerken tussen mantelzorggroepen te vergelijken. We gebruikten de Mann-Whitney U-test om de verschillen in ervaringen van mantelzorgers tussen de mantelzorggroepen te testen. Een principale componentenanalyse werd gebruikt om onderliggende structuren van familiezorg te onthullen. Om verschillen op deze constructen tussen zorgverlener groepen te identificeren, werd een ANOVA-analyse uitgevoerd. Constructen die significant geassocieerd waren met een mantelzorggroep groep ($p < 0.05$) werden opgenomen in multivariate ANOVA.

Voor het tweede doel hebben we een rapport opgesteld waarin we beschrijven hoe we stapsgewijs aan de hand van de Scrum methodologie tot de ontwikkeling van het psychoeducatieve thuis gebaseerde eHealth programma (iFOCUS) gekomen zijn. Daarnaast hebben we het onderzoeksprotocol toegevoegd voor de DIAdIC-studie waarin het eHealth iFOCUS-programma voor patiënten met gevorderde kanker en hun familie verzorgers deel uitmaakte van een internationale driearmige superioriteits-RCT. Deze studie was een internationale multicentrische parallelle groepsstudie met drie armen in zes landen (België, Nederland, Denemarken, Italië, het Verenigd Koninkrijk en Ierland), waarbij 1) de FOCUS+ face-to-face interventie (interventie 1) en 2) de iFOCUS web-interventie (interventie 2) werden vergeleken met 3) standaardzorg (controlegroep). Deze studie gebruikte zowel kwalitatieve als kwantitatieve gegevens om de uitkomsten van de interventie te meten. Gegevens werden drie keer verzameld van patiënt-mantelzorger-dyaden; (1) basismeting voor randomisatie naar de onderzoeksgroepen (T0), (2) eerste follow-up na 12 weken (T1) en (3) tweede follow-up na 24 weken (T2). De primaire eindpunten waren emotioneel functioneren en zelfeffectiviteit van zowel de persoon met gevorderde kanker als de familie verzorger op T1.

Voor het derde doel hebben we een analyse uitgevoerd van rekruteringsbestanden en gegevens verzameld tijdens baseline- en eerste follow-up vragenlijsten. Daarnaast hebben we resultaten geanalyseerd van de DIAdIC-studie met betrekking tot eigen-effectiviteit en emotioneel functioneren van patiënten met gevorderde kanker en hun mantelzorgers op T1 (12 weken na baseline). We voerden een 'intention-to-treat' (ITT) analyse uit als primaire analyse en per-protocol (PP) analyse als gevoeligheidsanalyse. Met betrekking tot het derde doel hebben we ook een rapport geschreven waarin onze ervaringen tijdens de ontwikkeling en implementatie van het dyadische face-to-face FOCUS+ en web gebaseerde iFOCUS-programma werden beschreven. Ten slotte hebben we kwalitatieve interviews uitgevoerd met stakeholders die betrokken kunnen zijn bij de implementatie van psychoeducatieve programma's om inzichten te verkrijgen in de barrières, facilitators, risico's en kansen voor duurzame implementatie van psychoeducatieve thuis gebaseerde programma's.

4. BELANGRIJKSTE BEVINDINGEN

In hoofdstuk 1 hebben we vastgesteld dat 7,6% van de totale bevolking gedurende de laatste 12 maanden mantelzorg verleende aan iemand met een ernstige ziekte. Meer dan een derde van de mantelzorgers was tussen 35 en 54 jaar oud of tussen 55 en 74 jaar oud. Mantelzorgers van mensen met een ernstige ziekte waren vaker vrouwen in vergelijking met mensen die geen mantelzorg verleenden. Meer dan een op de drie mantelzorgers werkte fulltime of was zelfstandige en 62,9% was getrouwd of wettelijk samenwonend. Bijna de helft van de mantelzorgers van mensen met een ernstige ziekte verleende zorg aan ouders of schoonouders. Vergeleken met personen met andere aandoeningen die mantelzorg kregen, waren degenen met een ernstige ziekte vaker mannen, tussen 35-54 jaar oud of tussen 55-74 jaar oud, en woonden vaker samen met andere familieleden dan de deelnemende mantelzorger. Bijna één op de drie mantelzorgers van mensen met een ernstige ziekte verleende dagelijks zorg en 44,7% verleende één of meerdere keren per week zorg; 31,8% verleende meer dan tien uur per week zorg. In vergelijking met mantelzorgers van mensen met andere aandoeningen, verleenden mantelzorgers van mensen met een ernstige ziekte vaker medische en verpleegkundige zorg. Vergeleken met mantelzorgers van mensen met andere aandoeningen, meldden mantelzorgers van mensen met een ernstige ziekte vaker dat het bieden van zorg psychisch veeleisend en betekenisvol was. Mantelzorgers van mensen met een ernstige ziekte ervaarden een hogere belasting dan mantelzorgers van mensen met andere aandoeningen, maar verschilden niet in

ervaren betekenisvolheid en werk-privé-conflict. Onze resultaten tonen echter aan dat, hoewel het verlenen van medische en verpleegkundige zorg leidde tot een verhoogde belasting voor beide groepen mantelzorgers, dit niet het geval was wanneer medische en verpleegkundige zorg niet verleend werd. In het tweede scenario, werd enkel een verhoogde belasting vastgesteld bij mantelzorgers voor iemand met een ernstige ziekte of aandoening.

In hoofdstuk 2 beschrijven we het ontwikkelingsproces van iFOCUS in zeven stappen: (1) conceptontwerp, (2) ontwikkeling van mock-ups, (3) verkrijgen van feedback van het internationale consortium, (4) technische ontwikkeling van het programma, (5) maken van land-specifieke versies voor elk van de zes deelnemende landen, (6) voorlopige testen door gebruikers- en functionele testen en (7) implementatie van de definitieve versie voor de RCT. Het gebruik van de Scrum-methodologie zorgde voor flexibiliteit in het ontwikkelingsproces, omdat het afwisselende periodes van programmaontwikkeling en evaluatie omvatte. De ontwikkeling van iFOCUS werd gedaan door vijf teams: (1) de kernontwikkelingsgroep bestond uit academici, klinici en gezondheidsprofessionals, (2) het web ontwikkelingsteam bestond uit softwareontwikkelaars, een gebruikersexpert/kankeroverlevende en de CEO van het IT-bedrijf, (3) het internationale consortium betrokken bij het DIAdIC-project, (4) experts op het gebied van video's en visualisatie en (5) potentiële eindgebruikers uit elk deelnemend land. De uitdagingen die we tegenkwamen hadden betrekking op het omzetten van ideeën in werkende functionaliteiten, verspreiding van de inhoud, tailoring, bepaling van de inlogprocedure, input van vertaald materiaal en bepaling van een aanmeldingsprocedure. Aan het einde van het ontwikkelingsproces vonden gebruikers het iFOCUS-programma acceptabel en bruikbaar.

In hoofdstuk 3 beschrijven we het protocol voor de DIAdIC-studie, waarin de internationale multicentrische driearmige gerandomiseerde gecontroleerde trial in België, Denemarken, Ierland, Italië, Nederland en het Verenigd Koninkrijk wordt uiteengezet. In elk land worden 156 dyaden (in totaal 936) van mensen met gevorderde kanker en hun mantelzorger willekeurig toegewezen aan een van de onderzoeksgroepen: 1) een door een verpleegkundige geleide face-to-face interventie (FOCUS+), 2) een webgebaseerde interventie (iFOCUS) of 3) een controlegroep (standaardzorg). De primaire uitkomsten zijn emotioneel functioneren en eigen-effectiviteit van de patiënt en de mantelzorger, respectievelijk. De secundaire uitkomsten zijn kwaliteit van leven, voordelen van de ziekte, coping, dyadische communicatie en manieren van ondersteuning van de patiënt en de mantelzorger.

In hoofdstuk 4 vonden we dat 37 van de 1752 niet-deelnemers (2,1%) expliciet ICT-gerelateerde factoren aanhaalden als reden voor het niet deelnemen. Patiënten met gevorderde kanker meldden significant lagere digitale competentie dan mantelzorgers. Patiënten en mantelzorgers verschilden significant in het gevoel van comfort, hoewel beiden meestal aangaven zich tamelijk comfortabel of zeer comfortabel te voelen bij het gebruik van een computer, smartphone of tablet. Patiënten meldden significant vaker dat ze niet bedreven waren in het gebruik van een computer, smartphone of tablet in vergelijking met mantelzorgers. Bij patiënten werd lagere digitale competentie gevonden bij degenen die ouder waren en degenen met financiële moeilijkheden, en hogere digitale competentie werd gevonden bij degenen uit Denemarken en degenen met hoger of secundair onderwijsniveau. Mantelzorgers meldden een hogere digitale competentie bij mannen, Denen en degenen met secundair of hoger onderwijs. Oudere mantelzorgers en degenen met financiële moeilijkheden meldden lagere digitale competentie. Na correctie voor leeftijd, geslacht en onderwijsniveau was zelf gerapporteerde digitale competentie op patiënt- en mantelzorger niveau niet significant geassocieerd met de behoud van deelname in zowel de onderzoeksgroep als de algehele trial.

In hoofdstuk 5 beschrijven we de resultaten van het face-to-face FOCUS+ en het web gebaseerde iFOCUS-programma als onderdeel van de DIAdIC-studie over de primaire uitkomsten (zelfeffectiviteit en emotionele functioneren bij patiënten met gevorderde kanker en hun mantelzorgers). iFOCUS leverde geen significante verbeteringen op vergeleken met de controlegroep op T1 voor zowel patiënten als mantelzorgers wat betreft emotioneel functioneren of eigen-effectiviteit. FOCUS+ leverde geen statistisch significante verbeteringen op T1 voor zowel patiënten als mantelzorgers wat betreft emotioneel functioneren, maar verbeterde significant de eigen-effectiviteit vergeleken met de controlegroep bij patiënten, maar niet bij mantelzorgers op T1. Er werden geen significante verbeteringen gevonden op T2.

In hoofdstuk 6 delen we onze ervaringen met de ontwikkeling en implementatie van twee psychoeducatieve thuisprogramma's als onderdeel van een internationale multicenter superioriteitsstudie. Ondanks rekruteringsuitdagingen, waaronder COVID-19-beperkingen en administratieve obstakels, werden 431 patiënt-mantelzorger-dyades ingeschreven in zes Europese landen. Uitdagingen in het beheer van de studie werden op een flexibele manier aangepakt met behulp van technische ondersteuning.

Als onderdeel van hoofdstuk 7 hebben we 13 belanghebbenden geïnterviewd in Vlaanderen België, afkomstig uit de ziekenhuis en thuissetting. We hebben barrières, facilitators, risico's en kansen geïdentificeerd voor duurzame implementatie op micro-, meso- en macroniveaus. Vier belangrijke categorieën kwamen naar voren: kenmerken van de interventie, bereiken van de doelpopulatie (microniveau), inbedding van het programma in zorgorganisaties (mesoniveau) en invloed op de externe omgeving (macroniveau).

5. ALGEMENE DISCUSSIE

Hoewel momenteel een aanzienlijk deel van de bevolking mantelzorg verleent, wordt de duurzaamheid van mantelzorg uitgedaagd door demografische verschuivingen richting een vergrijzende bevolking. Mantelzorgers van iemand met een ernstige ziekte ervaren aanzienlijke psychologische last. Deze bevinding is in lijn met bestaand onderzoek dat hogere percentages depressie aantoonde onder mantelzorgers van terminaal zieke patiënten en zou kunnen verklaren waarom de algehele last in deze populatie hoger is. Hoewel mantelzorgers van personen met ernstige ziekten vaker medische en verpleegkundige zorg verlenen, ervoeren zij alleen een hogere belasting in vergelijking met mantelzorgers van mensen met andere aandoeningen wanneer deze laatsten geen medische en verpleegkundige taken uitvoerden. Dit suggereert dat aanvullende factoren buiten de zorgtaken bijdragen aan de last van de mantelzorger, zoals de stress die voortvloeit uit het zien van de verminderde gezondheidstoestand van de patiënt en on vervulde zorgbehoeften, inclusief informatie- en coping strategieën. Angst voor het overlijden van een geliefde, vaker voorkomend bij patiënten met ernstige ziekten, verergert verder de last van de mantelzorger. Sociodemografische kenmerken zoals geslacht hingen niet significant samen met de last, in tegenstelling tot gangbare aannames, wat wijst op de noodzaak van verder onderzoek. Het begrijpen van de factoren die bijdragen aan de last van de mantelzorger is cruciaal voor de ontwikkeling van effectieve ondersteuningsinterventies.

Resultaten van de DIAdIC-studie tonen aan dat terwijl FOCUS+ een significante verbetering in zelfeffectiviteit van patiënten liet zien in vergelijking met de controlegroep, iFOCUS neutrale resultaten opleverde. Daarom hebben we drie belangrijke aspecten bekeken die dit kunnen verklaren, namelijk: de theoretische achtergrond en de implementatie van de programmatheorie (1), de inhoud van het programma (2) en de wijze van levering (3). Wat betreft de theoretische achtergrond is het mogelijk dat hoewel theoretische methoden als basis dienden voor de

ontwikkeling van iFOCUS, hun praktische toepassing onvoldoende was. Aangezien de gegevens van de procesevaluatie nog in analyse zijn, moeten definitieve conclusies over deze mogelijke kloof nog worden getrokken. Daarnaast, hoewel het gebruik van modellen zoals de Theory of Planned Behavior, Brandstadter's Dual Process Model of Skinner's Functional Approach mogelijk andere perspectieven op uitkomsten en onderliggende mechanismen had kunnen bieden, is het belangrijk op te merken dat deze modellen enkele concepten delen met het Transactioneel Model van Stress en Coping door Lazarus en Folkman, dat als basis fungeerde voor het iFOCUS programma. Bijgevolg is het niet zeker of het iFOCUS-programma of de uitkomsten significant anders zouden zijn geweest. Bijkomend wordt er gereflecteerd over de programma inhoud, en hoewel we kunnen stellen dat het bieden van emotionele steun aan patiënten met gevorderde kanker en hun familieleden cruciaal is, kunnen praktische informatie over symptoombeheer en financiële druk over het hoofd zijn gezien. Daarnaast, terwijl iFOCUS kan worden opgevat als een programma dat dyaden van informatie voorziet, is het ook ontworpen om dyadische communicatie te faciliteren, wederzijdse waardering van behoeften en sterke punten te bevorderen en coping mechanismen te verbeteren. Echter, er blijft onzekerheid bestaan of een eHealth-programma zoals het iFOCUS-programma de essentie van het FOCUS-programma volledig kan omvatten en kan overstijgen dan alleen worden gezien als een informatieverstrekend programma. Bovendien kan de digitale aard van iFOCUS ook uitdagingen met zich meebrengen die bijdragen aan de neutrale bevindingen over effectiviteit. Ten eerste vereist succesvolle toegang tot en gebruik van eHealth-programma's een bepaald niveau van digitale vaardigheden of affiniteit. Daarnaast waarderen zowel zorgontvangers als zorgverleners persoonlijk contact en de mogelijkheid om verbindingen met anderen aan te gaan. Verder is het ook belangrijk om het programma vernieuwend en actueel te houden, niet alleen voor de verwachtingen van de eindgebruiker, maar ook om de programveiligheid te waarborgen. Tot slot kan het op maat maken van iFOCUS voor gebruikersprofielen en voorkeuren de betrokkenheid en effectiviteit vergroten. Hoewel pragmatische keuzes zijn gemaakt in de ontwikkeling van iFOCUS, zou diepgaandere tailoring op demografische, gedrags- en psychologische profielen de tevredenheid en effectiviteit kunnen verbeteren. Verdere empirische onderzoeken naar tailoring is nodig om digitale interventies te optimaliseren. Niettemin is verder empirisch onderzoek naar het onderwerp van tailoring vereist, aangezien de mechanismen en effecten van deze vormen van tailoring mogelijk fundamenteel verschillend zijn.

Onze ervaring met de ontwikkeling van het iFOCUS-programma benadrukt de aanzienlijke tijd en middelen die nodig zijn voor de ontwikkeling van een psychoeducatief eHealth-programma, zelfs

wanneer voortgebouwd wordt op een bestaand raamwerk. Hoewel we een uitgebreid, flexibel ontwikkelingsproces hadden met input van verschillende teams, moeten we ook erkennen dat het ontwikkelingsproces plaatsvond in een relatief korte tijd, gedreven door beperkingen van de proef. Desalniettemin wordt een rigoureuus ontwikkelingsproces op basis van relevante theorie, beschikbaar bewijs en de betrokkenheid van gebruikers aanbevolen, aangezien dit de haalbaarheid, acceptatie en potentieel effectiviteit van het programma kan vergroten. Gebruikersbetrokkenheid wordt door ander onderzoek voorgesteld als een haalbare aanpak voor de ontwikkeling van eHealth-programma's. Echter, gebruikersbetrokkenheid moet breed en uitgebreid zijn, verdergaand dan een louter adviserende rol. Diverse ontwerpbenaderingen, zoals gebruikersgericht, mensgericht en co-design, worden benadrukt als mogelijke strategieën om de relevantie, tevredenheid en duurzaamheid van het programma te versterken. Desalniettemin heeft betrokkenheid van gebruikers ook zijn uitdagingen, waaronder steekproefbias en overmatig vertrouwen op input van eindgebruikers, wat de expertise van ontwerp- en ontwikkelingsteams kan overschaduwen. Bovendien heeft betrokkenheid van gebruikers ook praktische uitdagingen, zoals het schatten van ontwikkelingskosten en het omgaan met onvoorziene verstoringen zoals de COVID-19-pandemie.

Diverse studies benadrukken de wijdverbreide implementatie van eHealth-programma's, met name in elektronische patiëntendossiers en online cliëntportalen. Echter, de duurzame implementatie van psychoeducatieve eHealth-programma's, zoals iFOCUS, blijft schaars. We hebben barrières en oplossingen geïdentificeerd voor duurzame implementatie, waarbij we uitdagingen voor psychoeducatieve en eHealth-programma's hebben vergeleken. Macro-niveau factoren zoals vertraagde wetgeving en tekorten aan financiering hebben invloed op beide, wat wijst op gecentraliseerde regelgeving en gedecentraliseerde uitvoering. Meso-niveau uitdagingen omvatten organisatorische pasvorm en betrokkenheid van leiderschap, cruciaal voor zowel psycho-educatieve als eHealth-programma's. Het betrekken van professionele zorgverleners op microniveau is essentieel, omdat het invloed heeft op het bereiken van de doelgroep en scepsis over het programma.

Het iFOCUS-programma was nooit bedoeld als vervanging voor face-to-face psychoeducatie. Hoewel eHealth innovatieve benaderingen biedt, bestaan er nadelen zoals onpersoonlijkheid en uitdagingen bij de opvolging. Ethische overwegingen, waaronder privacy, welzijn en rechtvaardigheid, moeten worden aangepakt om de autonomie van de patiënt te waarborgen en gevoelige informatie te beschermen. Echter, erkennend dat zowel eHealth als face-to-face

programma's hun unieke sterke punten en uitdagingen hebben, wordt een gemengde aanpak voorgesteld waarbij eHealth en face-to-face methoden worden gecombineerd. Het integreren van digitale programma's met professionele begeleiding verbetert de naleving en resultaten. Echter, onderzoek naar gemengde zorg, vooral voor patiënten met gevorderde kanker en hun verzorgers, blijft beperkt, wat verdere verkenning van uitdagingen en strategieën noodzakelijk maakt.

6. AANBEVELINGEN VOOR ONDERZOEK, PRAKTIJK EN BELEID

6.1. Aanbevelingen voor onderzoek

- **De ontwikkeling van een eHealth psycho-educatief programma kan baat hebben bij vroegtijdige en uitgebreide betrokkenheid van verschillende belanghebbenden.** Een grondig ontwikkelingsproces, inclusief gebruikersbetrokkenheid, is cruciaal om de relevantie, effectiviteit en duurzaamheid van het programma te waarborgen. Deze betrokkenheid moet verder gaan dan alleen eindgebruikers en verschillende belanghebbenden vanaf het begin omvatten. Het aanpakken van mogelijke wervingsbias en het in evenwicht brengen van input van verschillende partijen zijn essentiële overwegingen. Gebruikersbetrokkenheid kan praktische uitdagingen met zich meebrengen, maar projectleiders moeten in staat zijn om doortastend op te treden om de projectdoelen en -tijdslijnen te beschermen.
- **Wees je bewust van de expliciete of subtiele invloed van digitale aspecten op rekrutering en retentie.** Hoewel expliciete vermeldingen van eHealth als reden voor non-participatie laag waren, gaf een aanzienlijk deel van de populatie geen specifieke reden of gebrek aan interesse aan, wat wijst op een bredere invloed van digitale componenten op de participatiegraad. Sociodemografische verschillen kunnen ook bijdragen aan digitale ongelijkheden en systematische uitsluiting van dergelijke proeven, wat leidt tot bevooroordeelde resultaten en conclusies. Het is daarom cruciaal om de redenen voor non-participatie te onderzoeken en te begrijpen welke populaties meer of minder geneigd zijn om deel te nemen, wat de interpretatie van proefresultaten informeert.
- **Inspanningen om retentiegraden in eHealth-proeven te verbeteren zijn van essentieel belang.** Ondanks over het algemeen bevredigende retentiegraden, kunnen er verschillen bestaan tussen proefgroepen, zoals waargenomen bij de lagere retentiegraden in de interventiegroep van de eHealth iFOCUS. Dit benadrukt de noodzaak om factoren te

identificeren die bijdragen aan studievermoeidheid en uitval. Hoewel digitale competentie niet direct gekoppeld was aan proefretentie, zouden andere programma- of deelnemersfactoren een rol kunnen spelen. Verder onderzoek is nodig om deze factoren en hun associatie met proefretentie te verkennen, inclusief potentiële demografische invloeden.

- **Verdere onderzoek naar de mechanismen van verandering die de effectiviteit van eHealth-programma's beïnvloeden is noodzakelijk.** Hoewel ons onderzoek geen significant effect vond van het psychoeducatieve eHealth iFOCUS-programma op zelfeffectiviteit en emotionele functies, suggereert ander onderzoek het potentieel van digitale ondersteuning om de psychosociale welzijn te verbeteren in vergelijkbare populaties. Daarom is een dieper inzicht in deze mechanismen cruciaal, waarbij inzichten worden verwacht uit de aankomende DIAdIC-procesevaluatie. Factoren zoals de relevantie van informatie en het niveau van personalisatie kunnen een belangrijke rol spelen. Het verkennen van de effectiviteit van oppervlakte- versus diepgaande personalisatie is essentieel, gezien hun implicaties voor de relevantie, betrokkenheid en effectiviteit van het programma

6.2. Aanbevelingen voor praktijk

- **Bied ondersteuning aan mantelzorgers van iemand met een ernstige ziekte, gezien de significante last die zij vaak dragen.** Veel volwassenen nemen langdurige en intensieve zorgverantwoordelijkheden op zich naast andere verplichtingen zoals werk. Ondanks dat ze hun rol als betekenisvol ervaren, ervaren mantelzorgers hogere niveaus van last vergeleken met anderen in soortgelijke rollen. Hun bijdrage aan langdurige zorg en ondersteuning is echter onschatbaar, vooral in het kader van een vergrijzende bevolking, maar de duurzaamheid van dit model kan in twijfel worden getrokken. Dyadische ondersteuningsprogramma's, ontworpen om te voldoen aan de behoeften van zowel patiënten als verzorgers, weerspiegelen niet alleen hun gedeelde realiteit maar hebben ook het potentieel voor positieve uitkomsten. Onderzoek suggereert dat dergelijke programma's het welzijn van zowel patiënten als verzorgers kunnen verbeteren, waarbij een holistische benadering van ondersteuning wordt geboden.
- **Stimuleer de implementatie en integratie van eHealth-programma's met oog op een gemengde eHealth – face-to-face benadering.** Hoewel deze dissertatie niet pleitte voor de vervanging van face-to-face psychoeducatieve ondersteuning, benadrukte het de

potentie van eHealth als waardevol instrument voor het bieden van aanvullende zorg op afstand en ondersteuning. Het integreren van eHealth in zorgpaden kan de toegankelijkheid verbeteren voor zowel patiënten als hun mantelzorgers. Om de integratie van eHealth-programma's te faciliteren, is steun van management- en uitvoerend personeel cruciaal. Het betrekken van deze belanghebbenden tijdens het ontwikkelingsproces kan scepsis wegnemen en duurzame programma integratie bevorderen zonder significante herorganisatie. Bovendien zou het aannemen van een gemengde benadering van psychoeducatieve ondersteuning voor patiënten met gevorderde kanker en hun verzorgers voordelig kunnen zijn door digitale en face-to-face elementen te combineren, gebruikmakend van de sterke punten van beide modaliteiten om programma retentie en effectiviteit te verbeteren.

6.3. Aanbevelingen voor beleid

- **Stimuleer initiatieven die zowel patiënten met gevorderde kanker als hun mantelzorgers ondersteunen.** Deze dissertatie benadrukt de gedeelde last die beide groepen ervaren, een last die naar verwachting zal toenemen door demografische verschuivingen die leiden tot een toename van deze populaties. Daarom wordt verder onderzoek naar innovatieve ondersteuningsprogramma's, waaronder eHealth of een gemengde aanpak, aanbevolen om hun kwaliteit van leven te verbeteren en toekomstige lasten op formele zorg te verminderen. Hoewel het iFOCUS-programma geen significante effecten op zelfeffectiviteit en emotionele functioneren liet zien, leidden wervingsproblemen tot een under-powered trial. Aanvullende financiering is nodig om onderzoek op deze gebieden te stimuleren en voldoende wervingstijd mogelijk te maken.
- **Er is behoefte aan duidelijk en gestructureerd beleid met betrekking tot psychoeducatieve eHealth-ondersteuning.** Het ontbreken van uniforme afspraken over de interoperabiliteit van eHealth-programma's en ambiguïteit in wetten met betrekking tot gegevensveiligheid, beveiliging en financieringsstructuren hebben geleid tot een complex eHealth-landschap. Beleidsmakers moeten worden betrokken om uniforme voorschriften te ontwikkelen die zich richten op technische modaliteiten, interoperabiliteit, beveiliging en vergoedingen. Door belanghebbenden op verschillende niveaus te betrekken, kunnen beleidsmakers haalbare regelgeving op macroniveau ontwikkelen en lokale bottom-up initiatieven stimuleren die interoperabel en toegankelijk zijn.

APPENDICES

Appendix 1: Procedure for analyzing data of functional testing

We identified four categories (“language and translations”, “logic”, “layout” and “video and audio”) that were subsequently divided into 1) applicable for all countries or 2) applicable for a specific country. To determine if, or in what order we would implement adaptations, the items within these categories were divided into two groups; “Simple solution identified” or “No simple solution identified”. To grade whether a solution was simple or not, questions were asked on: 1) the monetary burden on the national or international teams and 2) time consumption and its effect on planning and time management. All items where a simple solution was identified were adapted accordingly. For items with no simple solution on an international scale, pragmatic choices were made on what adaptations we could make. For all items with no simple solution on a national scale, the country reporting the issue was contacted to request if they would make these adaptations themselves.

Appendix 2: Interview guides for user testing without probes

iFOCUS user testing: SESSION ONE	
Starting your session	What was your experience logging in? Was the video with tips and tricks unclear?
Mutual support & family involvement	How was it to go through this chapter? What was/wasn't clear about the question on general support?
Communication	What are your experiences going through this chapter?
Emotions	What did you think going through the chapter on emotions?
Coping	How did you experience going through the information in the coping chapter?
Treatments	What are your thoughts on the treatments chapter?
RECAP	What do you think about the recap video?
General remarks iFOCUS SESSION 1 - Did you experience any bugs? - How do you evaluate the read aloud option? - How was the use of pictures? What effect did this have on you? - How do you evaluate the use of different exercises? - How do you evaluate the length of the tool?	

iFOCUS user testing: SESSION TWO	
Starting your session	What was your experience logging in?

	Was the video with tips and tricks unclear?
Impact of the illness	How was it to go through this chapter? How do you evaluate the option to send information to friends or family?
Talking with children	What are your experiences going through this chapter? Did you understand what the personal workbook was?
Uncertainty	What did you think going through the chapter on uncertainty? How useful is it to you to write down your uncertainties in this chapter, why is or isn't this useful?
Goals	How was going through the information in the goals chapter?
Symptom management	What are your thoughts on the symptom management chapter? How was it to rate your symptoms? What would or wouldn't you change?
RECAP	What do you think about the recap video?
<i>General remarks iFOCUS SESSION 2</i> 1. Did you experience any bugs? 2. How do you evaluate the read aloud option? 3. How was the use of pictures? What effect did this have on you? 4. How do you evaluate the use of different exercises? 5. How do you evaluate the length of the tool?	

<i>iFOCUS user testing: SESSION THREE</i>	
Starting your session	What was your experience logging in? Was the video with tips and tricks unclear?
Mutual support	How was it to go through this chapter?
Outlook	What are your experiences going through this chapter?
Stress & Healthy lifestyle	What did you think going through the chapter on Stress & Healthy lifestyle?
Uncertainty	How was going through the information in the uncertainty chapter?
Symptom management	What are your thoughts on the symptom management chapter?
RECAP	What do you think about the recap video?
<i>General remarks iFOCUS SESSION 3</i> 1. Did you experience any bugs? 2. How do you evaluate the read aloud option? 3. How was the use of pictures? What effect did this have on you? 4. How do you evaluate the use of different exercises?	

5. How do you evaluate the length of the tool?

iFOCUS user testing: SESSION FOUR

Starting your session	What was your experience logging in? Was the video with tips and tricks unclear? (to be put in)
Communication & mutual support	How was it to go through this chapter?
Outlook	What are your experiences going through this chapter?
Coping	What did you think going through the chapter on Coping?
Uncertainty	How was going through the information in the uncertainty chapter? What did you think about the offered extra information on different healthcare providers?
Symptom management	What are your thoughts on the symptom management chapter? How was it to rate your symptoms? What would or wouldn't you change? How was the description on the different symptoms?
RECAP	What do you think about the recap video?
<i>General remarks iFOCUS SESSION 4</i> 1. Did you experience any bugs? 2. How do you evaluate the read aloud option? 3. How was the use of pictures? What effect did this have on you? 4. How do you evaluate the use of different exercises? 5. How do you evaluate the length of the tool?	

Information about this questionnaire

You have received this questionnaire because you have agreed to participate in the DIAdIC trial investigating the effect of different kinds of support for patients and their carers across six European countries.

As part of your participation in the DIAdIC trial, you will receive three questionnaires. This is questionnaire X out of 3. The questionnaires ask questions about a lot of different topics, such as your health, how you cope and how you and your carer communicate. We are aware that some of the questions might seem rather similar and that some of the questions might also seem more relevant to your situation than others. However, we kindly ask that you try to reply to all questions as far as possible. The estimated time for completion of this questionnaire is about half an hour.

You will notice that some of the questions within this questionnaire refer to your 'carer'. By 'carer', we refer to the person (partner, family member or friend) together with whom you are participating in this trial.

At the end of the questionnaire, a series of questions about your visits to the hospital and your use of medicine will be asked. For these questions, it might be helpful to have your diary and/or lists of medicine that you take next to you.

Your answers to the questions within this questionnaire will be treated as strictly confidential. Data will be kept and used in accordance with the European 'General Data Protection Regulation' (GDPR) guidelines.

Should any of the questions in this questionnaire make you emotionally upset or distressed, do not hesitate to contact Professor Kevin Brazil (k.brazil@qub.ac.uk). You are also welcome to contact the your local research team if you have questions about the questionnaires or the DIAdIC trial in general.

Thank you very much for taking the time to participate!

Date of completion: _____

These first questions ask about you and your health. Please answer all of the questions yourself by marking the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

EORTC QLQ-C15-PAL +, emotional functioning

During the past week:

**Not at
all**

A little

**Quite a
bit**

**Very
much**

1. Do you have any trouble taking a <u>short</u> walk outside of the house?	1	2	3	4
2. Do you need to stay in bed or a chair during the day?	1	2	3	4
3. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4
4. Were you short of breath?	1	2	3	4
5. Have you had pain?	1	2	3	4
6. Have you had trouble sleeping?	1	2	3	4
7. Have you felt weak?	1	2	3	4
8. Have you lacked appetite?	1	2	3	4
9. Have you felt nauseated?	1	2	3	4
10. Have you been constipated?	1	2	3	4
11. Were you tired?	1	2	3	4
12. Did pain interfere with your daily activities?	1	2	3	4
13. Did you feel tense?	1	2	3	4
14. Did you feel depressed?	1	2	3	4
15. Did you worry?	1	2	3	4
16. Did you feel irritable?	1	2	3	4
17. Have you felt panic?	1	2	3	4

During the past week:	Not at all	A little	Quite a bit	Very much
18. Have you felt vulnerable?	1	2	3	4
19. Have you felt that nothing could cheer you up?	1	2	3	4
20. Have you felt miserable?	1	2	3	4

21. Have you felt desperate?	1	2	3	4
------------------------------	---	---	---	---

22. Have you been afraid of losing control?	1	2	3	4
---	---	---	---	---

23. Has your physical condition or medical treatment interfered with your <u>family</u> life?	1	2	3	4
---	---	---	---	---

24. Has your physical condition or medical treatment interfered with your <u>social</u> activities?	1	2	3	4
---	---	---	---	---

For the following questions please mark the number between 1 and 7 that best applies to you.

25. How would you rate your overall health during the past week?

1	2	3	4	5	6	7
Poor						Excellent

26. How would you rate your overall quality of life during the past week?

1	2	3	4	5	6	7
Poor						Excellent

EQ5D5L, Health economic measures

The following six questions are also about your health. Although some of the questions ask about similar areas to previous questions, we would be grateful if you could answer these as well.

Under each heading, please tick the ONE box that best describes your health TODAY.

27. MOBILITY

I have no problems in walking about	☐
I have slight problems in walking about	☐
I have moderate problems in walking about	☐
I have severe problems in walking about	☐

I am unable to walk about ☐

28. SELF-CARE

I have no problems washing or dressing myself ☐

I have slight problems washing or dressing myself ☐

I have moderate problems washing or dressing myself ☐

I have severe problems washing or dressing myself ☐

I am unable to wash or dress myself ☐

29. USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)

I have no problems doing my usual activities ☐

I have slight problems doing my usual activities ☐

I have moderate problems doing my usual activities ☐

I have severe problems doing my usual activities ☐

I am unable to do my usual activities ☐

30. PAIN / DISCOMFORT

I have no pain or discomfort ☐

I have slight pain or discomfort ☐

I have moderate pain or discomfort ☐

I have severe pain or discomfort ☐

I have extreme pain or discomfort ☐

31. ANXIETY / DEPRESSION

I am not anxious or depressed ☐

I am slightly anxious or depressed ☐

I am moderately anxious or depressed ☐

I am severely anxious or depressed ☐

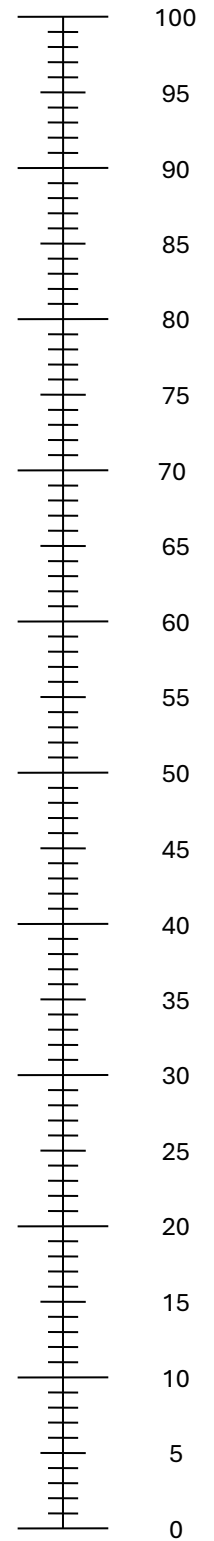
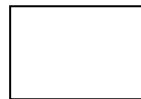
I am extremely anxious or depressed ☐

32. We would like to know how good or bad your health is TODAY.

- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
0 means the worst health you can imagine.
- Please mark an X on the scale to indicate how your health is TODAY.
- Now, write the number you marked on the scale in the box below.

The best health
you can
imagine

YOUR HEALTH



The worst
health you can
imagine

FACT-G, social wellbeing

Below is a list of statements that other people with your illness have said are important. Please mark one number per line to indicate your response as it applies to **the past 7 days**.

	Not at all	A little	Somewhat	Quite a bit	Very much
33. I feel close to my friends.	0	1	2	3	4
34. I get emotional support from my family.	0	1	2	3	4
35. I get support from my friends.	0	1	2	3	4
36. My family has accepted my illness.	0	1	2	3	4
37. I am satisfied with family communication about my illness.	0	1	2	3	4
38. I feel close to my partner (or the person who is my main support).	0	1	2	3	4

Regardless of your current level of sexual activity, please answer the following question.

If you prefer not to answer it, please mark this box ☐ and go to the next session.

	Not at all	A little	Somewhat	Quite a bit	Very much
39. I am satisfied with my sex life.	0	1	2	3	4

Case, Self-efficacy

We would like to know how confident or sure you feel about the statements listed below. Please rate your degree of confidence for each sentence using the scale shown. When you choose a higher number, you are telling us you are more confident.

Rate the confidence you feel TODAY	Not at all confident										Very confident
40. I am confident that I can use written information and resources (such as patient information and web information) to cope with the demands of cancer and its treatments.	0	1	2	3	4	5	6	7	8	9	10
41. I am confident that I can call on my inner strengths to pull myself through the cancer and its treatments.	0	1	2	3	4	5	6	7	8	9	10
42. I am confident that I have what it takes to help my family through this illness.	0	1	2	3	4	5	6	7	8	9	10
43. I am confident that I can maintain close communication with my carer about the cancer (<i>with 'carer', we refer to the person, partner, family member or friend, together with whom you participate in this study</i>).	0	1	2	3	4	5	6	7	8	9	10
44. I am confident that I can take the necessary steps to work through the demands from the cancer and its treatments.	0	1	2	3	4	5	6	7	8	9	10
45. I am confident that I have what it takes to help my family handle this cancer.	0	1	2	3	4	5	6	7	8	9	10
46. I am confident that I can handle the challenges from the cancer and its treatments.	0	1	2	3	4	5	6	7	8	9	10
47. I am confident that I have ways to manage the uncertainty brought on by the cancer.	0	1	2	3	4	5	6	7	8	9	10

Rate the confidence you feel TODAY	Not at all confident	Very confident

48. I am confident that I can manage difficult conversations with my doctors, nurses, and other health care providers.	0	1	2	3	4	5	6	7	8	9	10
49. I am confident that I can put the cancer into perspective in my life.	0	1	2	3	4	5	6	7	8	9	10
50. I am confident that I have the ability emotionally to help my family work through the issues caused by the cancer.	0	1	2	3	4	5	6	7	8	9	10
51. I am confident that I can deal with the physical changes caused by the cancer.	0	1	2	3	4	5	6	7	8	9	10
52. I am confident that I can manage what is being asked of me despite the cancer.	0	1	2	3	4	5	6	7	8	9	10
53. I am confident that I have the skills to deal with the pressures the cancer is causing in my close relationships.	0	1	2	3	4	5	6	7	8	9	10
54. I am confident that I have ways to manage the side effects caused by the treatments.	0	1	2	3	4	5	6	7	8	9	10
55. I am confident that I can keep a positive outlook in spite of the demands associated with the cancer and its treatments.	0	1	2	3	4	5	6	7	8	9	10
56. I am confident that I have ways to manage the potential stress associated with the cancer and its treatments.	0	1	2	3	4	5	6	7	8	9	10

Benefits of illness scale, Appraisal/benefits of illness

Having cancer can affect your life in different ways. We would like to know about your experience. How much do you agree with the following statements?

Having cancer has...	Not at all	A little	Some	A lot
57. Led me to be more accepting of things.	1	2	3	4

58. Helped me take things as they come.	1	2	3	4
59. Brought my family closer together.	1	2	3	4
60. Led me to deal better with stress and problems.	1	2	3	4
61. Helped me become more aware of the love and support available from other people.	1	2	3	4

SM, assertiveness to obtain information

The following two questions ask about your experiences with obtaining information and understanding information provided in relation to your cancer. How much do you agree with the following statements?

	Disagree a lot	Disagree a little	Neither agree nor disagree	Agree a little	Agree a lot
62. I know how to get access to information about my illness and treatment.	1	2	3	4	5
63. I often have trouble understanding the written patient information about my illness and treatment.	1	2	3	4	5

BC, Coping

These questions deal with the ways you cope with the stress in your life in relation to cancer. People deal with things in different ways. Each question says something about a particular way of coping. We want to know to what extent you've been doing what the question says during the last three months. How much or how frequently. Don't answer on the basis of whether it seems to be working or not - just whether or not you're doing it.

During the last three months...

**I
haven't
been
doing
this at
all**

**I've
been
doing
this a
little bit**

**I've
been
doing
this a
medium
amount**

**I've
been
doing
this a lot**

64. I've been turning to work or other activities to take my mind of things.

1

2

3

4

65. I've been concentrating my efforts on doing something about the situation I'm in.

1

2

3

4

66. I've been saying to myself "this isn't real".

1

2

3

4

67. I've been getting emotional support from others.

1

2

3

4

68. I've been giving up trying to deal with it.

1

2

3

4

69. I've been taking action to try to make the situation better.

1

2

3

4

70. I've been refusing to believe that it has happened.

1

2

3

4

71. I've been saying things to let my unpleasant feelings escape.

1

2

3

4

72. I've been getting help and advice from other people.

1

2

3

4

73. I've been criticizing myself.

1

2

3

4

74. I've been trying to come up with a strategy about what to do.

1

2

3

4

During the last three months...

**I
haven't
been
doing
this at
all**

**I've
been
doing
this a
little bit**

**I've
been
doing
this a
medium
amount**

**I've
been
doing
this a lot**

75. I've been getting comfort and understanding from someone.	1	2	3	4
76. I've been giving up the attempt to cope.	1	2	3	4
77. I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping, or shopping.	1	2	3	4
78. I've been accepting the reality of the fact that it has happened.	1	2	3	4
79. I've been expressing my negative feelings.	1	2	3	4
80. I've been trying to get advice or help from other people about what to do.	1	2	3	4
81. I've been learning to live with it.	1	2	3	4
82. I've been thinking hard about what steps to take.	1	2	3	4
83. I've been blaming myself for things that happened.	1	2	3	4

WoGs, Dyadic communication

The following statements focus on the way your carer deals with the fact that you are ill. With 'carer', we refer to the person together with whom you are participating in this study. Please indicate to what extent your carer does or does not act in the ways described.

	Never	Seldom	Now and then	Quite often	Very often
84. My carer tries to discuss it with me openly.	1	2	3	4	5
85. My carer asks me how I feel.	1	2	3	4	5

86. When something bothers me, my carer tries to discuss the problem.	1	2	3	4	5
87. My carer is full of understanding towards me.	1	2	3	4	5
88. My carer makes me feel that I 'm not alone in this.	1	2	3	4	5

DCI, coping

The following questions ask about how you and your carer cope with stress.

This section is about how you communicate your stress to your carer.	Very rarely	Rarely	Sometimes	Often	Very often
89. I let my carer know that I would appreciate his/her practical support, advice, or help.	1	2	3	4	5
90. I ask my carer to do things for me when I have too much to do.	1	2	3	4	5
91. I show my carer through my behavior when I am not doing well or have problems.	1	2	3	4	5
92. I tell my carer openly how I feel and that I would appreciate his/her support.	1	2	3	4	5
This section is about how your carer communicates when he/she is feeling stressed.	Very rarely	Rarely	Sometimes	Often	Very often
93. My carer lets me know that he/she appreciates my practical support, advice, or help.	1	2	3	4	5

94. My carer asks me to do things for him/her when he/she has too much to do.	1	2	3	4	5
95. My carer shows me through his/her behaviour that he/she is not doing well or when he/she has problems.	1	2	3	4	5
96. My carer tells me openly how he/she feels and that he/she would appreciate my support.	1	2	3	4	5
This section is about how you and your carer deal with stress together.	Very rarely	Rarely	Sometimes	Often	Very often
97. I am satisfied with the support I receive from my carer and the way we deal with stress together.	1	2	3	4	5
98. I am satisfied with the support I receive from my carer, and I find that the way we deal with stress together is effective.	1	2	3	4	5

FWS, computer skills

We are interested in your experiences with using technological devices. Please answer the following questions about your general experience using computers, smartphones and tablets.

In general,

99. I feel comfortable using a computer, a smartphone or tablet.

1	2	3	4
Not at all	A little	Quite a bit	Very much

100. I think I am skilled when it comes to using a computer, a smartphone or tablet.

1	2	3	4
Not at all	A little	Quite a bit	Very much

Process evaluation

We are very interested in your evaluation of the FOCUS/iFOCUS programme. Please select answers to the questions below that best describe your thoughts and feelings about the programme.

For each of the following questions about your overall experience using the programme, choose a number from 1 to 7 that best represents your view. To indicate your view, mark the number.

101. How useful was the programme to meeting your needs?

1	2	3	4	5	6	7
Not at all useful						Very useful

102. To what extent were you satisfied with the programme?

1	2	3	4	5	6	7
Very dissatisfied						Very satisfied

103. To what extent are you interested in using the programme materials for support in the future?

1	2	3	4	5	6	7
Not at all interested						Very interested

For each of the following questions about your overall experience using the programme, choose the response option/answer that best represents your view. To indicate your view, mark the answer.

104. To what extent did the programme meet your expectations?	Fell below my expectations	Met my expectations	Exceeded my expectations
---	----------------------------	---------------------	--------------------------

105. How would you rate the amount of information provided by the programme?

Not enough information

Just the right amount

Too much information

106. How often did you use the core materials provided as part of the programme?

Never

Only once/twice overall

Monthly

Weekly

Daily

For the following question about your overall experience using the programme, choose the response option/answer that best represents your view. To indicate your view, mark the answer.

107. Is the programme something that you would recommend to other people coping with cancer?

No

Don't know

Yes

Using the following scale (1 = "strongly disagree," 7 = "strongly agree"), please rate how much you agree or disagree with these statements. To indicate your view, mark the number.

108. The information I received in the programme was important to me.

1
Strongly
Disagree

2

3

4

5

6

7
Strongly
Agree

109. The information in the programme made me feel uncomfortable.

1
Strongly
Disagree

2

3

4

5

6

7
Strongly
Agree

110. The programme took too much time.

1
Strongly
Disagree

2

3

4

5

6

7
Strongly
Agree

111. I thought the programme was easy to understand.

1

2

3

4

5

6

7

Strongly Disagree							Strongly Agree
112. I can use the information from the programme in my day-to-day life.							
1	2	3	4	5	6	7	
Strongly Disagree						Strongly Agree	

CSRI, Health economic measure

We now have some questions about your healthcare and how you pay for it. For all questions, we are interested in all health care use whether related to your cancer diagnosis or not.

Please also notice that these questions are only about the care you received, and not the care received by anyone else.

OUTPATIENT HOSPITAL SERVICES

Please respond to the below question with the number of times you have used this service in **the last three months**. If you have not used this service, enter 0.

113. In the last three months, how many planned visits did you make to a hospital as an out-patient? (NOTE: Planned outpatient care is medical care provided by a hospital that does not require an overnight stay in the hospital. Examples include x-rays, laboratory tests, and face-to-face consultations).

INPATIENT HOSPITAL SERVICES

Please respond to each question with the number of times you have used this service in **the last three months**. If you have not used this service, enter 0.

114. In the last three months, how many times did you make an unplanned or emergency visit to a hospital as a patient?

115. In the last three months, how many times were you admitted to hospital overnight?

116. In the last three months, how many nights in total did you spend in a hospital overnight?

117. In the last three months, how many nights did you spend overnight in any other health care setting, e.g. hospice, nursing home?

PRIMARY AND COMMUNITY CARE SERVICES

118. Now we want to ask about health care use outside of hospitals. Please respond to each question with the number of times you have used this service in **the last three months** and the average contact time for each service you have used. This can include face-to-face, telephone or email consultations. If you have not used this service, enter 0.

Service	Total number of contacts over the last 3 months	Average contact time (minutes)
G.P./ primary care physician		
Public health or community health nurse		
Palliative care home care nurse		
Home help/care worker/health care assistant		
Psychologist		
Physiotherapist		
Occupational therapist		
Speech and language therapist		
Social worker		
Dentist		
Other medical specialist (please		

specify): _____

Other medical specialist (please specify): _____

Other (please specify): _____

Other (please specify): _____

MEDICATIONS

119. Other than hospital treatments (e.g. chemotherapy), please list below any drugs you have taken (prescribed or over the counter) during **the last one month**. Where possible copy name and dose from package or container. List all medications, whether related to your cancer diagnosis or not.

If you have not taken any medications, write 'No medications': _____

Name of drug	Dosage (if known)	Dose per day

If you do not know the answer to this question, please mark this box ☐

120. Please list below use of any specialist equipment you have used, e.g. special bed, wheelchair, breathing assistance.

If you have not used any equipment, write 'No equipment': _____

Name of equipment

Who paid all or most of the cost?

1. State or insurance
2. You or your family

1. State or Insurance
2. You or your family

1. State or Insurance
2. You or your family

INFORMAL CARE

In the **last three months**, have you received unpaid help from a friend or relative (including the carer participating in the study) on any of the following tasks as a consequence of your illness?

For each 'Type of help', please mark 'Yes' or 'No' and write in the average hours' help received each week.

Type of help

Mark

Average number of hours per week

121. Child care (choose 'no' if you have no children aged <18)

No

Yes

122. Personal care (e.g. washing, dressing, using the toilet, getting into bed)

No

Yes

123.Help in/around the house (eg. cooking, cleaning, moving around the house, taking medications, etc.)	No	Yes
---	----	-----

124.Help outside the home (e.g. shopping, transport etc.)	No	Yes
---	----	-----

PERSONAL COSTS

In the last three months, have you paid health care costs from your own pocket or lost income through missed work as a consequence of your illness?

For each 'Type of cost', please mark 'Yes' or 'No' and write in the average cost each week.

Type of cost	Mark		
125.Have you paid drug costs from out of your own pocket?	No	Yes	Average cost per week: _____
126.Have you paid for transport to and from health care appointments?	No	Yes	Average cost per week: _____
127.Have you taken time off work due to illness and lost income?	No	Yes	Average cost per week: _____ OR Average number of hours missed per week:_____
128.Have you taken time off work due to illness without loss of pay?	No	Yes	Average number of hours missed per week:_____
129.Did you receive a carer benefit/lump sum to support household expenses?	No	Yes	Total amount received: _____

The final questions ask you to provide some important background information about you and your current situation. Please tick the box that best applies.

130.Are you:

☐ Male

☐ Female

☐ Other

☐ Prefer not to answer

131.How old are you?

_____ years

132.What is your current relationship status?

☐ Married or in a relationship

☐ Separated/divorced/widowed

☐ Single/not in a relationship

☐ Prefer not to answer

133.Do you have children? (tick all the boxes that apply)

☐ I have children under the age of 18

☐ I have adult children age 18 years or older

☐ I don't have any children

134. Do you live:

☐ In a private household (flat, house etc.)

☐ In an institution/care facility (nursing home, sheltered housing etc.)

☐ Other. Please specify: _____

135. Together with whom do you live? (tick all the boxes that apply)

☐ With a spouse/partner

☐ With children under the age of 18

☐ With adult children age 18 years or older

☐ With other persons, please specify: _____

☐ I live alone

136. What is your relationship to the person who is participating in this study with you?

I am his/her...

☐ Spouse/partner

☐ Parent

☐ Sister/brother

☐ Daughter/son

☐ Other relative

☐ Friend

☐ Other, please specify: _____

137. What is the highest level of education you have completed?

☐ Pre-primary education

☐ Primary school education

☐ CSE, 'O' levels, GCSEs, entry level foundation diploma

☐ 'A' levels, AS levels, VCEs Higher diploma

☐ NVQ level 2, Intermediate GNVQ, City and Guilds, BTEC first general diploma, RSA diploma, Apprenticeship

☐ NVQ level 4, HND Foundation Degree, Diploma of Higher Education

☐ Bachelor's degree, Graduate Certificate, Graduate Diploma, Professional Graduate certificate in education

☐ MSc, NVQ level 5, Postgraduate Diploma, Postgraduate certificate

☐ PhD, Dphil, Professional doctorate

☐ Prefer not to answer

138. Are you currently employed? Tick one box only.

☐ Yes, but I am currently on sick / care leave (full time or part time)

☐ Yes, I work full time

☐ Yes, I work part time. Number of hours: _____ hours

☐ No, I am unemployed

☐ No, I am a homemaker

☐ No, I am retired

☐ No, I am a student

☐ Other, please specify: _____

☐ Prefer not to answer

139. What is the total monthly net income of your household (i.e. your income after tax and other deductions)?

- ☐ Approximately £0-894 per month
- ☐ Approximately £895-1789 per month
- ☐ Approximately £1790-2684 per month
- ☐ Approximately £2685-3579 per month
- ☐ Approximately £3580-4473 per month
- ☐ Approximately £4474-5368 per month
- ☐ More than £5369 per month
- ☐ Don't know
- ☐ Prefer not to answer

140. Which of the following descriptions comes closest to how you feel about your household income nowadays?

- ☐ Living comfortably on present income
- ☐ Coping on present income
- ☐ Difficult on present income
- ☐ Very difficult on present income
- ☐ Don't know
- ☐ Prefer not to answer

141. Has your physical condition or medical treatment caused you financial difficulties?

- ☐ Not at all
- ☐ A little

- ☐ Quite a bit
- ☐ Very much
- ☐ Prefer not to answer

The following question concerns an entirely different topic.

142. Do you agree with the following statement: 'I believe in God or in someone or something greater than myself'.

- ☐ Not at all
- ☐ A little
- ☐ Quite a bit
- ☐ Very much
- ☐ Prefer not to answer

143. Your country of birth: _____

If your mother or father was born in another country, please state it below:

Country of birth of mother: _____

Country of birth of father: _____

If you have any comments you would like to add after completing this questionnaire or as part of your participation within the DIAdIC trial, please write these below:

Thank you very much for completing this questionnaire. Your participation in the DIAdIC trial is much appreciated.

Information about this questionnaire

You have received this questionnaire because you have agreed to participate in the DIAdIC trial investigating the effect of different kinds of support for patients and their carers across six European countries.

As part of your participation in the DIAdIC trial, you will receive three questionnaires. This is questionnaire X out of 3. The questionnaires ask questions about a lot of different topics, such as your health, how you cope and how you and the person, together with whom you are participating in the DIAdIC trial, communicate. We are aware that some of the questions might seem similar and that some of the questions might also seem more relevant to your situation than others. However, we kindly ask that you try to reply to all questions as far as possible. The estimated time for completion of this questionnaire is about half an hour.

You will notice that some of the questions within this questionnaire refer to your 'partner/family member/friend'. By 'partner/family member/friend', we refer to the person together with whom you are participating in this trial.

At the end of the questionnaire, some questions about your possible visits to the hospital and use of medicine will be asked. For these questions, it might be helpful to have your diary and/or lists of any medicine you take next to you.

Your answers to the questions within this questionnaire will be treated as strictly confidential. Data will be kept and used in accordance with the European 'General Data Protection Regulation' (GDPR) guidelines.

Should any of the questions in this questionnaire make you emotionally upset or distressed, do not hesitate to contact Professor Kevin Brazil (k.brazil@qub.ac.uk). You are also welcome to contact the your local research team if you have questions about the questionnaires or the DIAdIC trial in general.

Thank you very much for taking the time to participate.

Date of completion: _____

These first questions ask about you and your health. Please answer all of the questions yourself by marking the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

EORTC EF10, Emotional functioning

During the past week:	Not at all	A little	Quite a bit	Very much
144. Did you feel tense?	1	2	3	4
145. Did you feel depressed?	1	2	3	4
146. Did you worry?	1	2	3	4
147. Did you feel irritable?	1	2	3	4
148. Have you felt panic?	1	2	3	4
149. Have you felt vulnerable?	1	2	3	4
150. Have you felt that nothing could cheer you up?	1	2	3	4
151. Have you felt miserable?	1	2	3	4
152. Have you felt desperate?	1	2	3	4
153. Have you been afraid of losing control?	1	2	3	4

EQ5D5L, Health economic measures

The following six questions are also about your health. Some questions might seem more relevant to your situation than others, however, we would be grateful if you could try to answer these as well.

Under each heading, please tick the ONE box that best describes your health TODAY.

154. MOBILITY

- | | |
|---|--------------------------|
| I have no problems in walking about | ☐ |
| I have slight problems in walking about | ☐ |
| I have moderate problems in walking about | ☐ |
| I have severe problems in walking about | ☐ |
| I am unable to walk about | ☐ |

155.SELF-CARE

- I have no problems washing or dressing myself ☐
- I have slight problems washing or dressing myself ☐
- I have moderate problems washing or dressing myself ☐
- I have severe problems washing or dressing myself ☐
- I am unable to wash or dress myself ☐

156.USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)

- I have no problems doing my usual activities ☐
- I have slight problems doing my usual activities ☐
- I have moderate problems doing my usual activities ☐
- I have severe problems doing my usual activities ☐
- I am unable to do my usual activities ☐

157.PAIN / DISCOMFORT

- I have no pain or discomfort ☐
- I have slight pain or discomfort ☐
- I have moderate pain or discomfort ☐
- I have severe pain or discomfort ☐
- I have extreme pain or discomfort ☐

158.ANXIETY / DEPRESSION

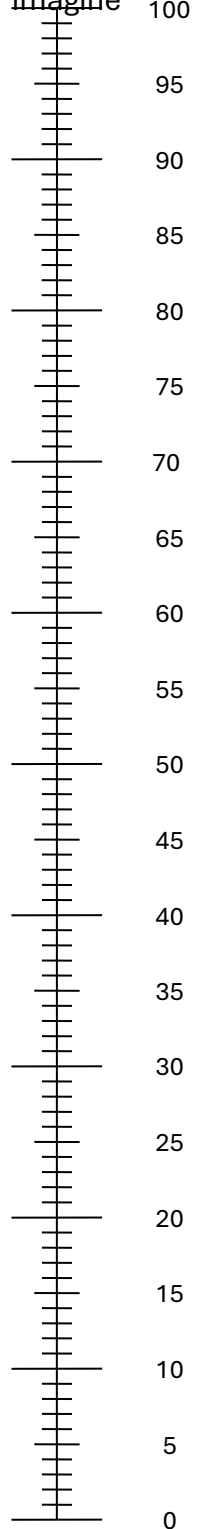
- I am not anxious or depressed ☐
- I am slightly anxious or depressed ☐
- I am moderately anxious or depressed ☐
- I am severely anxious or depressed ☐
- I am extremely anxious or depressed ☐

16. We would like to know how good or bad your health is TODAY.

- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
0 means the worst health you can imagine.
- Please mark an X on the scale to indicate how your health is TODAY.
- Now, write the number you marked on the scale in the box below.

YOUR HEALTH TODAY

The best health
you can
imagine



The worst
health you can
imagine

Below is a list of statements that other people caring for persons with cancer have said are important. By marking one number per line, please indicate how true each statement has been for you during the past 7 days.

Please note that with 'partner/family member/friend', we refer to the person together with whom you participate in this study. Depending on your relation to each other (whether you are in a relationship, are family or friends) some questions might seem more relevant than others. Please try to answer all questions.

During the past 7 days	Not at all	A little bit	Somewhat	Quite a bit	Very much
17. It bothers me that my daily routine is altered.	0	1	2	3	4
18. My sleep is restful.	0	1	2	3	4
19. My daily life is imposed upon.	0	1	2	3	4
20. I am satisfied with my sex life.	0	1	2	3	4
21. It is a challenge to maintain my outside interests.	0	1	2	3	4
22. I am under financial strain.	0	1	2	3	4
23. I am concerned about our insurance coverage.	0	1	2	3	4
24. My economic future is uncertain.	0	1	2	3	4
25. I fear my partner/family member/friend, will die.	0	1	2	3	4
26. I have more of a positive outlook on life since my partner/family member/friend's illness.	0	1	2	3	4

During the past 7 days	Not at all	A little bit	Somewhat	Quite a bit	Very much
27. My level of stress and worries has increased.	0	1	2	3	4
28. My sense of spirituality has increased.	0	1	2	3	4
29. It bothers me, limiting my focus to day-to-day.	0	1	2	3	4
30. I feel sad.	0	1	2	3	4
31. I feel under increased mental strain.	0	1	2	3	4
32. I get support from my friends and neighbors.	0	1	2	3	4
33. I feel guilty.	0	1	2	3	4
34. I feel frustrated.	0	1	2	3	4
35. I feel nervous.	0	1	2	3	4
36. I worry about the impact my partner/family member/friend's illness has had on my children or other family members.	0	1	2	3	4
37. I have difficulty dealing with my partner/family member/friend's changing eating habits.	0	1	2	3	4

During the past 7 days	Not at all	A little bit	Somewhat	Quite a bit	Very much
38. I have developed a closer relationship with my partner/family member/friend.	0	1	2	3	4
39. I feel adequately informed about my partner/family member/friend's illness.	0	1	2	3	4
40. It bothers me that I need to be available to chauffeur my partner/family member/friend to appointments.	0	1	2	3	4
41. I fear the adverse effects of treatment on my partner/family member/friend.	0	1	2	3	4
42. The responsibility I have for my partner/family member/friend's care at home is overwhelming.	0	1	2	3	4
43. I am glad that my focus is on getting my partner/family member/friend well.	0	1	2	3	4
44. Family communication has increased.	0	1	2	3	4
45. It bothers me that my priorities have changed.	0	1	2	3	4
46. The need to protect my partner/family member/friend bothers me.	0	1	2	3	4

During the past 7 days	Not at all	A little bit	Somewhat	Quite a bit	Very much
47. It upsets me to see my partner/family member/friend deteriorate.	0	1	2	3	4
48. The need to manage my partner/family member/friend's pain is overwhelming.	0	1	2	3	4
49. I am discouraged about the future.	0	1	2	3	4
50. I am satisfied with the support I get from my family.	0	1	2	3	4
51. It bothers me that other family members have not shown interest in taking care of my partner/family member/friend.	0	1	2	3	4

Case, self-efficacy

We would like to know how confident or sure you, as a carer to a person with cancer, feel about the statements listed below. Please rate your degree of confidence for each sentence using the scale shown. When you choose a higher number, you are telling us you are more confident.

Please note that with 'partner/family member/friend', we refer to the person together with whom you participate in this trial.

Rate the confidence you feel TODAY	Not at all confident										Very confident
52. I am confident that I can use written information and resources (such as patient information and web information) to cope with the demands of the cancer and its treatments.	0	1	2	3	4	5	6	7	8	9	10

53. I am confident that I can call on my inner strengths to pull myself through my partner/family member/friend's cancer and its treatments.	0	1	2	3	4	5	6	7	8	9	10
54. I am confident that I can maintain close communication with my partner/family member/friend about the cancer.	0	1	2	3	4	5	6	7	8	9	10
55. I am confident that I can take the necessary steps to work through the demands from the cancer and its treatments.	0	1	2	3	4	5	6	7	8	9	10
56. I am confident that I can handle the challenges from the cancer and its treatments.	0	1	2	3	4	5	6	7	8	9	10
57. I am confident that I have ways to manage the uncertainty brought on by the cancer.	0	1	2	3	4	5	6	7	8	9	10
58. I am confident that I can manage difficult conversations with the doctors, nurses, and other health care providers.	0	1	2	3	4	5	6	7	8	9	10
59. I am confident that I can put the cancer into perspective in my life.	0	1	2	3	4	5	6	7	8	9	10
Rate the confidence you feel TODAY	Not	at	all							Very	
	confident									confident	
60. I am confident that I can deal with the physical changes caused by my partner/family member/friend's cancer.	0	1	2	3	4	5	6	7	8	9	10
61. I am confident that I can manage what is being asked of me despite the cancer.	0	1	2	3	4	5	6	7	8	9	10
62. I am confident that I have the skills to deal with the pressures the cancer is causing in my close relationships.	0	1	2	3	4	5	6	7	8	9	10

63. I am confident that I have ways to help my partner/family member/friend manage the side effects caused by the cancer treatments.	0	1	2	3	4	5	6	7	8	9	10
--	---	---	---	---	---	---	---	---	---	---	----

64. I am confident that I can keep a positive outlook in spite of the demands associated with the cancer and its treatments.	0	1	2	3	4	5	6	7	8	9	10
--	---	---	---	---	---	---	---	---	---	---	----

65. I am confident that I have ways to manage the potential stress associated with the cancer and its treatments.	0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	---	----

Questions 66, 67 and 68 are to be answered by spouses/partners or family members only. If you are not the spouse/partner or a family member, please proceed to question 69.

66. I am confident that I have what it takes to help my family through the illness.	0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	---	----

67. I am confident that I have what it takes to help my family handle the cancer.	0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	---	----

68. I am confident that I have the ability emotionally to help my family work through the issues caused by the cancer.	0	1	2	3	4	5	6	7	8	9	10
--	---	---	---	---	---	---	---	---	---	---	----

Benefits of illness scale, Appraisal/benefits of illness

Being a carer to a person with cancer can affect your life in different ways. We would like to know about your experience. How much do you agree with the following statements?

Caring for my partner/family member/friend has...	Not at all	A little	Some	A lot
--	-------------------	-----------------	-------------	--------------

69. Led me to be more accepting of things.	1	2	3	4
--	---	---	---	---

70. Helped me take things as they come.	1	2	3	4
---	---	---	---	---

71. Brought my family closer together.	1	2	3	4
--	---	---	---	---

72. Led me to deal better with stress and problems.	1	2	3	4
---	---	---	---	---

73. Helped me become more aware of the love and support available from other people.	1	2	3	4
--	---	---	---	---

SM, assertiveness to obtain information

The following two questions ask about your experiences with obtaining information and understanding information provided in relation to your partner/family member/friend 's cancer. How much do you agree with the following statements?

	Disagree a lot	Disagree a little	Neither agree nor disagree	Agree a little	Agree a lot
74. I know how to get access to information about my partner/family member/friend 's illness and treatment.	1	2	3	4	5
75. I often have trouble understanding the written patient information about my partner/family member/friend 's illness and treatment.	1	2	3	4	5

BC, Coping

These questions deal with the ways you cope with the stress in your life in relation to your partner/family member/friend 's cancer. People deal with things in different ways. Each question says something about a particular way of coping. We want to know to what extent you've been doing what the question says during the last three months. How much or how frequently. Don't answer on the basis of whether it seems to be working or not - just whether or not you're doing it.

During the last three months...	I haven't been doing this at all	I've been doing this a little bit	I've been doing this a medium amount	I've been doing this a lot
76. I've been turning to work or other activities to take my mind of things.	1	2	3	4
77. I've been concentrating my efforts on doing something about the situation I'm in.	1	2	3	4
78. I've been saying to myself "this isn't real".	1	2	3	4
79. I've been getting emotional support from others.	1	2	3	4
80. I've been giving up trying to deal with it.	1	2	3	4
81. I've been taking action to try to make the situation better.	1	2	3	4
82. I've been refusing to believe that it has happened.	1	2	3	4
83. I've been saying things to let my unpleasant feelings escape.	1	2	3	4
84. I've been getting help and advice from other people.	1	2	3	4
85. I've been criticizing myself.	1	2	3	4
86. I've been trying to come up with a strategy about what to do.	1	2	3	4

During the last three months...	I haven't been doing this at all	I've been doing this a little bit	I've been doing this a medium amount	I've been doing this a lot
87. I've been getting comfort and understanding from someone.	1	2	3	4

88. I've been giving up the attempt to cope.	1	2	3	4
89. I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping, or shopping.	1	2	3	4
90. I've been accepting the reality of the fact that it has happened.	1	2	3	4
91. I've been expressing my negative feelings.	1	2	3	4
92. I've been trying to get advice or help from other people about what to do.	1	2	3	4
93. I've been learning to live with it.	1	2	3	4
94. I've been thinking hard about what steps to take.	1	2	3	4
95. I've been blaming myself for things that happened.	1	2	3	4

WoGs, Dyadic communication

The following statements focus on the way you deal with the fact that your partner/family member/friend is ill. Please indicate to what extent you do or do not act in the ways described.

	Never	Seldom	Now and then	Quite often	Very often
96. I try to discuss it with my partner/family member/friend openly.	1	2	3	4	5
97. I ask my partner/family member/friend how he or she feels.	1	2	3	4	5

98. When something bothers my partner/family member/friend, I try to discuss the problem.	1	2	3	4	5
99. I am full of understanding towards my partner/family member/friend.	1	2	3	4	5
100. I make my partner/family member/friend feel that he or she is not alone in this.	1	2	3	4	5

DCI, coping

The following questions ask about how you and your partner/family member/friend cope with stress.

This section is about how you communicate your stress to your partner/family member/friend.	Very rarely	Rarely	Sometimes	Often	Very often
101. I let my partner/family member/friend know that I would appreciate his/her practical support, advice, or help.	1	2	3	4	5
102. I ask my partner/family member/friend to do things for me, when I have too much to do.	1	2	3	4	5
103. I show my partner/family member/friend through my behavior, when I am not doing well or have problems.	1	2	3	4	5
104. I tell my partner/family member/friend openly how	1	2	3	4	5

I feel and that I would appreciate his/her support.

This section is about how your partner/family member/friend communicates when he/she is feeling stressed.

Very rarely

Rarely

Sometimes

Often

Very often

105. My partner/family member/friend lets me know that he/she appreciates my practical support, advice, or help.

1

2

3

4

5

106. My partner/family member/friend asks me to do things for him/her, when he/she has too much to do.

1

2

3

4

5

107. My partner/family member/friend shows me through his/her behavior that he/she is not doing well or when he/she has problems.

1

2

3

4

5

108. My partner/family member/friend tells me openly how he/she feels and that he/she would appreciate my support.

1

2

3

4

5

This section is about how you and your partner/family member/friend deal with stress together.

Very rarely

Rarely

Sometimes

Often

Very often

109. I am satisfied with the support I receive from my partner/family

1

2

3

4

5

member/friend and the way we deal with stress together.

110. I am satisfied with the support I receive from my partner/family member/friend, and I find that the way we deal with stress together is effective.	1	2	3	4	5
---	---	---	---	---	---

FWS, computer skills

We are interested in your experiences with using technological devices. Please answer the following questions about your general experience using computers, smartphones and tablets.

In general,

111. I feel comfortable using a computer, a smartphone or tablet.

1	2	3	4
Not at all	A little	Quite a bit	Very much

112. I think I am skilled when it comes to using a computer, a smartphone or tablet.

1	2	3	4
Not at all	A little	Quite a bit	Very much

Process evaluation

We are very interested in your evaluation of the FOCUS/iFOCUS programme. Please select answers to the questions below that best describe your thoughts and feelings about the programme.

For each of the following questions about your overall experience using the programme, choose a number from 1 to 7 that best represents your view. To indicate your view, mark the number.

113. How useful was the programme to meeting your needs?

1	2	3	4	5	6	7
---	---	---	---	---	---	---

Not at all useful							Very useful
114. To what extent were you satisfied with the programme?							
1	2	3	4	5	6	7	
Very dissatisfied							Very satisfied
115. To what extent are you interested in using the programme materials for support in the future?							
1	2	3	4	5	6	7	
Not at all interested							Very interested

For each of the following questions about your overall experience using the programme, choose the response option/answer that best represents your view. To indicate your view, mark the answer.

116. To what extent did the programme meet your expectations?	Fell below my expectations	Met my expectations	Exceeded my expectations		
117. How would you rate the amount of information provided by the programme?	Not enough information	Just the right amount	Too much information		
118. How often did you use the core materials provided as part of the programme?	Never	Only once/twice overall	Monthly	Weekly	Daily
119. Is the programme something that you would recommend to other people coping with cancer?	No	Don't know	Yes		

Using the following scale (1 = “strongly disagree,” 7 = “strongly agree”), please rate how much you agree or disagree with these statements. To indicate your view, mark the number.

120. The information I received in the programme was important to me.							
1	2	3	4	5	6	7	
Strongly Disagree							Strongly Agree
121. The information in the programme made me feel uncomfortable.							
1	2	3	4	5	6	7	

Strongly Disagree							Strongly Agree
122.The programme took too much time.							
1	2	3	4	5	6	7	
Strongly Disagree						Strongly Agree	
123.I thought the programme was easy to understand.							
1	2	3	4	5	6	7	
Strongly Disagree						Strongly Agree	
124. I can use the information from the programme in my day-to-day life.							
1	2	3	4	5	6	7	
Strongly Disagree						Strongly Agree	

CSRI, Health economic measures

We now have some questions about your healthcare and how you pay for it. Please notice that these questions are only about the care you received, and not the care received by your partner/family member/friend or anyone else.

We know from experience that some of these questions might not seem relevant to your situation as a carer. However, we kindly ask you to try to answer all the questions as they will provide important information for our health economics analysis.

OUTPATIENT HOSPITAL SERVICES

Please respond to the below question with the number of times you have used this service in **the last three months**. If you have not used this service, enter 0.

125.In the last three months, how many planned visits did you make to a hospital as an out-patient? (NOTE: Planned outpatient care is medical care provided by a hospital that does not require an overnight stay in the hospital. Examples include x-rays, laboratory tests, and face-to-face consultations).

INPATIENT HOSPITAL SERVICES

Please respond to each question with the number of times you have used this service in **the last three months**. If you have not used this service, enter 0.

126. In the last three months, how many times did you make an unplanned or emergency visit to a hospital as a patient?

127. In the last three months, how many times were you admitted to hospital overnight?

128. In the last three months, how many nights in total did you spend in a hospital overnight?

PRIMARY AND COMMUNITY CARE SERVICES

129. Now we want to ask about health care use outside of hospitals. Please respond to each question with the number of times you have used this service in **the last three months** and the average contact time for each service you have used. This can include face-to-face, telephone or email consultations. If you have not used this service, enter 0.

Service	Total number of contacts over the last 3 months	Average contact time (minutes)
G.P./ primary care physician		
Public health or community health nurse		
Palliative care home care nurse		
Home help/care worker/health care assistant		
Psychologist		
Physiotherapist		
Occupational therapist		

Speech and language therapist

Social worker

Dentist

Other medical specialist (please specify): _____

Other medical specialist (please specify): _____

Other (please specify): _____

Other (please specify): _____

MEDICATIONS

130. Please list below any drugs you have taken (prescribed or over the counter) during **the last one month**. Where possible copy name and dose from package or container.

If you have not taken any medications, write 'No medications': _____

Name of drug	Dosage (if known)	Dose per day

If you do not know the answer to this question, please mark this box ☐

PERSONAL COSTS

In **the last three months**, have you paid health care costs from your own pocket, or lost income through missed work as a consequence of being a carer?

For each 'Type of cost', please mark 'Yes' or 'No' and write in the average cost each week.

Type of cost	Mark		
131. Have you taken time off work and lost income?	No	Yes	Average cost per week: _____ OR Average number of hours missed per week: _____
132. Have you taken time off work without loss of pay?	No	Yes	Average number of hours missed per week: _____

The final questions ask you to provide some important background information about you and your current situation as a carer to a person with cancer. Please tick the box that best applies.

133. Are you:

☐ Male

☐ Female

☐ Other

☐ Prefer not to answer

134. How old are you?

_____ years

135. What is your current relationship status?

☐ Married or in a relationship

☐ Separated/divorced/widowed

☐ Single/not in a relationship

☐ Prefer not to answer

136. Do you have children? (tick all the boxes that apply)

☐ I have children under the age of 18

☐ I have adult children age 18 years or older

☐ I don't have any children

137. Do you live:

☐ In a private household (flat, house etc.)

☐ In an institution/care facility (nursing home, sheltered housing)

☐ Other. Please specify: _____

138. Together with whom do you live? (tick all the boxes that apply)

- ☐ With a spouse/partner
- ☐ With children under the age of 18
- ☐ With adult children age 18 years or older
- ☐ With other persons, please specify: _____
- ☐ I live alone

139. Do you live together with the person with whom you participate in this study?

- ☐ Yes
- ☐ No

140. What is your relationship to the person who is participating in this study with you?
I am his/her...

- ☐ Spouse/partner
- ☐ Parent
- ☐ Sister/brother
- ☐ Daughter/son
- ☐ Other relative
- ☐ Friend
- ☐ Other, please specify: _____

141. What is the highest level of education you have completed?

- ☐ Pre-primary education
- ☐ Primary school education
- ☐ CSE, 'O' levels, GCSEs, entry level foundation diploma
- ☐ 'A' levels, AS levels, VCEs Higher diploma
- ☐ NVQ level 2, Intermediate GNVQ, City and Guilds, BTEC first general diploma, RSA diploma, Apprenticeship)
- ☐ NVQ level 4, HND Foundation Degree, Diploma of Higher Education
- ☐ Bachelor's degree, Graduate Certificate, Graduate Diploma, Professional Graduate certificate in education
- ☐ MSc, NVQ level 5, Postgraduate Diploma, Postgraduate certificate
- ☐ PhD, Dphil, Professional doctorate
- ☐ Prefer not to answer

142. Are you currently employed? Tick one box only.

- ☐ Yes, but I am currently on sick / care leave (full time or part time)
- ☐ Yes, I work full time
- ☐ Yes, I work part time. Number of hours: _____ hours
- ☐ No, I am unemployed
- ☐ No, I am a homemaker
- ☐ No, I am retired
- ☐ No, I am a student
- ☐ Other, please specify: _____
- ☐ Prefer not to answer

143. What is the total monthly net income of your household (i.e your income after tax and other deductions)?

- ☐ Approximately £0-894 per month
- ☐ Approximately £895-1789 per month
- ☐ Approximately £1790-2684 per month
- ☐ Approximately £2685-3579 per month
- ☐ Approximately £3580-4473 per month
- ☐ Approximately £4474-5368 per month
- ☐ More than £5369 per month
- ☐ Don't know
- ☐ Prefer not to answer

144. Which of the following descriptions comes closest to how you feel about your household income nowadays?

- ☐ Living comfortably on present income
- ☐ Coping on present income
- ☐ Difficult on present income
- ☐ Very difficult on present income
- ☐ Don't know
- ☐ Prefer not to answer

145. Has the physical condition or medical treatment of your partner/family member/friend with cancer caused you financial difficulties?

- ☐ Not at all
- ☐ A little
- ☐ Quite a bit
- ☐ Very much
- ☐ Prefer not to answer

The following question concerns an entirely different topic.

146. Do you agree with the following statement: 'I believe in God or in someone or something greater than myself'.

- ☐ Not at all
- ☐ A little
- ☐ Quite a bit
- ☐ Very much
- ☐ Prefer not to answer

147. Your country of birth: _____

If your mother or father was born in another country, please state it below:

Country of birth of mother: _____

Country of birth of father: _____

If you have any comments you would like to add after completing this questionnaire or as part of your participation within the DIAdIC trial, please write these below:

Thank you very much for completing this questionnaire. Your participation in the DIAdIC trial is much appreciated.

Appendix 5: Figures 1-6 DAG model

Figure 1: Model 1

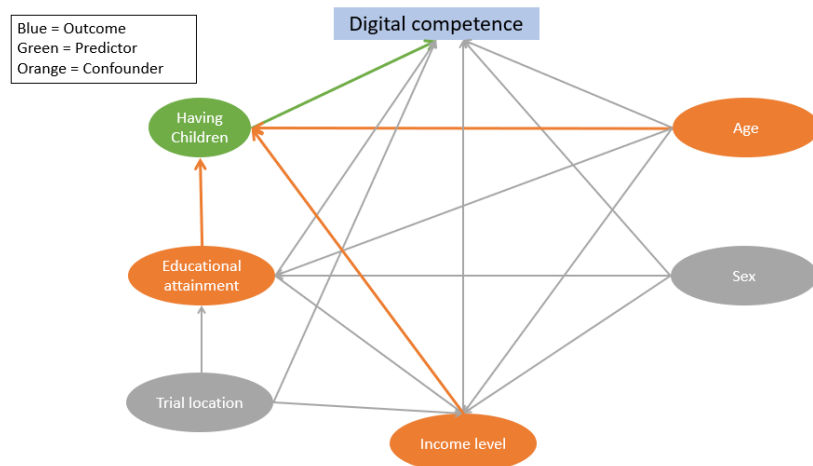


Figure 2: Model 2

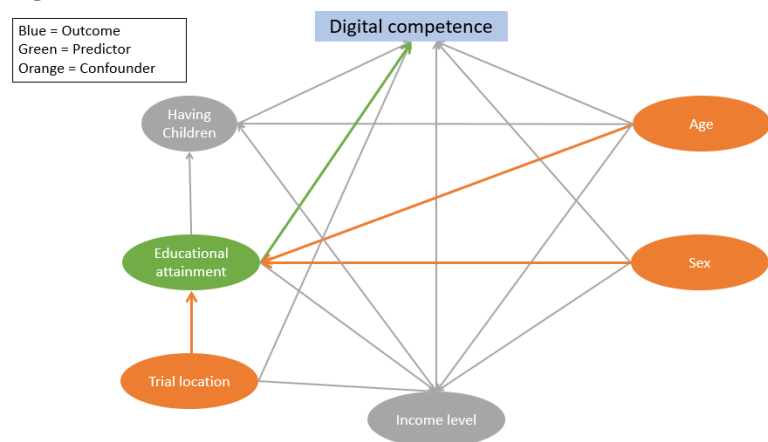


Figure 3: Model 3

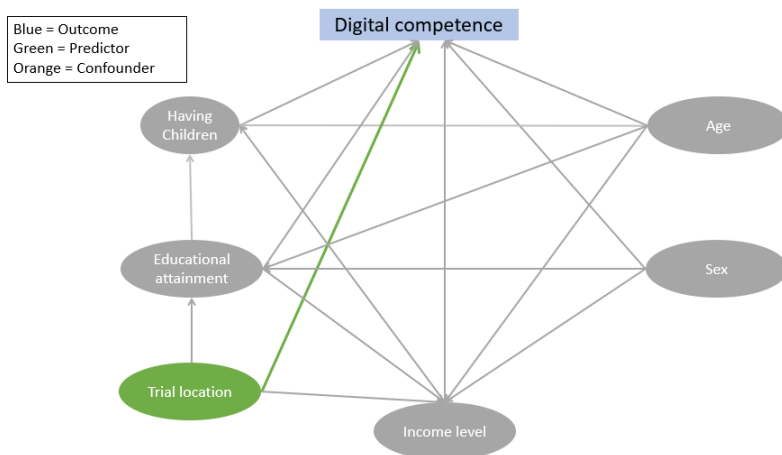


Figure 4: Model 4

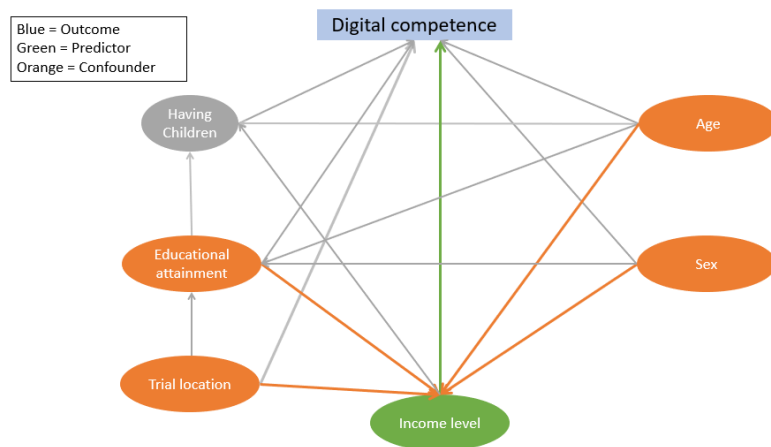


Figure 5: Model 5

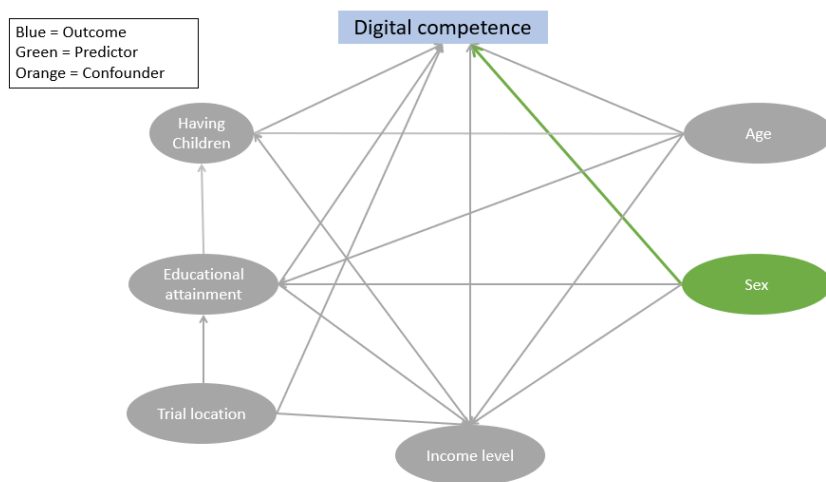
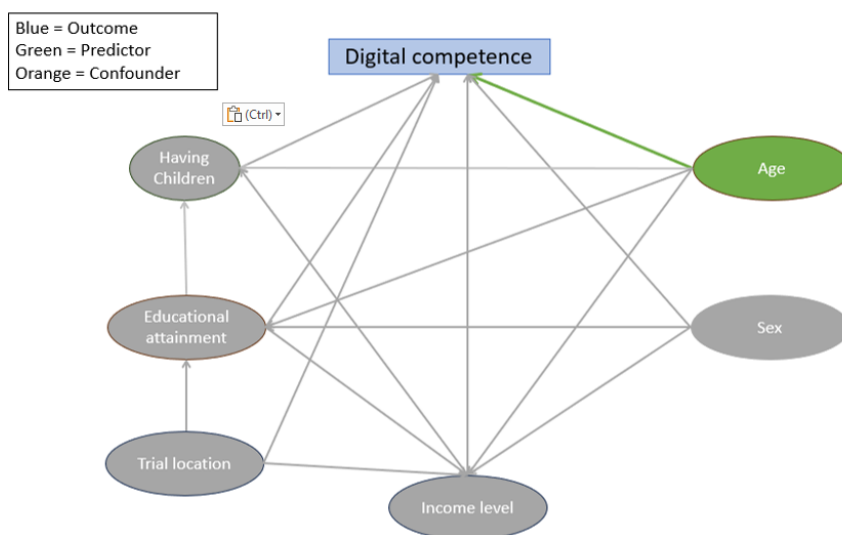


Figure 6: Model 6



Appendix 6: overview of recruiting hospitals and departments

Name hospital	City (country)	Department
Universitair Ziekenhuis Gent	Ghent (Belgium)	Medical oncology, Pneumology, Gastroenterology
AZ Maria Middelaes	Ghent (Belgium)	Medical oncology
AZ Damiaan	Oostende (Belgium)	Medical oncology
AZ Sint-Lucas	Ghent (Belgium)	Medical oncology
Rigshospitalet University Hospital	Copenhagen (Denmark)	Oncology
Herlev University Hospital	Herlev (Denmark)	Oncology
St Francis Hospice (SFH)	Dublin (Ireland)	Medical oncology
St Vincent's University Hospital	Dublin (Ireland)	Medical oncology
Azienda USL-IRCCS di Reggio Emilia	Reggio Emilia (Italy)	Oncology
Reinier de Graaff Hospital	Delft (The Netherlands)	Medical oncology
Amphia Hospital	Breda (The Netherlands)	Medical oncology
King's College Hospital NHS Foundation	London (United Kingdom)	Oncology / Palliative Care
Guy's and St Thomas' Hospitals NHS Foundation Trust	London (United Kingdom)	Oncology / Palliative Care
Belfast City Hospital, Belfast Health and Social Care Trust	Belfast (United Kingdom)	Oncology

Appendix 7: The face-to-face FOCUS+ and iFOCUS intervention according to the TIDieR checklist

A: The face-to-face FOCUS+ intervention according to the TIDieR checklist

The intervention that was evaluated in the DIAdIC project can be described as follows.

WHY

The FOCUS+ intervention is a multi-component, psychosocial, dyadic intervention, tailored to the specific needs of the dyad, that can substantially improve the quality of life and well-being of cancer patients and their family caregivers. The overarching aim is to enhance dyads' quality of life. The specific aims are:

1. Improve dyad's mutual communication
2. Identify dyads' identity and meaning-making

3. Increase dyads' coping skills
4. Help dyads reduce their uncertainty
5. Improve dyads' self-efficacy

A number of factors have been identified in the research literature that positively influence the quality of life of patients and their family caregivers. These factors include higher family support¹⁻⁴, greater optimism or less hopelessness⁴⁻⁶, less uncertainty about the illness or treatments^{4,7}, less symptom distress⁸, and the use of more active coping strategies^{9,10}. These findings provided the rationale for developing a program that facilitates family support, enhances a positive outlook, and encourages active coping, while also reducing uncertainty and symptom distress. These factors became the core components of The FOCUS Program. We anticipate that participation in the program will help dyads to respond to the impact of an advanced cancer diagnosis more favourably and that their quality of life will therefore be enhanced.

WHAT

The FOCUS+ intervention is a family-based intervention designed to provide patients with advanced cancer and their caregivers with information and support. The program consists of five core content areas, with the first letter of each area forming the acronym FOCUS: Family involvement, positive Outlook, Coping effectiveness, Uncertainty reduction, and Symptom management. Each of the five core content areas was derived from prior research. A more detailed description of the program has been reported previously¹¹.

To standardize the implementation of the FOCUS+ intervention across various nurses and sites, a 17-page protocol manual was developed that outlines the interventions for each home visit and phone call. The manual has a checklist format so that intervention nurses can document that each of the five core content areas are covered with all dyads. In addition to the core content areas, the program has flexibility that enables nurses to tailor program content to the needs of specific family dyads. For example, some dyads need more assistance with symptom management, while others need more assistance with maintaining a positive outlook. The intervention is delivered by a trained nurse. She meets with the dyad using the manual that includes instructions on what to discuss. All FOCUS items (F, O, C, U, S) are discussed in every session. The manual includes references to leaflets or websites where the dyad can find information or support. The nurse can provide the dyad with (links to) these materials, considering their needs. The nurse tailors the intervention to the needs of the dyad and supports the dyad in discussing items that are identified as important to the dyad. A **FOCUS+ guide** will be handed out in a print version to the dyad before the first session. This guide is a supporting guide for the dyads that they can refer to at their own discretion between and during sessions and reinforces key intervention messages linked to the core components of the intervention.

WHO

The nurse is the key to the success of the intervention through their ability to form relationships with the patient-carer dyad and by implementing the intervention consistently and with empathy. Nurses are trained in delivering the intervention during an online training program. They need to have the following competencies and qualifications:

- Able to communicate in the language appropriate for their country and sufficiently proficient in English to be able to participate in the training which will be delivered in English.
- A professional nursing grade, such as a BSc in Nursing in the UK.
- Experience in caring for patients with advanced cancer and/or in palliative care.
- Excellent communication, listening and questioning skills.
- Ability to cope with emotionally demanding situations.
- Willingness and ability to work flexible hours.

HOW

The first session is a face-to-face session of the nurse and the dyad. The second session is a telephone or video call of the nurse and the dyad. The third session is face to face between the nurse and the dyad.

However, in light of the COVID-19 pandemic, possible measures to contain it, and possible consequences to the feasibility of home visits delivery of the FOCUS+ sessions via a GDPR-approved online platform (e.g. MTeams, Zoom, ...) were allowed as an option, if necessary. The following decision-making tree was then followed and standardly recorded in each country:

Is face-to-face delivery of FOCUS + feasible?

- No → we specify why and move to online sessions
- Yes → *Does the dyad agree with the face-to-face sessions?*
 - If not, we specify why and move to online sessions
 - If yes, we keep the face-to-face sessions

WHERE

Face-to-face sessions will take place at the home of the patient-caregiver dyad (or in the location of the dyad's preference).

WHEN and HOW MUCH

The intervention consists of 3 sessions over a 12-week period. The first session is scheduled in week 0 for about 90 minutes. The second session is scheduled around week 4-5 for about 30 minutes. The third session is scheduled at week 9-10 and lasts about 90 minutes.

TAILORING

The nurse discusses all the FOCUS elements at each session, using the intervention manual. In addition, the nurse discusses other needs of the patient and caregiver. Depending on the dyad's situation and the personal needs of both, a wide variety of problems can be addressed. If there is a need for support, the nurse either provides such support or refers the dyad to appropriate health care professionals, organizations or information sources. When additional personal problems of the dyad are discussed during the first session, the nurse makes notes to ensure that these problems are evaluated during the second and third session.

The intervention manual and an overview of associated materials are uploaded as separate deliverables.

B: The web-based iFOCUS intervention according to the TIDieR checklist

The DIAdIC project is a European project with an international team of researchers conducted in 6 countries (Belgium, The Netherlands, Denmark, Ireland, the UK and Italy). The project consists of a face-to-face intervention (FOCUS+) and a web-based intervention (iFOCUS). Both are reported using the TIDieR checklist. Below you can find the report for the **web-based iFOCUS intervention**.

WHY

Cancer is the second most common cause of death in the European Union with an estimated 1.36 million cancer-related deaths in 2015. The costs of care for people with cancer, combined with their loss of productivity was estimated to be 126 euros in 2009. It is expected that formal care will come under increasing pressure as the need for adequate care in the population will increase because of the expected rise in the number of people with cancer, the increase of the ageing population, governments' efforts to limit health care spending and shortages of professional healthcare providers¹². Family caregivers already play a vital role in providing various aspects of palliative care in the advanced stages of the disease, by providing psychosocial support, symptom management, personal care, and assistance with the basic activities of daily living.

A large body of evidence has demonstrated the negative effect of advanced cancer on the quality of life of patients and their family caregivers. Besides the symptom burden, patients with advanced cancer also often experience high levels of serious psychosocial care needs. They report emotional and spiritual suffering, increased impairment in their daily life and a decline in their quality of life (QOL)^{13–15}. Family caregivers report similar levels of role adjustment problems and emotional distress as patients do. In addition, they often provide complex care in the home with little support from others, which increases their distress. Psychosocial problems in family caregivers of patients with advanced cancer are various with anxiety and depression being present in up to 40% progression¹⁶. Hence, both patients with advanced cancer and their family caregivers form a large group of citizens who could benefit from palliative care interventions aimed at promoting quality of life and wellbeing.

Despite the serious problems that advanced cancer creates for patients and their family caregivers, there are surprisingly few rigorously developed intervention programs to help both patients and their family caregivers self-manage the effects of illness and maintain their QOL. Reviews of psychosocial interventions in chronic illnesses that are life limiting however indicate that dyadic interventions, i.e. interventions that target both patient and family caregiver together, are more likely to result in better outcomes for both parties than single target interventions (i.e. targeting patient or family caregiver in isolation), and are potentially more cost-effective¹⁷. To address these challenges, new models of care that are accessible, affordable, scalable, and sustainable are needed. Therefore, the use of e-Health technologies in the field of psychosocial care provides a relevant opportunity for the provision of psychosocial support to both patients and caregivers. e-Health technologies have been shown to improve access to more services, increase the efficiency of the services provided while at the same time minimising the associated costs. The integration of these technologies within existing care provision is therefore considered a potentially feasible and valuable means of improving quality of life and well-being of advanced

cancer patients and their family caregivers, despite only limited evidence concerning e-health in the field of palliative care^{18,19}.

As part of the DIAdIC project, the iFOCUS intervention is a web-based, multi-component, psychoeducational intervention, tailored to the specific needs of patient-caregiver pairs (referred to as dyads). The overarching aim is to enhance dyad's quality of life by improving the emotional functioning and self-efficacy of cancer patients and their family caregivers.

The specific aims are:

1. Improve dyad's mutual communication
2. Identify dyads' identity and meaning-making
3. Increase dyads' coping skills
4. Help dyads reduce their uncertainty
5. Improve dyads' self-efficacy

Research shows that several factors can have a positive influence on the quality of life of patients and their family caregivers. These factors include higher family support¹⁻⁴, greater optimism or less hopelessness⁴⁻⁶, less uncertainty about the illness or treatments^{4,7}, less symptom distress⁸, and the use of more active coping strategies^{9,10}. These findings provided the rationale for developing a program that facilitates family support, enhances a positive outlook, and encourages active coping, while also reducing uncertainty and symptom distress. These factors became the core components of The FOCUS Program. The efficacy of the face-to-face FOCUS program was demonstrated in three randomized controlled trials (RCTs) conducted in the US. These studies found that the face-to-face program improved the QOL and well-being of both patients and caregivers. Both the face-to-face and the web-based intervention have also demonstrated good feasibility²⁰⁻²². We anticipate that participation in the program will help dyads to respond to the impact of an advanced cancer diagnosis more favourably and that their quality of life will therefore be enhanced.

WHAT

The iFOCUS intervention is a **self-managed psycho-educational intervention** aimed at dyads, designed to provide patients with advanced cancer and their caregivers with information and support. The program is internet (web)-based, which explains the prefix "i", furthermore it consists of five core content areas, with the first letter of each area forming the acronym FOCUS: Family involvement, positive Outlook, Coping effectiveness, Uncertainty reduction, and Symptom management. Each of the five core content areas was derived from prior research. The main content and information is as similar as possible across the participating countries (i.e. Belgium, The Netherlands, Denmark, Ireland, the UK and Italy). For the content of the iFOCUS web program national and international resources were gathered, revised and summarised in an English base-document and sent out for revision and translation to the European partners. Despite the similarities for some countries and languages (Dutch in the Netherlands and Belgium / English in the UK and Ireland), we chose to make country-specific versions to increase the

likeliness of acceptance from the population in said countries. The process of translation does not only apply to the written text and exercises, but to all materials such as voice-overs, video's, etc. Next to having six language versions of iFOCUS, all countries had the possibility to insert country-specific information. These adaptations are of no effect to the main content and message of the program but are of informative nature. This can be, e.g. referrals to external information sources or instances for support. The iFOCUS program consists of 4 web-based sessions and a personal workbook. Across the 4 web-based sessions information all FOCUS items are discussed in each session (Table 1). Each of the four web-sessions follows an approach similar to that of the FOCUS+ program, but fully automated by a web-program. Dyads are asked to assess their strengths, problems and needs. Based on their assessment tailored educational feedback is presented and they are asked to discuss this between themselves. The overarching content is divided in such a way that each session/topic builds further on the previous one.

Table 1: iFOCUS brief session overview

Session	F	O	C	U	S
1	Establish alliance Assess roles and teamwork Identify additional needs for support Communication patterns	Normalizing emotions Maintaining a positive outlook	Different coping styles	Different treatments	Side-effects of treatments
2	Reflection on previous session Impact on family and friends	Acknowledging difficulties Setting goals	Communication towards others	Mapping uncertainties Acknowledging uncertainties	Side-effect assessment Information on side-effects
3	Reflection on mutual support	Impact on body image	Managing body changes Tips to cope with stress Encouraging a healthy lifestyle	Talking about uncertainties to a healthcare provider	Intimacy and sexuality Evaluation of symptoms
4	Reflection on previous sessions Refer to extra sources	Evaluate change in attitude Advance care planning Refer to extra sources	Coping with stress and energy management Refer to extra sources for help	Evaluate capability for managing uncertainty Inform about help for uncertainty	Evaluate symptom development

Information across sessions is delivered in various ways. This to make the tool more engaging for the patient-caregiver dyads. For most larger pieces of text, the users can choose to have the text read aloud by clicking on a sound icon. Information is also provided through animated video's, testimonials and exercises. The content of the web-sessions is written at a lower secondary education reading level, using principles of plain language (i.e. easy to read and understand).

Additional resources

As the sessions are completed by the dyads a personal workbook is generated. The personal workbook functions as a logbook where the patient-caregiver dyad will on one hand receive standard information based on the content of the sessions and on the other hand personalised information based on the answers they gave to the exercises and assessments during the sessions. In the sessions they also have the option to indicate if they would like to have certain existing information brochures for patients, caregivers or both added to the workbook.

Tailoring

Tailoring is used in several facets of the program. Based on the information patients and caregivers provided at enrolment (names and demographic characteristics such as age, sex and relationship of the dyad) the program will react differently, e.g. by addressing the patient-caregiver dyad by name. Furthermore, the exercises allow us to tailor the web-sessions to the needs of the patient-caregiver dyad by taking in account the answers they gave to exercises. For example, an exercise might make clear that the patient-caregiver dyad has trouble with pain or sleep, which will result in providing information specifically for this topic. The personal workbook will also be tailored as it will contain dyad-specific information such as answers on exercises and related information.

WHO

The iFOCUS intervention is aimed at patients with advanced solid organ cancer (except brain cancer) and their primary family caregiver. Patients with brain cancer are excluded as they may have difficulty completing the intervention and questionnaires. Patients with a prognosis of less than 3 months were also excluded as they may be too vulnerable, and the intervention is tested over a time period of 3 months. A helpdesk is available (via email or telephone) in case the dyad experiences any technical difficulties.

HOW

Only patient-caregiver dyads that completed the baseline measurement and are allocated to the web-intervention will have access to the iFOCUS web-program. Access to the 4 sessions will be provided via a link sent by email. The dyad can log-in using their registered email address and password. For the first invitation the dyad will receive a generated password. The dyad is encouraged to change this to a personal password upon logging in. The four sessions are spread over a period of 12 weeks (where the foreseen plan is to have 3 weeks between sessions). Patient-caregiver dyads have flexibility as to when they want to complete the intervention session. When a trial manager notices that a session has not yet or partly been completed after a few weeks, a reminder can be sent out to the dyad. The invitations are automated but with a possibility for the national trial managers to make alterations. The sessions are fully web-based and accessible by

desktop, laptop or tablet. The sessions are completed simultaneously by the patient and the family caregiver, sitting side by side at a computer. At the beginning of each session, a wizard explains how dyads can navigate through the sessions.

Invitations are automated but with a possibility for the national trial managers to make alterations.

The personal workbook is accessible on the homepage. The personal workbook contains the information presented throughout the four sessions and is automatically filled in upon completion of said sessions. The information is both standard (information that everyone receives) and tailored (e.g. replies to exercises). They can access their personal workbook at each given moment, but it will be empty up till completing the first session. The personal workbook can also be downloaded as a PDF and saved locally.

WHERE

The web-based iFOCUS sessions will take place at the home of the patient-caregiver dyad (or in the location of the dyad's preference), where both will access the tool side-by-side at the same time.

WHEN and HOW MUCH

The intervention consists of 4 sessions over a 12-week period. All sessions are estimated to take up to 90 minutes but can be accessed for a longer/shorter period. The personal workbook can be used upon completion of at least one session and can be viewed at any time.

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Appendix 8: Loss to follow-up by arm by characteristics at T1 (Emotional functioning)

Characteristics	Patient				Family caregiver			
	Overall l, N = 95 (28%)	iFOCU S, N = 46 (31,1%)	FOCUS +, N = 25 (17,9%)	Control l Group, N = 24 (16,8%)	Overall l, N = 91 (21,1%)	iFOCU S, N = 47 (31,8%)	FOCUS +, N = 19 (13,6%)	Control l Group, N = 25 (17,5%)
Age in years								
18-55	19 (17,4%)	11 (24,4%)	2 (6,7%)	6 (17,6%)	32 (19,8%)	16 (25,4%)	4 (9,3%)	12 (21,4%)
56-75	62 (21,7%)	30 (32,3%)	18 (18,8%)	14 (14,4%)	51 (21,1%)	26 (34,7%)	13 (15,1%)	12 (14,8%)
>76	14 (38,9%)	5 (50%)	5 (35,7%)	4 (33,3%)	8 (29,6%)	5 (50%)	2 (18,2%)	1 (16,7%)
Sex								
Male	48 (24,6%)	22 (31%)	15 (24,2%)	11 (17,7%)	37 (21%)	18 (36,7%)	9 (14,1%)	10 (15,9%)
Female	47 (19,9%)	24 (31,2%)	10 (12,8%)	13 (16%)	54 (21,2%)	29 (29,3%)	10 (13,2%)	15 (18,8%)
Educational attainment								
Primary Education	4 (30,8%)	1 (33,3%)	3 (42,9%)	0 (0%)	2 (25%)	0 (0%)	1 (33,3%)	1 (50%)
Secondary Education	58 (24,3%)	27 (31,4%)	12 (15,6%)	19 (25%)	55 (21,7%)	27 (32,1%)	10 (11,6%)	18 (21,7%)
Higher Education	32 (18,6%)	18 (31%)	9 (17%)	5 (8,2%)	32 (19,2%)	19 (32,2%)	7 (14%)	6 (10,3%)
Unknown/Prefer not to answer	1 (14,3%)	0 (0%)	1 (33,3%)	0 (0%)	1 (50%)	0 (0%)	1 (100%)	0 (0%)
Recruitment Country								
Belgium	32 (21,6%)	14 (30,4%)	11 (21,6%)	7 (13,7%)	30 (20,3%)	13 (28,3%)	9 (17,6%)	8 (15,7%)
Italy	31 (24,6%)	14 (26,9%)	8 (21,6%)	9 (24,3%)	23 (18,3%)	13 (25%)	5 (13,5%)	5 (13,5%)

Appendix 8: Loss to follow-up by arm by characteristics at T1 (Emotional functioning)

Characteristics	Patient				Family caregiver			
	Overall l, N = 95 (28%)	iFOCU S, N = 46 (31,1%)	FOCUS +, N = 25 (17,9%)	Control l Group, N = 24 (16,8%)	Overall l, N = 91 (21,1%)	iFOCU S, N = 47 (31,8%)	FOCUS +, N = 19 (13,6%)	Control l Group, N = 25 (17,5%)
Denmark	12 (11,2 %)	9 (25,7%)	1 (2,9%)	2 (5,4%)	15 (14%)	12 (34,3%)	0 (0%)	3 (8,1%)
The Netherlands	4 (40%)	3 (60%)	0 (0%)	1 (100%)	3 (30%)	3 (60%)	0 (0%)	0 (0%)
Ireland	3 (25%)	2 (66,7%)	1 (20%)	0 (0%)	4 (33,3 %)	2 (66,7%)	1 (20%)	1 (25%)
UK	13 (46,4 %)	4 (57,1%)	4 (50%)	5 (38,5 %)	16 (57,1 %)	4 (57,1%)	4 (50%)	8 (61,5 %)
Relationship with family caregiver								
Spouse/Partner	72 (22,1 %)	35 (32,7%)	18 (16,5%)	19 (17,3 %)	68 (20,9 %)	33 (30,8%)	14 (12,8%)	21 (19,1 %)
Other	22 (21,4 %)	11 (27,5%)	6 (20%)	5 (15,2 %)	22 (21,4 %)	14 (35%)	4 (13,3%)	4 (12,1 %)
Unknown	1 (50%)	0 (0%)	1 (100%)	0 (0%)	1 (50%)	0 (0%)	1 (100%)	0 (0%)
Cancer Type								
Gastrointestinal	30 (24,2 %)	14 (34,1%)	7 (19,4%)	9 (19,1 %)				
Breast	15 (13,6 %)	7 (20,6%)	2 (5,4%)	6 (15,4 %)				
Lung	16 (26,2 %)	6 (25%)	6 (33,3%)	4 (21,1 %)				
Prostate	10 (30,3 %)	5 (33,3%)	4 (33,3%)	1 (16,7 %)				
Gynecological	8 (29,6 %)	7 (77,8%)	1 (10%)	0 (0%)				

Appendix 8: Loss to follow-up by arm by characteristics at T1 (Emotional functioning)

Characteristics	Patient				Family caregiver			
	Overall l, N = 95 (28%)	iFOCU S, N = 46 (31,1%)	FOCUS +, N = 25 (17,9%)	Control l Group, N = 24 (16,8%)	Overall l, N = 91 (21,1%)	iFOCU S, N = 47 (31,8%)	FOCUS +, N = 19 (13,6%)	Control l Group, N = 25 (17,5%)
Kidney	4 (19%)	2 (33,3%)	1 (12,5%)	1 (14,3%)				
Other	12 (21,8%)	5 (26,3%)	4 (21,1%)	3 (17,6%)				
Days since diagnosis Mean (SD)								
Relationship status								
Single/Not in a relationship	7 (25,9%)	6 (37,5%)	1 (14,3%)	0 (0%)	4 (13,3%)	3 (18,8%)	0 (0%)	1 (10%)
Married/in a relationship	77 (21,4%)	38 (31,9%)	18 (15,7%)	21 (16,7%)	81 (21,2%)	41 (32,3%)	16 (12,6%)	24 (18,8%)
Separated/Divorced/Widowed	10 (24,4%)	1 (8,3%)	6 (35,3%)	3 (25%)	6 (40%)	3 (60%)	3 (42,9%)	0 (0%)
Prefer not to answer	1 (33,3%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Treatment type (multiple answers possible)								
Chemotherapy	70 (23%)	33 (32%)	20 (19,6%)	17 (17%)				
Radiotherapy	4 (23,5%)	0 (0%)	2 (20%)	2 (33,3%)				
Antihormonal therapy	8 (18,2%)	5 (29,4%)	1 (6,7%)	2 (16,7%)				
Immunotherapy	15 (16,5%)	8 (26,7%)	6 (20,7%)	1 (3,1%)				
Surgery	2 (10,5%)	0 (0%)	1 (14,3%)	1 (14,3%)				

Appendix 8: Loss to follow-up by arm by characteristics at T1 (Emotional functioning)

Characteristics	Patient				Family caregiver			
	Overall l, N = 95 (28%)	iFOCU S, N = 46 (31,1%)	FOCUS +, N = 25 (17,9%)	Contro l Group, N = 24 (16,8%)	Overall l, N = 91 (21,1%)	iFOCU S, N = 47 (31,8%)	FOCUS +, N = 19 (13,6%)	Contro l Group, N = 25 (17,5%)
Targeted therapy	6 (28,6 %)	2 (50%)	1 (12,5%)	3 (33,3 %)				
Other	1 (3,1%)	1 (7,1%)	0 (0%)	0 (0%)				
None	5 (41,7 %)	4 (66,7%)	1 (50%)	0 (0%)				
Children (multiple answer possible)								
Under the age of 18	10 (20,4 %)	5 (27,8%)	3 (17,6%)	2 (14,3 %)	16 (22,9 %)	7 (25%)	3 (16,7%)	6 (25%)
Over the age of 18	73 (21,9 %)	35 (31,8%)	19 (17,4%)	19 (16,5 %)	60 (20,8 %)	29 (32,6%)	14 (13,5%)	17 (17,9 %)
No Children	2 (10,5 %)	11 (31,4%)	3 (13,6%)	6 (20%)				
Living situation (multiple answer possible)								
With spouse/partner	77 (22,1 %)	38 (33%)	19 (16,7%)	20 (16,8 %)	78 (21,2 %)	39 (32,8%)	16 (12,7%)	23 (18,7 %)
With children < 18	10 (20,4 %)	5 (25%)	3 (18,8%)	2 (15,4 %)	13 (21,3 %)	7 (25,9%)	1 (6,7%)	5 (26,3 %)
With children > 18	9 (12%)	3 (12,5%)	3 (12%)	3 (11,5 %)	10 (19,2 %)	1 (6,3%)	4 (20%)	5 (31,3 %)
With other person	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Alone	8 (16,7 %)	3 (15,8%)	4 (26,7%)	1 (7,1%)	6 (27,3 %)	3 (33,3%)	2 (28,6%)	1 (16,7 %)
Financial difficulties								
Not at all	52 (19,6 %)	28 (29,2%)	11 (14,1%)	13 (14,3 %)	62 (20,9 %)	37 (33,6%)	11 (12%)	14 (14,9 %)

Appendix 8: Loss to follow-up by arm by characteristics at T1 (Emotional functioning)

Characteristics	Patient				Family caregiver			
	Overall l, N = 95 (28%)	iFOCU S, N = 46 (31,1%)	FOCUS +, N = 25 (17,9%)	Control l Group, N = 24 (16,8%)	Overall l, N = 91 (21,1%)	iFOCU S, N = 47 (31,8%)	FOCUS +, N = 19 (13,6%)	Control l Group, N = 25 (17,5%)
A little	19 (20,7 %)	7 (25,9%)	4 (13,3%)	8 (22,9 %)	21 (24,1 %)	6 (27,3%)	5 (15,6%)	10 (30,3 %)
Quite a bit	12 (31,6 %)	5 (50%)	5 (25%)	2 (25%)	6 (22,2 %)	3 (27,3%)	2 (25%)	1 (12,5 %)
Very Much	7 (26,9 %)	4 (33,3%)	2 (28,6%)	1 (14,3 %)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Prefer not to answer	5 (50%)	2 (66,7%)	3 (60%)	0 (0%)	2 (15,4 %)	1 (25%)	1 (33,3%)	0 (0%)
Living together with person with whom you participate in the study with								
Yes					72 (20,6 %)	35 (30,4%)	14 (12,4%)	23 (19%)
No					19 (24,1 %)	12 (38,7%)	5 (19,2%)	2 (9,1%)
Unknown								

Appendix 8: Loss to follow-up by arm by characteristics at T1 (Self-efficacy)

Characteristics	Patient				Family caregiver			
	Overall, N = 95 (22%)	iFOCUS, N = 47 (31,8%)	FOCUS +, N = 24 (17,9%)	Control Group, N = 24 (16,8%)	Overall, N = 114 (21,1%)	iFOCUS, N = 56 (31,8%)	FOCUS +, N = 25 (13,6%)	Control Group, N = 33 (17,5%)
Age in years								
18-55	18 (16,5%)	11 (24,4%)	2 (6,7%)	5 (14,7%)	40 (24,7%)	19 (30,2%)	6 (14%)	15 (26,8%)
56-75	63 (22%)	31 (33,3%)	17 (17,7%)	15 (15,5%)	63 (26%)	30 (40%)	16 (18,6%)	17 (21%)
>76	14 (38,9%)	5 (50%)	5 (35,7%)	4 (33,3%)	11 (40,7%)	7 (70%)	3 (27,3%)	1 (16,7%)
Sex								
Male	48 (24,6%)	23 (32,4%)	14 (22,6%)	11 (17,7%)	44 (25%)	19 (38,8%)	9 (14,1%)	16 (25,4%)
Female	47 (19,9%)	24 (31,2%)	10 (12,8%)	13 (16%)	70 (27,5%)	37 (37,4%)	16 (21,1%)	17 (21,3%)
Educational attainment								
Primary Education	4 (30,8%)	1 (33,3%)	3 (42,9%)	0 (0%)	3 (37,5%)	2 (0%)	2 (66,7%)	1 (50%)
Secondary Education	59 (24,7%)	28 (32,6%)	11 (14,3%)	20 (26,3%)	71 (28,1%)	35 (41,7%)	12 (14%)	24 (28,9%)
Higher Education	31 (18%)	18 (31%)	9 (17%)	4 (6,6%)	38 (22,8%)	20 (33,9%)	10 (20%)	8 (13,8%)
Unknown/Prefer not to answer	1 (14,3%)	0 (0%)	1 (33,3%)	0 (0%)	1 (50%)	1 (0%)	1 (100%)	0 (0%)
Recruitment Country								
Belgium	30 (20,3%)	14 (30,4%)	10 (19,6%)	6 (11,8%)	37 (25%)	17 (37%)	11 (21,6%)	9 (17,6%)
Italy	32 (25,4%)	15 (28,8%)	8 (21,6%)	9 (24,3%)	38 (30,2%)	18 (34,6%)	9 (24,3%)	11 (29,7%)
Denmark	13 (12,1%)	9 (25,7%)	1 (2,9%)	3 (8,1%)	16 (15%)	12 (34,3%)	0 (0%)	4 (10,8%)

Appendix 8: Loss to follow-up by arm by characteristics at T1 (Self-efficacy)

Characteristics	Patient				Family caregiver			
	Overall, N = 95 (22%)	iFOCUS, N = 47 (31,8%)	FOCUS +, N = 24 (17,9%)	Control Group, N = 24 (16,8%)	Overall, N = 114 (21,1%)	iFOCUS, N = 56 (31,8%)	FOCUS +, N = 25 (13,6%)	Control Group, N = 33 (17,5%)
The Netherlands		3		1 (100%)	3	3		
Ireland	4 (40%)	(60%)	0 (0%)		(30%)	(60%)	0 (0%)	0 (0%)
UK	3 (25%)	2 (66,7%)	1 (20%)	0 (0%)	4 (33,3%)	2 (66,7%)	1 (20%)	1 (25%)
Relationship with family caregiver		4		5	16	4		
Spouse/Partner	13 (46,4%)	(57,1%)	4 (50%)	(38,5%)	(57,1%)	(57,1%)	4 (50%)	8 (61,5%)
Other		36	18	19	85	40	18	27
Unknown	73 (22,4%)	(33,6%)	(16,5%)	(17,3%)	(26,1%)	(37,4%)	(16,5%)	(24,5%)
Cancer Type		11		5	27	15		
Gastrointestinal	21 (20,4%)	(27,5%)	5 (16,7%)	(15,2%)	(26,2%)	(37,5%)	6 (20%)	6 (18,2%)
Breast			1		2	1		
Lung	1				(100%)	(100%)	(100%)	0 (0%)
Prostate		15	6	8				
Gynecological	29 (23,4%)	(36,6%)	(16,7%)	(17%)				
Kidney	7			6	27	15		
	15 (13,6%)	(20,6%)	2 (5,4%)	(15,4%)				
	16 (26,2%)	6 (25%)	6 (33,3%)	(21,1%)				
	10 (30,3%)	(33,3%)	4 (33,3%)	(16,7%)				
	7							
	8 (29,6%)	(77,8%)	1 (10%)	0 (0%)				
	2			1				
	4 (19%)	(33,3%)	1 (12,5%)	(14,3%)				

Appendix 8: Loss to follow-up by arm by characteristics at T1 (Self-efficacy)

Characteristics	Patient				Family caregiver			
	Overall, N = 95 (22%)	iFOCUS, N = 47 (31,8%)	FOCUS +, N = 24 (17,9%)	Control Group, N = 24 (16,8%)	Overall, N = 114 (21,1%)	iFOCUS, N = 56 (31,8%)	FOCUS +, N = 25 (13,6%)	Control Group, N = 33 (17,5%)
Other	13 (23,6%)	5 (26,3%)	4 (21,1%)	4 (23,5%)				
Days since diagnosis Mean (SD)								
Relationship status								
Single/Not in a relationship	6 (22,2%)	6 (37,5%)	0 (0%)	0 (0%)	5 (16,7%)	4 (25%)	0 (0%)	1 (10%)
Married/in a relationship	77 (21,4%)	39 (32,8%)	18 (15,7%)	20 (15,9%)	102 (26,7%)	49 (38,6%)	22 (17,3%)	31 (24,2%)
Separated/Divorced/Widowed	11 (26,8%)	1 (8,3%)	6 (35,3%)	4 (33,3%)	6 (40%)	3 (60%)	3 (42,9%)	0 (0%)
Prefer not to answer	1 (33,3%)	1 (100%)	0 (0%)	0 (0%)	1 (25%)	0 (0%)	0 (0%)	1 (50%)
Treatment type (multiple answers possible)								
Chemotherapy	70 (23%)	34 (33%)	19 (18,6%)	17 (17%)				
Radiotherapy				2 (33,3%)				
Antihormonal therapy	4 (23,5%)	0 (0%)	2 (20%)	2 (16,7%)				
Immunotherapy	8 (18,2%)	5 (29,4%)	1 (6,7%)	2 (16,7%)				
Surgery	15 (16,5%)	8 (26,7%)	6 (20,7%)	1 (3,1%)				
Targeted therapy	2 (10,5%)	0 (0%)	1 (14,3%)	1 (14,3%)				
Other	6 (28,6%)	2 (50%)	1 (12,5%)	3 (33,3%)				
None	1 (3,1%)	1 (7,1%)	0 (0%)	0 (0%)				
	5 (41,7%)	4 (66,7%)	1 (50%)	0 (0%)				

Appendix 8: Loss to follow-up by arm by characteristics at T1 (Self-efficacy)

Characteristics	Patient				Family caregiver			
	Overall, N = 95 (22%)	iFOCUS, N = 47 (31,8%)	FOCUS +, N = 24 (17,9%)	Control Group, N = 24 (16,8%)	Overall, N = 114 (21,1%)	iFOCUS, N = 56 (31,8%)	FOCUS +, N = 25 (13,6%)	Control Group, N = 33 (17,5%)
Children (multiple answer possible)								
Under the age of 18	10 (20,4%)	5 (27,8%)	3 (17,6%)	2 (14,3%)	20 (28,6%)	8 (28,6%)	3 (16,7%)	9 (37,5%)
Over the age of 18	72 (21,6%)	36 (32,7%)	18 (16,5%)	18 (15,7%)	77 (26,7%)	36 (40,4%)	19 (18,3%)	22 (23,2%)
No Children	14 (22,6%)	7 (28%)	4 (22,2%)	3 (15,8%)	22 (25,3%)	12 (34,3%)	4 (18,2%)	6 (20%)
Living situation (multiple answer possible)								
With spouse/partner	78 (22,4%)	39 (33,9%)	19 (16,7%)	20 (16,8%)	97 (26,4%)	46 (38,7%)	21 (16,7%)	30 (24,4%)
With children < 18	10 (20,4%)	5 (25%)	3 (18,8%)	2 (15,4%)	16 (26,2%)	8 (29,6%)	1 (6,7%)	7 (36,8%)
With children > 18	9 (12%)	4 (16,7%)	3 (12%)	2 (7,7%)	12 (23,1%)	2 (12,5%)	4 (20%)	6 (37,5%)
With other person	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Alone	7 (14,6%)	3 (15,8%)	3 (20%)	1 (7,1%)	6 (27,3%)	3 (33,3%)	2 (28,6%)	1 (16,7%)
Financial difficulties								
Not at all	53 (20%)	28 (29,2%)	11 (14,1%)	14 (15,4%)	74 (25%)	42 (38,2%)	13 (14,1%)	19 (20,2%)
A little	19 (20,7%)	8 (29,6%)	4 (13,3%)	7 (20%)	29 (33,3%)	8 (36,4%)	9 (28,1%)	12 (36,4%)
Quite a bit	11 (28,9%)	5 (50%)	4 (20%)	2 (25%)	8 (29,6%)	4 (36,4%)	2 (25%)	2 (25%)
Very Much	7 (26,9%)	4 (33,3%)	2 (28,6%)	1 (14,3%)	1 (14,3%)	1 (100%)	0 (0%)	0 (0%)
Prefer not to answer	5 (50%)	2 (66,7%)	3 (60%)	0 (0%)	2 (15,4%)	1 (25%)	1 (33,3%)	0 (0%)

Appendix 8: Loss to follow-up by arm by characteristics at T1 (Self-efficacy)

Characteristics	Patient				Family caregiver			
	Overall, N = 95 (22%)	iFOCUS, N = 47 (31,8%)	FOCUS+, N = 24 (17,9%)	Control Group, N = 24 (16,8%)	Overall, N = 114 (21,1%)	iFOCUS, N = 56 (31,8%)	FOCUS+, N = 25 (13,6%)	Control Group, N = 33 (17,5%)
Living together with person with whom you participate in the study with								
Yes					91 (26,1%)	43 (37,4%)	19 (16,8%)	29 (24%)
No					23 (29,1%)	13 (41,9%)	6 (23,1%)	4 (18,2%)
Unknown								

Appendix 9: Mean scores at baseline, t1 and t2 for the primary outcomes (intention-to-treat)

		Mean score at baseline (T0) (95% CI)			Mean score at 12 weeks (T1) (95% CI)			Mean score at 24 weeks (T2) (95% CI)		
		<i>Control group</i>	<i>iFOCUS</i>	<i>FOCUS+</i>	<i>Control group</i>	<i>iFOCUS</i>	<i>FOCUS+</i>	<i>Control group</i>	<i>iFOCUS</i>	<i>FOCUS+</i>
Emotional functioning	Patient	47.61 (46.19 to 49.03)	47.17 (45.74 to 48.60)	47.69 (46.38 to 49.00)	49.03 (47.63 to 50.43)	48.50 (47.07 to 49.93)	49.18 (47.91 to 50.45)	48.52 (4.05 to 49.99)	49.91 (48.52 to 51.30)	48.60 (47.19 to 50.02)
	Family caregiver	46.71 (45.35 to 48.07)	45.91 (44.44 to 47.38)	46.53 (45.24 to 47.83)	46.73 (45.31 to 48.15)	46.56 (45.31 to 47.81)	46.89 (45.65 to 48.13)	46.62 (45.18 to 48.06)	47.17 (45.76 to 48.58)	45.94 (44.71 to 47.17)
Self-efficacy	Patient	119.67 (114.46 to 124.88)	118.25 (112.64 to 123.87)	122.66 (118.13 to 127.19)	115.62 (109.77 to 121.47)	114.68 (109.27 to 120.09)	126.43 (122.12 to 130.74)	116.82 (111.39 to 122.25)	117.00 (111.82 to 122.18)	120.24 (115.07 to 125.41)
	Family caregiver	118.30 (112.96 to 123.64)	113.24 (108.24 to 118.24)	114.68 (109.19 to 120.17)	114.34 (108.64 to 120.04)	114.56 (109.44 to 119.68)	116.05 (110.90 to 121.20)	114.19 (108.49 to 119.89)	113.67 (108.73 to 118.61)	115.56 (110.16 to 120.96)

Appendix 10: Primary endpoints effect (per-protocol)

Mean difference (95% CI)				Effect size (Cohen's d) (95% CI)				p-value			
T1		T2		T1		T2		T1		T2	
<i>iFOCUS vs control group</i>	<i>FOCUS+ vs control group</i>	<i>iFOCUS vs control group</i>	<i>FOCUS+ vs control group</i>	<i>iFOCUS vs control group</i>	<i>FOCUS+ vs control group</i>	<i>iFOCUS vs control group</i>	<i>FOCUS+ vs control group</i>	<i>iFOCUS vs control group</i>	<i>FOCUS+ vs control group</i>	<i>iFOCUS vs control group</i>	<i>FOCUS+ vs control group</i>

Emotional functioning	Patient	0.01	(-	-0.01	(-	2.59	(-	-0.10	(-	0.00	(-	-0.00	(-	0.44		0.02	(-	0.990	0.988	0.017	0.917
		2.36	to	2.16	to	0.01	to	2.24	to	0.29,		0.27,		(0.13	to	0.27	to				
		2.39)		2.14)		5.20)		2.44)		0.29)		0.26)		0.76)		0.30)					
	Family caregiver	0.64	(-	0.07	(-	1.80	(-	-0.91	(-	0.092	(-	0.01	(-	0.35		-0.17	(-	0.500	0.939	0.118	0.387
		1.63	to	1.98	to	0.96	to	3.42	to	0.20,		0.25,		(0.03	to	0.46	to				
		2.91)		2.11)		4.56)		1.61)		0.38)		0.27)		0.66)		0.11)					
Self-efficacy	Patient	2.99	(-	9.13		3.87	(-	2.15	(-	0.16	(-	0.47		0.18	(-	0.10	(-	0.420	0.006	0.338	0.554
		5.92	to	(1.18	to	5.83	to	6.56	to	0.14,		(0.21,		0.13	to	0.19	to				
		11.90)		17.08)		13.56)		10.86)		0.45)		0.74)		0.49)		0.38)					
	Family caregiver	6.64	(-	4.63	(-	5.22	(-	4.49	(-	0.34		0.24	(-	0.25	(-	0.22	(-	0.087	0.180	0.200	0.223
		2.65	to	3.65	to	4.55	to	4.35	to	(0.04,		0.03,		0.07	to	0.08	to				
		15.93)		12.91)		14.99)		13.33)		0.64)		0.50)		0.57)		0.51)					

Appendix 11: Mean scores at baseline, t1 and t2 for the primary outcomes (per-protocol)

		Mean score at baseline (T0) (95% CI)			Mean score at 12 weeks (T1) (95% CI)			Mean score at 24 weeks (T2) (95% CI)		
		<i>Control group</i>	<i>iFOCUS</i>	<i>FOCUS+</i>	<i>Control group</i>	<i>iFOCUS</i>	<i>FOCUS+</i>	<i>Control group</i>	<i>iFOCUS</i>	<i>FOCUS+</i>
Emotional functioning	Patient	48.36 (46.77 to 49.95)	48.86 (46.92 to 50.80)	48.75 (47.37 to 50.14)	49.50 (48.30 to 50.70)	49.52 (47.99 to 51.05)	49.49 (48.20 to 50.78)	49.08 (47.25 to 50.92)	51.68 (49.61 to 53.74)	49.19 (47.35 to 51.02)
	Family caregiver	47.62 (46.19 to 49.04)	46.45 (44.19 to 47.72)	47.29 (45.71 to 48.86)	46.64 (44.54 to 48.74)	47.28 (45.00 to 49.56)	46.70 (44.59 to 48.82)	46.84 (45.27 to 48.42)	48.64 (46.75 to 50.54)	45.94 (44.28 to 47.60)
Self-efficacy	Patient	121.35 (115.61 to 127.09)	126.71 (119.17 to 134.25)	125.81 (120.94 to 130.67)	118.01 (112.79 to 123.23)	121.00 (114.60 to 127.40)	127.14 (121.68 to 132.59)	120.63 (113.94 to 127.33)	124.50 (116.91 to 132.10)	122.78 (116.06 to 129.50)
	Family caregiver	121.29 (115.73 to 126.85)	112.97 (105.81 to 120.13)	115.61 (108.98 to 122.24)	112.91 (107.39 to 118.42)	119.55 (112.94 to 126.15)	117.54 (111.96 to 123.12)	113.071 (106.60 to 119.54)	118.29 (110.85 to 125.73)	117.56 (110.90 to 124.22)

Appendix 12: Overview of the instruments, underlying measured concepts and their 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 Function	For patients (10 items): - EORTC 10 emotional function items For caregivers (10 items): - EORTC 10 item emotional function scale	✓	✓	✓
Self-efficacy	The Lewis' Cancer self-efficacy scale from FOCUS - 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 <i>plus</i> two social function items + two items about overall health from EORTC C30 - Social well-being scale from FACT-G For caregivers (35 items): - The 35 item Caregiver Quality of Life Index-Cancer (CQOLC)	✓	✓	✓
Benefits of illness	Benefits of illness scale - For patients (5 items) - For caregivers (5 items)	✓	✓	✓
Coping	A shortened version of Brief Cope - For patients (20 items) - For caregivers (20 items)	✓	✓	✓
Dyad communication	The five items 'Active engagement scale' from the 'Ways of giving support questionnaire'. Three scales (10 items) from the 'Dyadic Coping Inventory': '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 and CSRI - 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: - 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 evaluated:				
Items about computer skills	Two FOCUS items about computer skills - For patients (2 items) - For caregivers (2 items)	✓		
Process evaluation	FOCUS items asking about experience and satisfaction with the intervention. - For patients (12 items) - For caregivers (12 items)		✓	
Process evaluation	Experiences with the intervention: - Interviews with patients and family caregivers - Interviews with nurses delivering the intervention Fidelity: FOCUS+ - Session characteristics (e.g. length, timing), random sample intervention checklists (see Appendix A2.4c), random sample audio-taped intervention sessions Fidelity: iFOCUS - Data from web-based program (e.g. number of sessions logged into, time taken to complete session) Routine data on recruitment (e.g. potential participants, initial engagement, eligible participants, enrolment)		✓ ✓ ✓	

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Appendix 13: Consolidated criteria for Reporting Qualitative Research (COREQ)

COREQ (COnsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
<i>Personal characteristics</i>			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	4
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	4
Occupation	3	What was their occupation at the time of the study?	4
Gender	4	Was the researcher male or female?	4
Experience and training	5	What experience or training did the researcher have?	4
<i>Relationship with participants</i>			
Relationship established	6	Was a relationship established prior to study commencement?	4
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	4
Interviewer characteristics	8	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	
Domain 2: Study design			
<i>Theoretical framework</i>			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	4
<i>Participant selection</i>			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	4
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	4
Sample size	12	How many participants were in the study?	5
Non-participation	13	How many people refused to participate or dropped out? Reasons?	5
<i>Setting</i>			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	4
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	4
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	5
<i>Data collection</i>			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	4
Repeat interviews	18	Were repeat interviews carried out? If yes, how many?	4
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	4
Field notes	20	Were field notes made during and/or after the interview or focus group?	4
Duration	21	What was the duration of the interviews or focus group?	5
Data saturation	22	Was data saturation discussed?	4
Transcripts returned	23	Were transcripts returned to participants for comment and/or	

Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			
<i>Data analysis</i>			
Number of data coders	24	How many data coders coded the data?	4
Description of the coding tree	25	Did authors provide a description of the coding tree?	
Derivation of themes	26	Were themes identified in advance or derived from the data?	4
Software	27	What software, if applicable, was used to manage the data?	4
Participant checking	28	Did participants provide feedback on the findings?	
<i>Reporting</i>			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	6
Data and findings consistent	30	Was there consistency between the data presented and the findings?	6
Clarity of major themes	31	Were major themes clearly presented in the findings?	6
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	6

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.

Appendix 14: original interview guide stakeholder interviews

Introduction of interview

- Thank you for taking the time for this interview. I am very grateful that you were able to make yourself available.
- This is a qualitative research project exploring the perspectives of experts and their experience on psychosocial and educational support for people with advanced cancer and their informal caregivers. We are interested in:
 - o In your opinion, what are psychoeducational forms of support?
 - o In your opinion, what are the goals of psychoeducational forms of support?
- The project is part of the DIAdIC study - an international randomised trial to evaluate the effectiveness of a nurse-delivered (FOCUS+) and a web-based (iFOCUS) psychoeducational intervention for people with advanced cancer and their informal caregivers, in which Ghent University and UZ Gent are collaborating.
- Both iFOCUS and FOCUS+ are psycho-educational interventions. FOCUS+ is a nurse-led face-to-face intervention and iFOCUS is a web-based intervention. Both interventions are based on the FOCUS program, which stands for Family involvement, Outlook, Coping effectiveness, Uncertainty reduction and Symptom management. FOCUS+ has 3 sessions spread over 12 weeks, iFOCUS has 4 sessions spread over 12 weeks. Both interventions are accessible at the place of preference of the participating dyads- most often at home.
- The aim of this study is to explore the context of psychoeducational support for people with advanced cancer and their informal caregivers in Belgium. In particular, we are interested in possible barriers or facilitators to implement these forms of support.
- Check whether signed informed consent is obtained
 - o YES: I received your information and consent leaflet well.

Or

- NO: I have sent you an information and consent leaflet. If you are happy with that, could you please type your name in the interviewee line and email it back to me?
- Do you have any general questions about the study before we start?
- I would like to record the interview. Is this OK? I will delete the video recording after the interview and keep only the audio recording, making a transcription of the interview for analysis purpose.

Definitions (if necessary)

Advanced cancer: The patients we aim for within this study no longer receive curative treatment, the emphasis is on palliative treatment such as pain control, management of quality of life; the treating physician would not be surprised if the person died within two years .

Psychoeducational interventions: psychological support designed to enhance people's ability to cope with the disease. Programmes can be offered face-to-face or online. Some examples: psychoeducational groups, cognitive-behavioural groups, support groups, one-to-one interactions with the nurse delivering the programme, web-based support.

Dyadic interventions: interventions addressed to a dyad, i.e. two people.

eHealth (programmes) (programmes aimed at) supporting or improving the health/wellbeing of patients/participants, using Internet and Computer Technology (ICT) such as laptops, tabletops, tablets, mobile phones or equivalents.

The interview

Prompts/additional questions throughout the interview

- Can you tell a little more about this experience?
- What led to these thoughts or feelings?
- What do you think is important about this aspect of support for patients and family caregivers?
- Do you think this would be a general experience/vision?

For each question on psychoeducational support:

- Reflection on possible difference between eHealth and face-to-face support programmes
- Who else might offer this programme?
- Why is this person/service suitable/not suitable to offer this?

Do you know of any other persons/services that could offer this?

Before we start the interview, we would like to collect some general descriptive information about you. This information will not be used to identify you, we will only collect some general demographic data.

Sociodemographic data

- How old are you?
- What is your gender?
- What is your professional background?
- What is your current role or position?

- Can you tell me something about your experience regarding oncology care delivery?

Knowledge of psychoeducational support

- What types of psychoeducational support for people with advanced cancer and/or their family caregivers are you familiar with?
- In your opinion, how do psychoeducational programmes function and what are its effects or purposes for people with advanced cancer and their family caregivers?
- In your opinion, what are potential strengths and weaknesses of these programmes?
- What are your views on the added value of this type of support for people with advanced cancer and/or their family caregivers?
- What recommendations do you have for the development of these forms of support?

Involvement in psychoeducational support

- What is the role of your organization and others regarding the provision of psychoeducational support for people with advanced cancer and/or their family caregivers?
- What recommendations would you make regarding implementing/embedding these support programmes in organisations or workings such as yours?
- What are the challenges and opportunities you experience within your work in providing this type of support?

Embedding of psychoeducational support

- Reflecting on the broader healthcare context of people with advanced cancer and their family caregivers, what do you think are the barriers and facilitators in offering these types of programmes?
- What challenges do you think there are in embedding these kinds of programmes in different care contexts?
- Are there any changes that would support the wider implementation/integration of this type of programme? If so, which ones?
- Does the current context regarding COVID-19/Coronavirus have specific implications for the need for, or provision of, psychosocial support to this group?

Other comments

- Do you have any other comments or additions?

Closing

- What did you think of the interview?
- Would you have liked to tell me anything else?

Before the start of the interview

The researcher/interviewer contacts the potential participant to introduce the study and to ask if they would be interested to participate. This first contact can be made through mail or phone. As part of the introduction, the researcher/interviewers give the following information;

- His/her name and function
- Explain the project (DIAdIC, iFOCUS and FOCUS+)
- The goal of the interview (to develop guidelines for program embedding and implementation)
- What they can expect from us (online interview, at the moment of their choice, will be recorded)
- Our contact information (phone nr., mail)

Furthermore they are referred to the DIAdIC website and are encouraged to watch the video there. If they agree to participate, the information letter and informed consent can be sent in following correspondence. Participants are asked to return the informed consent signed before the start of the interview. In this follow-up contact, the participant can once again be referred to the DIAdIC website.

Interview guide stakeholder interviews

Introduction of interview

- Thank you for taking the time for this interview. I am very grateful that you were able to make yourself available.
- This is a qualitative research project exploring the perspectives of experts and their experience on psychosocial and educational support for people with advanced cancer and their informal caregivers.
- The project is part of the DIAdIC study - an international randomised trial to evaluate the effectiveness of a nurse-delivered (FOCUS+) and a web-based (iFOCUS) psychoeducational intervention for people with advanced cancer and their informal caregivers, in which Ghent University and UZ Gent are collaborating.
- Both iFOCUS and FOCUS+ are psycho-educational interventions. FOCUS+ is a nurse-led face-to-face intervention and iFOCUS is a web-based intervention. Both interventions are based on the FOCUS program, which stands for Family involvement, Outlook, Coping effectiveness, Uncertainty reduction and Symptom management. FOCUS+ has 3 sessions spread over 12 weeks, iFOCUS has 4 sessions spread over 12 weeks. Both interventions are accessible at the place of preference of the participating dyads- most often at home.
- The aim of this study is to explore the context of psychoeducational support for people with advanced cancer and their informal caregivers in Belgium. In particular, we are interested in possible barriers or facilitators to implement these forms of support.

<i>Definitions (if necessary)</i>

Advanced cancer: The patients we aim for within this study no longer receive curative treatment, the emphasis is on palliative treatment such as pain control, management of quality of life; the treating physician would not be surprised if the person died within two years .

Psychoeducational interventions: psychological support designed to enhance people's ability to cope with the disease. Programmes can be offered face-to-face or online. Some examples: psychoeducational groups, cognitive-behavioural groups, support groups, one-to-one interactions with the nurse delivering the programme, web-based support.

iFOCUS is a psychoeducational WEBprogram for people with advanced cancer and their family caregiver. iFOCUS has 4 sessions spread over 3 months where dyads can go through the program together without further support or assistance.

FOCUS+ is a psychoeducational face-to-face program for people with advanced cancer and their informal caregiver. FOCUS+ has 3 sessions spread over 3 months where a nurse will organize the conversation with both of them.

Dyadic interventions: interventions addressed to a dyad, i.e. two people.

eHealth (programmes) (programmes aimed at) supporting or improving the health/wellbeing of patients/participants, using Internet and Computer Technology (ICT) such as laptops, tabletops, tablets, mobile phones or equivalents.

- Check whether signed informed consent is obtained
 - o YES: I received your information and consent leaflet well.
- Or
- o NO: I have sent you an information and consent leaflet. If you are happy with that, could you please type your name in the interviewee line and email it back to me?
- Do you have any general questions about the study before we start?
- I would like to record the interview. Is this OK? I will delete the video recording after the interview and keep only the audio recording, making a transcription of the interview for analysis purpose.

The interview

Prompts/additional questions throughout the interview

- Can you tell a little more about this experience?
- What led to these thoughts or feelings?
- What do you think is important about this aspect of support for patients and family caregivers?
- Do you think this would be a general experience/vision?

For each question on psychoeducational support:

- Reflection on possible difference between eHealth and face-to-face support programmes
- Who else might offer this programme?
- Why is this person/service suitable/not suitable to offer this?

Do you know of any other persons/services that could offer this?

Before we start the interview, we would like to collect some general descriptive information about you. This information will not be used to identify you, we will only collect some general demographic data.

Sociodemographic data

- How old are you?
- What is your gender?
- What is your educational and professional background?
- What is your current role or position?

Involvement in psychoeducational support

- What is the role of your organization regarding the provision of psychoeducational support such as iFOCUS and FOCUS+ for people with advanced cancer and/or their family caregivers?
- What are the challenges and opportunities you experience within your work in providing this type of support, similar to iFOCUS and FOCUS+?
 - o Specific challenges for dyadic programs?
 - o Specific opportunities for dyadic programs?
 - o Specific challenges for programs accessed at home?
 - o Specific opportunities for programs accessed at home?
 - o Specific challenges for programs which dyads have to manage themselves?
 - o Specific opportunities for programs which dyads have to manage themselves?
- What recommendations would you make regarding implementing/embedding these support programmes such as iFOCUS and FOCUS+ in organizations or workings such as yours?

Embedding of psychoeducational support

- What are facilitating factors when it comes to implementation embedding these programs such as iFOCUS and FOCUS+ into organizations, but on a broader perspective, beyond the limits of your organization on a broader scale?
- What are hindering factors when it comes to implementation embedding these programs such as iFOCUS and FOCUS+ into organizations, but on a broader perspective, beyond the limits of your organization on a broader scale?
- Which primary care organization or profiles would be fitting partners to introduce or provide access to potential participants to the FOCUS+ and iFOCUS program, and why? (If not clear, primary care can be accessed without referral)
 - o Who should we reach out to within this organization?
 - o Who should take on what role in providing iFOCUS and FOCUS+
 - o How can we facilitate embedding in this structure?
- Which secondary care organization or profiles would be fitting partners to introduce or provide access to potential participants to the FOCUS+ and iFOCUS program, and why? (If not clear, Secondary care is care which is accessible upon referral)
 - o Who should we reach out to within this organization?
 - o Who should take on what role in providing iFOCUS and FOCUS+
 - o How can we facilitate embedding in this structure?
- Which societal changes need to happen to increase the likelihood of embedding psychoeducational programs such as iFOCUS and FOCUS+ into different organizations?

- Does the current context regarding COVID-19/Coronavirus have specific implications for the need for, or provision of, psychosocial support to this group?

Other comments

- Closing, is there anything else which you think is of the utmost importance when it comes to embedding or implementing psychoeducational programs such as iFOCUS or FOCUS+

Closing

- What did you think of the interview?
- Would you have liked to tell me anything else?
- Can we reach out to you for a follow-up interview?
- Would you recommend anyone else in your network who we can reach out to for this interview?

Contributions of the PhD student – Vincent Van Goethem

Below we will provide a brief description of the contributions of the PhD student, Vincent Van Goethem, author of this dissertation, first author of chapters 1, 2, 4,6 and 7, and fifth author of chapters 3 and 5. Vincent Van Goethem began his PhD trajectory in May 2019. Consequently, he was not involved in drafting the DIAdIC trial protocol or any decisions made at that stage. During his PhD trajectory his primary responsibilities focused on the development and evaluation of the eHealth iFOCUS program, which was part of the DIAdIC trial where a face-to-face (FOCUS+) and eHealth (iFOCUS) program were compared to care as usual.

More specifically, Vincent Van Goethem was involved in the following activities during his PhD:

- Development of the iFOCUS program and overseeing user- and functional testing.
- Data collection as part of the DIAdIC trial.
- Data cleaning.
- Data analysis for chapters 1, 2, 4,6 and 7.
- Overseeing Belgian process evaluation, which is forthcoming.
- Scientific output (3 published articles, two submitted).
- Reporting.
- Engagement in dissemination activities.

CURRICULUM VITAE AND LIST OF PUBLICATIONS OF VINCENT VAN GOETHEM

Vincent Van Goethem, born May 17th, 1994 obtained his bachelor's degree in Occupational Therapy in 2016 at the Artevelde University College in Ghent. He graduated cum laude from Ghent University in 2018, earning a Master of Science degree in Health Education and Health Promotion. From 2018 to 2019, Vincent worked at the Belgian Cancer Registry as a junior researcher. In 2019, he joined the End-of-Life Care Research Group as a PhD student. Vincent worked for 5 years on research titled *“Developing and evaluating an eHealth application to develop palliative care capacity in people with advanced cancer and their family carer”*, which was part of the CAPACITY project. Additionally he worked on the DIAdIC (Dyadic psychoeducational Interventions for people with Advanced cancer and their Informal Caregivers) project, which was an international multicentre Randomized Clinical trial evaluating the effectiveness of two psychoeducational home-based programs.

EDUCATION

MSc in Health Education and Health Promotion
Ghent University, 2016-2018

Bachelor Occupational Therapy
Arteveldehogeschool, 2012-2016

Extra credits voor de vakken 'Management en accountancy', 'Creativiteit en innovatie' en 'Human Resources Management en leadership' binnen de opleiding KMO-Management

TSO, Gezondheids- en Welzijnswetenschappen
Technisch Instituut Sint-Carolus, Sint-Niklaas, 2007-2012

PROFESSIONAL CAREER

PhD Researcher: Development and evaluation of a psychoeducational eHealth program to support and empower patients with advanced cancer and their family caregivers.
Ghent University/VUB, 2019 – Heden

Researcher: Quality of life in patients with cancer and the influence of the socio-economic background on the incidence and prevalence of cancer.
Stichting kankerregister: 2018-2019

PUBLICATIONS:

Van Goethem V, Dierickx S, Deliens L, De Vleminck A, Lapeire L, Cohen J. *Size and characteristics of family caregiving for people with serious illness: A population-based survey*. Palliative and Supportive Care. 2022;21(4):634-643. doi:10.1017/S1478951522001079 [2022 Web of Science impact factor: 2,2; journal ranking Q2; ranking n° 45/117 in Health policy & Services]

Van Goethem, V., Dierickx, S., Matthys, O., Northouse, L., Lund, L., Jordan, C., ... & Cohen, J. (2023). *A self-management psychoeducational eHealth program to support and empower people with advanced cancer and their family caregivers: Development using the scrum methodology*. Internet Interventions, 33, 100659. <https://doi.org/10.1016/j.invent.2023.100659>. [2022 Web of Science impact factor: 2,3; journal ranking Q1; ranking n° 25/106 in Health Care Sciences & Services]

Matthys, O., De Vleminck, A., Dierickx, S., Deliens, L., **Van Goethem, V.**, Lapeire, L., ... & 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, 1-18. [2021 Web of Science impact factor: 2,113; journal ranking Q2; ranking n° 37/88 in Health policy & Services]

Van Goethem, V., Dierickx, S., Matthys, O., Deliens, L., Lapeire, L., Surmont, V., ... & Cohen, J. (2024) *Influence of digital competence on participation and retention of patients with advanced cancer and their family caregivers in a randomized controlled trial with an eHealth component: findings from the DIAdIC trial*. Telemedicine and e-Health [Accepted 01/03/2024, 2022 Web of Science Impact factor: 5.541; journal ranking Q1; ranking n° 16/115 in Health Informatics]

Matthys, O., Turola, E., Dierickx, S., Dombrecht, L., **Van Goethem, V.**, Deliens, L., ... & Cohen, J., (2024) *The DIAdIC advanced cancer psychoeducational intervention RCT: impact on emotional function and self-efficacy* [Ready for submission]

De Vleminck, A. & **Van Goethem, V.**, Dierickx, S., Matthys, O., Beernaert, K.,... & Cohen, J., (2024) *Developing and implementing a nurse-delivered and a web-based dyadic psychoeducational program for people with advanced cancer and their family caregivers: sharing experiences from a three-arm international randomized controlled trial (DIAdIC)*. [Submitted]

Van Goethem, V., Dierickx, S., Matthys, O., Beernaert, K., Guerin, S., Deliens, L., ... & Cohen, J., *Implementation of dyadic psychoeducational support programs at home for people with advanced cancer and their family caregivers: Stakeholder perspectives on barriers, facilitators, risks and opportunities*. [Submitted]

Rammant, E., Fonteyne, V., **Van Goethem, V.**, Verhaeghe, S., Raes, A., Van Hemelrijck, M., ... & Van Hecke, A. (2021, December). *Supportive Roles of the Health Care Team throughout the illness trajectory of bladder Cancer patients undergoing Radical Cystectomy: a qualitative study exploring the patients' perspectives*. In Seminars in oncology nursing (Vol. 37, No. 6, p. 151226). WB Saunders. [Web of Science Impact factor: 2.2; Journal Ranking Q2; Ranking n° 10/21 in Oncology (Nursing)]

