Improving the wellbeing of people with advanced cancer and their family carers: protocol for an effectiveness-implementation trial of a dyadic digital health intervention (FOCUSau)

Peter L Hudson, Jill Francis, Joachim Cohen, Suzanne Kapp, Richard De Abreu Lourenco, Lisa Beatty, Kathleen Gray, Michael Jefford, Ilona Juraskova, Laurel Northouse, Aline de Vleminck, Sungwon Chang, Patsy Yates, Sophy Athan, Shaira Baptista, Marlena Klaic, Jennifer Philip

Submitted to: JMIR Research Protocols
on: December 08, 2023

Table of Contents

Improving the wellbeing of people with advanced cancer and their family carers: protocol for an effectiveness-implementation trial of a dyadic digital health intervention (FOCUSau)

Peter L Hudson[1, 2]; Jill Francis[3, 4, 5, 6]; Joachim Cohen[1]; Suzanne Kapp[3]; Richard De Abreu Lourenco[7]; Lisa Beatty[8]; Kathleen Gray[9]; Michael Jefford[4, 10]; Ilona Juraskova[11]; Laurel Northouse[12]; Aline de Vleminck[1]; Sungwon Chang[13]; Patsy Yates[14]; Sophy Athan[15]; Shaira Baptista[3, 16]; Marlena Klaic[3]; Jennifer Philip[17]

[1]Vrije Universiteit Brussel Brussels BE
[2]Centre for Palliative Care, c/o St Vincent's Hospital and The University of Melbourne Melbourne AU
[3]Melbourne School of Health Sciences, The University of Melbourne Melbourne AU
[4]Sir Peter MacCallum Department of Oncology, The University of Melbourne Melbourne AU
[5]Centre for Implementation Research, Ottawa Hospital Research Ottawa CA
[6]Centre for Health Economics Research and Evaluation (CHERE), University of Technology Sydney Sydney AU
[7]College of Education, Psychology and Social Work, Flinders Institute for Mental Health and Wellbeing, Flinders University Adelaide AU
[8]Centre for Digital Transformation of Health, The University of Melbourne Melbourne AU
[9]Department of Health Services Research, Peter MacCallum Cancer Centre Melbourne AU
[10]School of Psychology, Faculty of Science, University of Sydney Sydney AU
[11]School of Nursing, University of Michigan Ann Arbor US
[12]Improving Palliative, Aged and Chronic Care through Clinical Research and Translation (IMPACCT), Faculty of Health, University of Technology Sydney Sydney AU
[13]Queensland University of Technology Queensland AU
[14]Cancer Consumer Advisory Committee, Victorian Comprehensive Cancer Centre Alliance Melbourne AU
[15]School of Public Health and Preventative Medicine, Monash University Melbourne AU
[16]The University of Melbourne, St. Vincent's Hospital and the Victorian Comprehensive Cancer Centre Melbourne AU

Corresponding Author:
Peter L Hudson
Centre for Palliative Care, c/o St Vincent's Hospital and The University of Melbourne
41 Victoria Parade, Fitzroy
Melbourne
AU

Abstract

Background: Advanced cancer significantly impacts patients' and family carers' quality of life. When patients and carers are supported concurrently as a dyad, the wellbeing of each person is optimised. FOCUS is a dyadic, psychoeducational intervention developed in the USA, shown to improve the wellbeing and Quality of Life (QoL) of patients with advanced cancer and their primary carers. Originally a nurse-delivered in-person intervention, FOCUS has been adapted into a self-administered web-based intervention for European delivery.

Objective: To: 1) adapt FOCUS to the Australian context (FOCUSau); 2) evaluate the effectiveness of FOCUSau in improving the emotional wellbeing and self-efficacy of patients with advanced cancer and their primary carer relative to a usual care control group, 3) compare health care utilisation between the intervention and control groups; and 4) assess the acceptability, feasibility and scalability of FOCUSau in order to inform future sustainable implementation of the intervention within the Australian health care system.

Methods: FOCUS will be adapted prior to trial commencement, using an iterative stakeholder feedback process to create FOCUSau. To examine the efficacy and cost-effectiveness of FOCUSau and assess the acceptability, feasibility and scalability we will use a pragmatic phase III hybrid effectiveness-implementation trial, with an integrated research design that includes a digital health evaluation. Participants will include patients with cancer who are over 18 years of age; able to access the internet and can identify a primary support person/carer who can be also approached for participation. Sample size: 173 dyads in each arm (i.e. 346 dyads in total). Patient-carer dyad data will be collected at three time points: baseline (T0) completed pre-

randomisation, first follow-up (T1) at 12 weeks post-baseline; second follow-up (T2) at 24 weeks post-baseline.

Results: Funded March 2022. Recruitment anticipated to commence by March 2024.

Conclusions: If shown to be effective, this intervention will improve the wellbeing of patients with advanced cancer and their family carer, regardless of their location or current level of health care support. Clinical Trial: ClinicalTrials.gov on the 13th of October 2023 (ID: NCT06082128)

(JMIR Preprints 08/12/2023:55252)
DOI: https://doi.org/10.2196/preprints.55252

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✓ **Please make my preprint PDF available to anyone at any time (recommended).**
Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.
Only make the preprint title and abstract visible.
No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**
Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v
Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

Original Manuscript

Improving the wellbeing of people with advanced cancer and their family carers: protocol for an effectiveness-implementation trial of a dyadic digital health intervention (FOCUSau)

Authors

Peter Hudson [A,B,*], *Jill Francis* [C,D,E,F], *Joachim Cohen* [B], *Suzanne Kapp* [C], *Richard De Abreu Lourenco* [G], *Lisa Beatty* [H], *Kathleen Gray* [I], *Michael Jefford* [D,E], *Ilona Juraskova* [J], *Laurel Northouse* [K], *Aline DeVleminck* [B], *Sungwon Chang* [L], *Patsy Yates* [M], *Sophy Athan* [N], *Shaira Baptista* [C,O], *Marlena Klaic* [C], *Jennifer Philip* [P].

[A] Centre for Palliative Care, c/o St Vincent's Hospital and The University of Melbourne, Australia.; [B] Vrije Universiteit Brussel, Belgium.; [C] Melbourne School of Health Sciences, The University of Melbourne, Australia.; [D] Department of Health Services Research, Peter MacCallum Cancer Centre, Melbourne, Australia.; [E] Sir Peter MacCallum Department of Oncology, The University of Melbourne, Australia.; [F] Centre for Implementation Research, Ottawa Hospital Research, Ontario, Canada.; [G] Centre for Health Economics Research and Evaluation (CHERE), University of Technology Sydney, Australia.; [H] College of Education, Psychology and Social Work, Flinders Institute for Mental Health and Wellbeing, Flinders University, Adelaide, South Australia.; [I] Centre for Digital Transformation of Health, The University of Melbourne, Australia.; [J] School of Psychology, Faculty of Science, University of Sydney, Australia.
[K] School of Nursing, University of Michigan, USA.; [L] Improving Palliative, Aged and Chronic Care through Clinical Research and Translation (IMPACCT), Faculty of Health, University of Technology Sydney, Australia.; [M] Queensland University of Technology, Australia.; [N] Cancer Consumer Advisory Committee, Victorian Comprehensive Cancer Centre Alliance, Melbourne, Australia.; [O] School of Public Health and Preventative Medicine, Monash University, Melbourne, Australia.; [P] The University of Melbourne, St. Vincent's Hospital and the Victorian Comprehensive Cancer Centre, Melbourne, Australia.

*Corresponding author. Email: phudson@unimelb.edu.au , Address: 41 Victoria Parade, Fitzroy VIC 3065.

Total word count: 5274

Clinical Trial Registration: ClinicalTrials.gov on the 13th of October 2023 (ID: NCT06082128)

Keywords: Advanced Cancer, Clinical Trial, Digital Health Intervention, Palliative Care, Health Economics, Implementation Science.

Abstract

Background: Advanced cancer significantly impacts patients' and family carers' quality of life. When patients and carers are supported concurrently as a dyad, the wellbeing of each person is optimised. FOCUS is a dyadic, psychoeducational intervention developed in the USA, shown to improve the wellbeing and Quality of Life (QoL) of patients with advanced cancer and their primary carers. Originally a nurse-delivered in-person intervention, FOCUS has been adapted into a self-administered web-based intervention for European delivery.

Objectives: To: 1) adapt FOCUS to the Australian context (FOCUSau); 2) evaluate the effectiveness of FOCUSau in improving the emotional wellbeing and self-efficacy of patients with advanced cancer and their primary carer relative to a usual care control group, 3) compare health care utilisation between the intervention and control groups; and 4) assess the acceptability, feasibility and scalability of FOCUSau in order to inform future sustainable implementation of the intervention within the Australian health care system.

Methods: FOCUS will be adapted prior to trial commencement, using an iterative stakeholder feedback process to create FOCUSau. To examine the efficacy and cost-effectiveness of FOCUSau and assess the acceptability, feasibility and scalability we will underake a Hybrid type 1 implementation study consisiting of a Phase 3 (cinical effectiveness) trial along with an observational implementation study. Participants will include patients with cancer who are over 18 years of age; able to access the internet and can identify a primary support person/carer who can be also approached for participation. Sample size: 173 dyads in each arm (i.e. 346 dyads in total). Patient-carer dyad data will be collected at three time points: baseline (T0) completed pre-randomisation, first follow-up (T1) (N=346) at 12 weeks post-baseline; second follow-up (T2) at 24 weeks post-baseline.

Results: Funded March 2022. Recruitment anticipated to commence by March 2024.

Conclusion: If shown to be effective, this intervention will improve the wellbeing of patients with advanced cancer and their family carer, regardless of their location or current level of health care support.

Clinical trial registration : ClinicalTrials.gov on the 13th of October 2023 (ID: NCT06082128)

Introduction

Advanced cancer is a 'family affair' significantly affecting the wellbeing of the person with cancer and their family [1].Family carers are at the core of patient care; they are typically unpaid lay people, comprising close family members or friends or others who provide a significant level of support (practical, social or emotional) to the person with cancer. Additionally, their contributions alleviate some of the burden on the Australian healthcare system, resulting in significant cost savings [2]. As a result, addressing the needs of both patients and their family carers is a priority in many countries, with established standards, policies, and guidelines [3-5].

Furthermore, The World Health Organization advocates that palliative care should be 'family centered', enhancing the Quality of Life (QoL) of the patient and their family carers [6], and includes supporting those still receiving curative treatment in addition to those receiving end of life (EoL) care [7]. Palliative care, when effectively delivered, can restore choice regarding options for care [8], improve patients' and carers' sense of control, self-efficacy, coping ability, communication about the illness, and reduce emotional distress [9]. Research has shown benefits of early access to palliative care for patients, their family carers and the health care system; there has been an increased and proactive approach to early integration of palliative care to improve QoL and symptom management of patients and family carers [7]. Hence intervening earlier in the disease trajectory to assist the family unit prepare for, and respond to, the implications of life-threatening illness constitutes best practice.

Despite policy, clinical and research evidence advocating a family approach to palliative care, systemic inadequacies such as inability of many family carers to access health professional support and fragmented, inconsistent, variable palliative care services, along with lack of preparation for death have impeded family centered care [10]. Patients may undergo potentially unecessary treatment, report high levels of pain, difficulty coping, poor physical and emotional health and their EoL wishes are not always upheld [10]. This translates to many carers reporting high emotional distress, unmet needs and difficulties with providing complex home-based care, especially during the advanced stages of illness and EoL [11]. Around 40% of carers are reported to experience psychological distress [12] which is typically under-recognised [13]. Furthermore; these impacts may be more pronounced in underserved groups.

The overwhelming majority of Australians would prefer to die at home [14], yet Australian acute hospitals provide EoL care to approximately 50% of people who die [15]. Comprehensive family support is a key factor determining whether the preference of home care and death can be realised [16]. Yet, effective systematically applied psychosocial support for family carers in the EoL context is still underdeveloped [16,17].

Patients and family carers experience illness together, with one person's ability to cope affecting the other's [18]. In a longitudinal study of dyads including people with advanced cancer and their carers, carer mental health at baseline significantly influenced patient mental health three months later [11], whilst in a study of dyads affected by brain cancer greater carer competence in the caregiver role predicted longer patient survival [19]. Dyadic interventions, targeting the patient and family carer together, are more likely to result in better outcomes for both parties than single target interventions, and may be more cost-effective [18,20,21]. Consequently, dyadic interventions focusing on the QoL of both the patient and carer from the point of advanced disease diagnosis are necessary to promote wellbeing and cost effective care.

Historically, much of the psychological and psychoeducational palliative care intervention research has been delivered in-person, with demonstrated improvements in patient QoL [22] and family carer wellbeing, sense of preparedness, reduction of unmet needs and more favourable bereavement outcomes [21,23-25]. While these in-person delivered interventions produce promising results they can be time and resource intensive. These resource requirements constitute a major barrier to longer term implementation and integration of these interventions into the health care system, particularly in the context of current shortages of staff and other resources.

Digital-health interventions offer an innovative modality for the delivery of health care services [26]. They provide considerable resource advantages to in-person interventions [27] such as improving, information-sharing, decision-making and communication [26,28,29]. Advantages for users also include lower cost of delivery, greater reach (including for rural and remote areas), and convenience, less travel time, reduced risk of infections due to reduced exposure associated with face-to-face consultations and recipients feeling more empowered [27,29]. A meta-analysis of internet therapy studies has provided strong support for the adoption of online psychological interventions [30] and the increasing use of digital health has ushered in a new era of patient-centred cancer care that moves beyond the traditional in-person care model [31].

Digital health within the context of palliative care should not be considered a replacement for, but complementary to, in-person care in this con (which has numerous benefits) [29]. Indications are that digital health communication in this context may result in patients and carers receiving more reliable information; it can be more feasibly applied; and at organisational and societal levels, digital health may contribute to more efficient and equitable use of resources [29]. Furthermore, disseminating dyadic interventions via the internet and other technologies may be more scalable from a health systems perspective [18]. Reduced labour costs, as well as lower ongoing program charges, suggest the longer-term cost-effectiveness of digital health interventions compares favourably with traditional in-person care [18]. However, compared to the rapid increase of digital health interventions in other areas of health care, there is limited application of digital health interventions within advanced cancer and palliative care settings. No rigorously tested interventions applied systematically in Australia have targeted the psychosocial wellbeing of the patient-carer dyad [26,29]. There is an urgent need, therefore, to develop evidence based, dyadic digital health approaches that are meaningful, accessible and sustainable for integration into the Australian health system.

FOCUS intervention background

The FOCUS intervention has been developed in accordance with guidelines for complex interventions [32-36]. Co-designed with consumers, patients and family carers, the intervention consists of five core components underpinning the FOCUS acronym: (1) supporting **F**amily involvement, (2) supporting **O**utlook and meaning, (3) increasing **C**oping effectiveness, (4) reducing **U**ncertainty, and (5) **S**ymptom management. The original in-

person FOCUS program was developed in the USA as a nurse-delivered in-person intervention, being multi-component and psychoeducational in its framework, and providing tailored informational and emotional support to patients with advanced cancer and their family carers [32]. The efficacy of this in-person FOCUS intervention was demonstrated in three randomised control trials and two pilot effectiveness studies conducted in the USA [32-35,37], with the patient-carer dyads reporting significantly improved QoL and wellbeing, less negative appraisal of illness and caregiving, reduced uncertainty and hopelessness, improved communication, and enhanced self-efficacy. To make the FOCUS (USA) intervention more accessible, the main component (family involvement) of this in-person intervention was then adapted into a tailored, digital/web-based format [38]. Significant intervention effects were found in a pre-post study on dyads' QoL, emotional distress, perceived benefits of illness/caregiving, and on carers' self-efficacy [38].

The strong empirical base and utility of the FOCUS (USA) intervention have been acknowledged by the European Union (EU) through successful grant funding awarded to test European-adapted versions of both programs (in-person (FOCUS+) and digital (iFOCUS) in a Phase III trial, currently being conducted across six countries (England, Ireland, Belgium, Denmark, Netherlands and Italy) [39,40,41].

For the present study; we aim to test the FOCUS EU digital version (iFOCUS) for the Australian setting ('FOCUSau'), given the need to reach regional and rural areas and address the cost-effectiveness and sustainability issues that arise for in-person interventions.

Research aim and hypotheses

We seek to determine the effectiveness and sustainability of a digital health intervention (iFOCUS) aimed at improving the wellbeing of patients with advanced cancer and their primary family carer. Our objectives are: 1) adapt iFOCUS to the Australian context to create FOCUSau; 2) examine the effectiveness of FOCUSau in improving the wellbeing (primary outcomes: emotional wellbeing and self-efficacy) of patients with advanced cancer and their primary family carer, compared to control group (usualcare); 3) compare the type and costs of health service use by participants in the intervention and control group; and 4) assess the acceptability, feasibility and scalability of FOCUSau in order to inform sustainable implementation of the intervention within the Australian health care system.

Our hypotheses are that compared to the control group, patent-carer dyads in the intervention group (who receive the intervention in additional to usual care) will, at 12 weeks follow up, report: a) higher levels of emotional wellbeing and self-efficacy (i.e., confidence in managing illness) (primary outcomes); b) higher QoL, less negative appraisal of illness/caregiving, better communication about the illness and improved coping ability (secondary outcomes). In addition, FOCUSau will be cost-effective compared with the control group in terms of the incremental cost (change in health care use) per additional participant with a meaningful

change in (1) emotional wellbeing and (2) self-efficacy.

Methods

The study addresses the objectives in three stages:

Stage one: Adaptation of iFOCUS to the Australian healthcare setting (objective 1)

The Adaptation of iFOCUS to create FOCUSau will involve appraisal of the intervention by consumer representatives and research team participants along with detailed feedback to inform modifications . The process will be underpinned by the ADAPT process [42] whereby we will also evaluate the quality, acceptability, appropriateness, comprehensibility, accessibility and feasibility of the intervention before and after adaptation. We have concurrently review compatibility of the intervention software with Australian digital health infrastructure and ensure alignment with Australian standards for digital accessibility, security, privacy and shareability of personal data, and capacity to interoperate with other systems.

Consumer representatives and research team participants (n =16) viewed the iFOCUS intervention and provided detailed feedback to inform the modifications. Participants also completed the Adapted Mobile Application Rating Scale [43] the Theoretical framework of Acceptability questionnaire [44] and commented on the quality, acceptability, appropriateness, comprehensibility, accessibility and feasibility of the intervention before and after adaptation. We collected data using RedCap (need to add the correct citation here) and analysed data using descriptive statistics, thematic analysis [45] and content analysis [46]. Data analysis led to suggestions for modifications to the intervention which were voted favourably by participants.

The full method and results of the adaptation study will be reported elsewhere.

Stage two: Pragmatic Phase III hybrid effectiveness-implementation trial of FOCUSau (objectives 2 & 3)

Design

Hybrid type 1 implementation study consisiting of a Phase 3 (cinical effectiveness) trial along with an observational impmentation study.[47] This integrated research design includes digital health evaluation [48] to account for the interaction between conventional health effects and human-computer engagement [49]. This includes: i) randomisation of participating dyads to the intervention versus standard care (control group), to examine FOCUSau effectiveness in relation to clinical outcomes and health service use, while simultaneously ii) exploring acceptability, feasibility, sustainability and scalability of the intervention – that are recognised in both implementation science methods [47] and digital health evaluation methods [50]. Hybrid designs have a dual focus: a priori assessment of clinical effectiveness and implementation [47]. These pragmatic designs offer

novel ways of testing intervention effectiveness and potential uptake and are recommended for multisite psychosocial related interventions in cancer care [51].

Participants

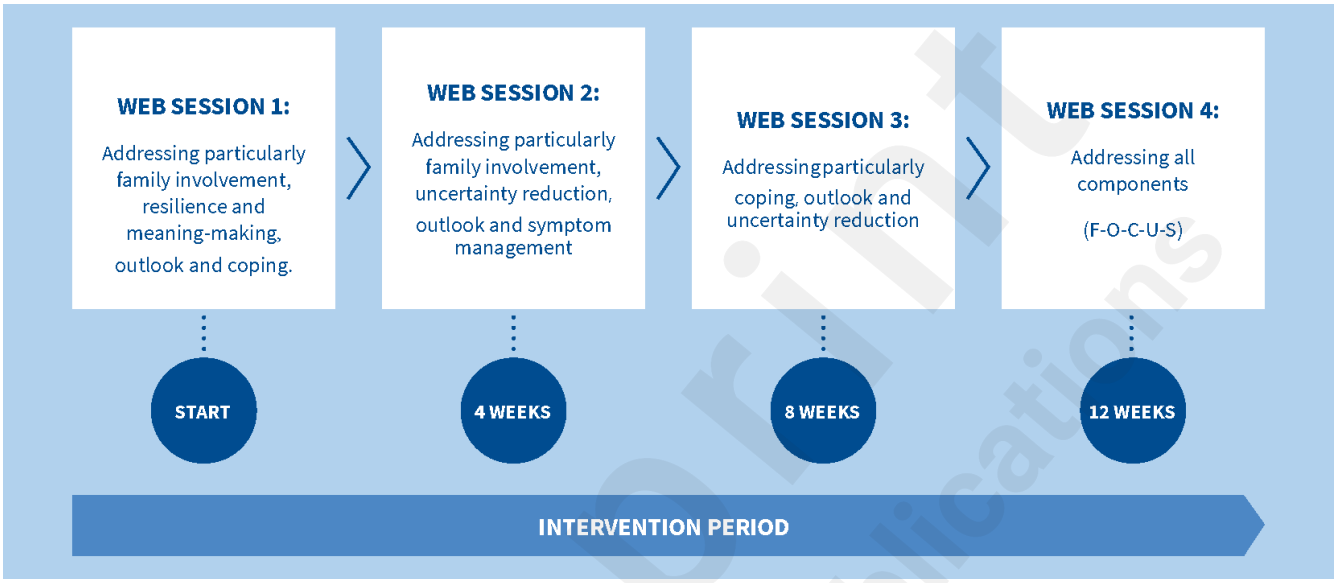
Patient inclusion criteria: Diagnosis of advanced cancer; over 18 years of age; able to comprehend written or spoken English; no visual, hearing, and/or cognitive impairment that would preclude participation; patient can commit to research participation requirements (including data collection and completion of the FOCUSau intervention if randomised to that group); able to access the internet (on their own desktop computer, laptop computer or tablet device); and able to identify a primary support person/carer, who is an unpaid individual (not necessarily a partner or family member) who is providing them with physical, social or emotional support. Patient exclusion criteria: involvement in an advanced cancer non-drug trial that focuses on improving QoL. Family carer inclusion criteria: identified by the patient as their primary support person who is related to them biologically, legally or emotionally, is willing to accept this support role; aged over 18 years; no visual, hearing, and/or cognitive impairment that would preclude participation; commits to research participation requirements; and is able to access the internet. Dyad inclusion criteria: capacity to effectively utilise the internet (as determined through a short practical online exercise as part of the screening and consent process).

The FOCUSau intervention

Aim and core features: The overall aim is to enhance dyads' emotional wellbeing and self-efficacy; addressed by five core components of the intervention [32] (as outlined above). The transactional model of stress and coping underpins the intervention [52]. *Delivery mode, dose and timeline:* self-administered, completed autonomously via the internet by the patient-carer dyads. It encompasses four prescribed consecutive sessions (with three weeks between each session) over a period of 12 weeks that collectively cover the five core components; the core content of which is outlined in Figure 1. The sessions are completed simultaneously by the patient and family carer, together at a computer. At the beginning of each session, a computer prompt (wizard) explains how dyads can navigate through the sessions. Access to the four sessions is provided via an automated link sent by email. The content of the sessions is written at a lower secondary education reading level, using principles of plain language. Audio instead of text provision of material is also available to allow for participation by those with visual impairment. Written content is complemented by images and videos of patients and carers reflecting on their advanced cancer experience which is linked to five core components. *Additional resources:* Dyads are provided with an online personal workbook containing information tailored to their responses to questions completed during the internet sessions. Any information sheets that the dyad indicated as 'of interest to them' during the internet sessions are included as a hyperlink in their personal workbook which also contains evidence-based local advanced cancer related resources. Assistance via a helpdesk (via email or telephone) is available to resolve any technical difficulties with accessing the online

materials. *Tailoring of the intervention:* Tailoring enhances the intervention's efficacy by providing dyads with information personally relevant to them. Three types of tailoring strategies are used: personalisation, tailored feedback, and content matching [53]. Participants receive tailored individual and dyadic messages according to their own demographic characteristics (age, sex, dyadic relationship) provided at study enrolment and their responses to questions within the sessions.

Figure 1. Intervention overview



The control – usual care

Participants in the control group will receive usual care. Usual care advanced cancer care is known to be heterogeneous. Nonetheless, we will collect relevant health services usage data (see below) to describe and compare the control and intervention arms.

Setting and recruitment procedures

The patient-carer dyads will be recruited via two methods: (1) referral from hospitals or (2) self-referral. For method one, approximately six hospitals and/or cancer centres (metropolitan and regional) across several states of Australia will be selected. The specific selection of institutions will be undertaken by the Cancer Symptoms Trials group (CST, a national cooperative trials group see https://www.uts.edu.au/research/impacct/cancer-symptom-trials/cst-clinical-trials) as the trial coordinating centre. The CST will undertake a feasibility assessment process to ensure institutions are selected on their ability to demonstrate they have the internal resources and patient population to refer sufficient dyads to achieve the site-specific sample size and broad coverage of services across Australia. As part of the CST site selection process, participating institutions will identify multidisciplinary staff in relevant departments to undertake an initial eligibility screen. The study will be verbally explained to eligible patients who receive a brief written project summary. With their permission, the contact details of patients interested in the study will be submitted to the project website by the relevant

referring clinician. Thereafter the patient will be contacted by a research officer who will undertake the screening and consenting process incorporating obtaining permission to contact the patient's primary family carer to seek their interest in participating, then scheduling a video meeting with the dyad which will also serve as a further check of their capacity to engage in an internet intervention. If all inclusion criteria are met, electronic consent via standard ethical requirements will be undertaken.

For the self-referral recruitment method, patients who have been made aware of the project (but have not been officially screened by a clinician) may self-refer via a form on the project website. These patients will be made aware via consumer/carer/cancer advocacy groups, or social media advertisement. A research officer will then review the self-referral form and liaise directly with the patient to advise if they meet the criteria and if so recruiting and consent procedures as per method one will be undertaken. There will be a second videoconference arranged (after consent and subsequent randomisation) to explain to the dyad which group they have been allocated to and brief orientation to the FOCUSau platform and the associated data collection methods.

Allocation and Blinding

Following informed consent and completion of baseline measures, block randomisation will occur via an embedded randomiser within the FOCUSau platform to create the randomisation table based on blocks of multiplicators of 2, blocks of 4, 6, 8. The block randomisation method is designed to randomise subjects into groups to ensure a balance in sample size across groups over time. A research officer will initiate the randomisation process which will involve logging into the FOCUSau platform, entering relevant participant details and then block randomisation will occur. Due to the nature of the intervention the patient-carer dyads cannot be blinded to allocation. Data collection will occur electronically and the research team will remain blind to which trial arm the dyads were randomised until the end of the final data-collection point. The first ten consented dyads who are allocated to the intervention group will additionally be invited to participate in the final step of the aforementioned intervention adaptation process and be provided with a specific (additional) Participant Information Sheet and Consent Form.

Data collection: primary and secondary psychosocial outcomes:

Patient-carer dyad data will be collected at three time points: baseline (T0) completed pre-randomisation, first follow-up (T1) at 12 weeks post-baseline; second follow-up (T2) at 24 weeks post-baseline. All data will be completed by the dyads (regardless of allocation) using the FOCUSau software platform; whereby they will complete a suite of online questionnaires. The platform enables the application of data validation rules to ensure that required data is entered or that an annotation is provided to explain any missing data. The FOCUSau platform automatically generates a unique ID number used by the dyad to log into the platform. Data collection will be completed separately by the patient and carer (regardless of allocation). The data

collection points, outcomes and measures have been selected in accordance with those used in the aforementioned EU trial to enhance international comparison and potential generalisability [39].

The list of variables and associated measures to be completed by the dyad are summarised in Table 1 and are as follows, *for the primary outcomes*: emotional wellbeing (10 items describing emotional functioning from The European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 [54,55] and self- efficacy (The Lewis´ Cancer self-efficacy scale [56]); *for the secondary outcomes*: QoL of patients (EORTC QLQ-palliative care [57], two social functioning items (#26, 27) + one item about overall health (#29) from EORTC QLQ-C30, Social well-being scale from FACT-G) and family carers (The Caregiver Quality of Life Index–Cancer [58]), appraisal of illness (Benefits of illness scale [59]), coping (Brief cope [60]), and dyad communication (Ways of giving support questionnaire [61] + 1- items from the Dyadic Coping Inventory).

In addition, we will administer a sociodemographic questionnaire at baseline (T0) and Modified version of Eastern Cooperative Oncology Group (ECOG) Performance Status Assessment [62] (response option 5 “death” removed as not relevant for this study).

Data collection: Health services utilisation

The impact on health care costs of FOCUSau will be determined by analysing patterns and costs of healthcare utilisation, including the costs of administering the intervention. Information will be collected on the time required to administer FOCUSau (per patient and overall). The impact of FOCUSau and usual care on health care services’ utilisation will be assessed by consenting participants for access to their Medicare (Australian Government health services) data (to obtain information on the use of outpatient medical and pharmaceutical services) and using the Client Services Receipt Inventory (CSRI) [63]; modified to reduce overlap with Medicare data. The CSRI will also allow us to explore the use of hospital versus in-patient palliative EoL care, and the use of informal care or services provided outside of the health care system (to be completed by carers).

Data collection: Implementability

Table 1 also outlines data to be collected to measure factors related to implementability of the intervention. This will include piloting and administering a new acceptability questionnaire [64]. Interview topic guides (one for patients; a parallel guide for carers) will be informed by the Theoretical Domains Framework (TDF) of behaviour change [65].

Table 1: Trial data collection measures

Objective	**Outcome/variable**	**Instrument**	**Timing**		
			T_0: Before randomization	T_1:T_0 + 12 wks	T_2: T_0 + 24 wks

Outcome measures used for the primary outcomes					
1. Psychosocial Effectiveness	Emotional wellbeing	For **patients** EORTC QLQ-C30 emotional function items (10 items) For **carers** EORTC QLQ-C30 item emotional function scale (10 items)	✓	✓	✓
	Self-efficacy	For **patients** and **carers** The Lewis´ Cancer self-efficacy scale (17 items)	✓	✓	✓
Outcome measures used for the secondary outcomes					
	Quality of life	For **patients** EORTC QLQ-C15-PAL (23 items) *plus* two social function items + two items about overall health from EORTC QLQ- C30 Social well-being scale from the FACT-G (6 items) For **carers** The Caregiver Quality of Life Index-Cancer (CQOLC) (35 items)	✓ ✓	✓ ✓	✓ ✓
	Appraisal of illness	For **patients** and **carers** Benefits of illness scale (5 items)	✓	✓	✓
	Coping	For **patients** and **carers** A shortened version of Brief Cope (20 items)	✓	✓	✓
	Communication	For **patients** and **caregivers** The ’Active engagement scale’ (5 items) 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’	✓	✓	✓
	Level of functioning	For **patients** (4 items) Modified version of Eastern Cooperative Oncology Group (ECOG) Performance Status Assessment (item 5 “death” removed)	✓	✓	✓
2. Cost effectiveness	Health economic measures	For patients (23 items) 17 and for carers (14 items) Client Services Receipt Inventory (CSRI) including use of hospital versus in-patient palliative EoL care and the use of informal care or services provided outside of the health care system (to be completed by carers) and modified to reduce overlap with Medicare data .	✓	✓	✓
	Primary outcome expressed as cost per participant with a	For patients and carers EuroQol EQ5D5L (5 item)	✓	✓	✓

	meaningful change in wellbeing/self-efficacy for the intervention compared with control Secondary outcomes expressed as cost per quality adjusted life year for the intervention compared with control	For patients and carers Services Australia data: Use of outpatient medical and pharmaceutical services	✓	✓	✓
3. Implementability	Acceptability	For patients and for carers (intervention group) Theoretical Framework of Acceptability (TFA) survey (9 items) – perceptions based on info provided and actual after completion	✓	✓	✓
		For patients and for carers (control group)1 Theoretical Framework of Acceptability (TFA) survey (9 items) perceptions based on info provided only	✓		
		For patients and for carers (intervention group only) Qualitative (interviews) to explore acceptability and barriers and enablers to uptake of FOCUSau by dyads, the latter informed by the Theoretical Domains Framework of behaviour		✓	
	Satisfaction with intervention	For patients and for carers (intervention group) FOCUS items asking about experience and satisfaction with the intervention. (intervention group only) For patients (12 items) For caregivers (12 items)		✓	✓
	Uptake	Study log: Recruitment data including reasons for accepting or declining participation, sociodemographic profile of invited dyads, capacity to reach vulnerable populations (with lower socioeconomic status, cultural minorities, and from rural/remote locations)	✓	✓	✓
	Intervention fidelity	Study log: Communication between trial managers and participants, whether for technical problem-solving or for other reasons. Aspects of adherence (intervention as received) are built into the FOCUSau intervention. Completion rates of individual FOCUSau sessions.	✓	✓	✓
	Technical	Interviews /focus groups with health IT experts:	✓	✓	✓

	feasibility	Data and infrastructure standards adherence System architecture for interoperability/ integration with electronic patient records Extensibility and scalability potential			
4.Other characteristics	Socio demographics characteristics	For patients (14 items) and for carers (15 items) Sex, age, relationship status, living situation, children, educational level, employment status, income, financial difficulties, medical insurance, ethnicity, dyad's relationship	✓		
	Patient level of functioning	For patients (1 item) Modified version of Eastern Cooperative Oncology Group (ECOG) Performance Status Assessment (response option 5 "death" removed as not relevant)	✓	✓	✓

Sample size

A pre-determined strict fixed sequence (FS) procedure defines prospectively hierarchical ordering of the primary endpoints; emotional wellbeing (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 wellbeing) compared to the other methods, as it does not save any portion of alpha for testing later hypothesis. The reference mean value from EORTC for all cancer patients, stage III-IV is 71.5 (SD: 23.8). To maintain rigorous control over Type I errors due to multiple comparisons, the alpha level is set at 0.025 instead of the more common 0.05. This adjustment accounts for the multiple comparisons required in the study, including comparisons between a control group and two participant groups (patients and carers). We set statistical power at 0.80. The expected difference between the control group and the intervention arm in the primary outcomes is 0.375 SD at T1 (12 weeks). With these parameters n=173 dyads are needed in each arm (i.e. 346 dyads in total). Anticipating a maximum 80% retention rate at T1 (USA FOCUS retention was 86% [66]) we will require approximately 433 dyads to be recruited. An enrolment rate of 55% of those eligible was achieved in prior digital health FOCUS study from 2014 [66], however we anticipate this will be higher for FOCUSaus (estimating 70%) given the internet is much more widely available now and our digital recruitment approach; meaning that we will need to identify approximately 618 dyads who meet eligibility criteria. Evidence also suggests that recruitment rates can increase when a digital health intervention is offered [67]. To meet these targets the CTS has calculated that approximately six referral sites will be required complemented by our aforementioned self-referral strategy.

Data analysis

The effectiveness of FOCUSau will be compared with the standard care (control group) for each participant population (patients/carers). Our hypotheses will be tested using a mixed model (per participant population)

with the T1 measurement values for emotional wellbeing and self-efficacy as primary outcomes using significance level of alpha=0.025. These mixed models will be implemented using IBM SPSS for Windows Version 27.0 and R with recruitment centre treated as a random effect and randomization group as predictor variables. 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 wellbeing). Additionally, we will incorporate other factors identified in the literature as potentially predictive by including them as covariates in the mixed models. We will perform analyses on both 'intention-to-treat' and per-protocol principles. To interpret the magnitude of the effects for the different outcomes, we will estimate effect sizes (Cohen's d). Our analysis will encompass all primary and secondary outcomes. Primary endpoints, including emotional well-being and self-efficacy measured at T1, will be analysed first. Following that, secondary endpoints, comprising outcomes measured at T1 that are not primary endpoints, as well as all outcomes measured at T2 (occurring 24 weeks from T0), will be assessed. This approach allows for a comprehensive evaluation, including the examination of longer-term effects.

The robustness and validity of the results will be explored using sensitivity analyses by varying the parameter inputs (including sensitivity to the use of values for missing observations). The analysis will be conducted for the within trial period; the potential to extrapolate results over the longer-term will be assessed based on the proportion of patients alive at the end of follow-up.

For the cost-effectiveness analysis, costs will be reported as the mean costs of care per dyad in each arm of the study. Costs applied to health care service use will be as per Australian standard fees (e.g., via the Medicare Benefits Schedule). If a difference in outcomes is observed, as hypothesised, the incremental cost effectiveness of FOCUSau compared with control will be estimated in terms of the: (1) cost per additional patient with a meaningful improvement in emotional wellbeing (as assessed using the EORTC QLQ-C30 emotional wellbeing scale); and separately, (2) cost per additional carer with a meaningful change in self-efficacy (as assessed using the The Lewis´ Cancer self-efficacy scale). The base case analysis of cost-effectiveness will be conducted from a health care system perspective. Subsequent sensitivity analyses will modify the assessment of costs to adopt a societal perspective to capture the impact of informal care costs, as well as testing the robustness of the analysis results to variations in other parameter inputs.

Missing data for costs and outcomes will be described and summarised. Where missing data can be regarded as missing at random, likelihood (interpolation) methods will be used for analysis of those data as appropriate.

Stage Three - acceptability, feasibility and scalability of FOCUSau (Objective 4)

Our approach is underpinned by a conceptual framework which highlights the link between acceptability,

fidelity and feasibility, and potential implementability [68]. An investigation of fidelity will also inform internal validity and thus our interpretation of the effectiveness findings. If prospective acceptability, uptake and engagement with the intervention are moderate (based on conventional cut-off scores of 50%) [69, 70], then FOCUSau is feasible to deliver in other settings; if participants receive and comprehend FOCUSau as designed (i.e., fidelity is high), then the effectiveness findings will represent a valid test of the intervention; if participant retention and retrospective acceptability are high, then FOCUSau is likely to be sustainable; and if FOCUSau is cost-effective and additional workforce requirements are minimal, then the intervention is likely to be scalable. *Acceptability* is "the extent to which people receiving FOCUSau consider it to be appropriate, based on anticipated (prospective) or experienced (retrospective) cognitive and emotional responses to the intervention" [71]. Informed by a new and influential theoretical framework of acceptability [71], we will pilot test a questionnaire [64] to be administered at baseline and follow-up (T0 and T2). As acceptability is ideally assessed both quantitatively and qualitatively [36], a diverse subsample of participants (~ 30 dyads) will be recruited from the intervention group and be interviewed via video conference immediately following completion of FOCUSau (T1), to gain a greater insight into intervention acceptability, including potential for further enhancements. Uptake: We will document the recruitment process, including reasons for accepting or declining participation and examine the sociodemographic profile of dyads invited to participate in the trial, capturing our capacity to reach relevant populations (with lower socioeconomic status, cultural minorities, and from rural/remote locations). We will also use the aforementioned T1 interviews to explore barriers and enablers to uptake by dyads. Interview topic guides (one for patients; a parallel guide for carers) will be informed by the Theoretical Domains Framework (TDF) of behaviour change [65]. Intervention fidelity encompasses whether the intervention is delivered and received as planned [72]. We will document communication between trial managers and participants, whether for technical problem-solving or for other reasons, to assess whether components have been added to FOCUSau as designed. Aspects of adherence (intervention as received) are built into the FOCUSau internet-module and include a readily accessible 'help' function. Dyads who experience problems with onboarding for the FOCUSau sessions will receive help from the trial manager via phone; they will confirm their presence and indicate whether they are utilising the computer or phone; dyads who exit an FOCUSau session before completion will be sent a reminder email or text message. Completion rates of individual FOCUSau sessions will be monitored.

The audiotaped semi-structured interviews with dyads to assess FOCUSau acceptability will be transcribed verbatim and thematically analysed using the Framework method [73]. To ensure methodological rigour, the analysis will follow: i) a step-by-step guide outlined by Gale et al. [74] and ii) criteria for trustworthiness [75]. Deductive analysis will be informed by the theoretical framework of acceptability (component constructs: affective attitude, burden, ethicality, intervention coherence, opportunity costs, perceived effectiveness, self-efficacy) ascertaining whether particular elements of FOCUSau were experienced as positive or negative and will include themes from previous intervention evaluations. Coding of established themes and subthemes will

be computer-assisted using NVivo software. Statistical descriptions of the quantitative data from the intervention checklist and routine monitoring will be used to describe fidelity, utilising conventional cut-off points for acceptable intervention adherence.

For technical aspects of implementability we will consider key factors in scalability, that is "the ability of a health intervention shown to be efficacious on a small scale or under controlled conditions, to be expanded under real world conditions to reach a greater proportion of the eligible population, while retaining effectiveness" [76]. This study will follow the previous stages, and will be the subject of additional human research ethics approval. It will use health IT expert consensus methods, to determine the technical feasibility of implementing and operating the FOCUSau program as an ongoing service at each site that is participating in the clinical trial, as well as at other potential hosting sites for the program that are identified during the clinical trial. The assessment of this aspect of implementability [68] will entail either semi-structured interviews or focus groups with health IT stakeholders who may include: trial managers, software proprietors, digital health specialists in health service management and governance roles, and experts in deployment of software in routine clinical care. The interview / focus group schedule will use two probes: 1) a technical specification of the software as it has been adapted for use in the trial, based on work done by the proprietor with the research computing services group; 2) a summary of the intervention's clinical and socio-economic value proposition, based on preliminary findings of project studies up to this point. The interview / focus group schedule will collect and thematically analyse data, based on stakeholders' knowledge of current local, national and international best practice approaches to digital health implementation planning [77,78], including the Australian Digital Health Agency technical standards and specifications. (https://developer.digitalhealth.gov.au/initiatives/interoperability-and-digital-health-standards/).

Data management, monitoring and risk management

CST has a suite of Standard Operating Procedures that will be used in support for the management of study data including electronic data handling, case report forms, archiving of research materials and record destruction. Referral and recruiting reviews will be undertaken via monthly trials management video calls and ongoing oversight by the lead investigator. Monitoring will be conducted remotely, including the following: data quality, protocol deviations/violations, adverse event reporting, participant consent and eligibility. We will also monitor recruitment status and target achievement; review any adverse events or serious adverse events (suspected or actual); and review of participant withdrawals and mortality.

Ethical considerations

This research protocol was approved by the Human Research Ethics Committee of St Vincents Hospital Melbourne (ERM ID Number: 84479 SAGE Project ID Number: 2022/PID06577 SVHM Local Ref ID: 262/22). FOCUSau is non-invasive with no known risk of protocol-related injury. As a psychoeducational

intervention focused on the provision of information we anticipate the risk of any adverse events to be low. Nevertheless, information is available in FOCUSau about where participants may access additional medical and/or psychosocial support. Our project team is experienced in leading complex psychosocial interventions involving recruitment of patients with advanced disease and their family carers. If necessary, any adverse events will be reported to the CTS Ethical and Data Monitoring committee. Due to the nature of the study population, some deaths due to advance disease progress are expected. A protocol for liaising with the carer of the deceased has been developed for these situations. This includes advising carers allocated to the intervention arm that they will not be required to continue with the study.

Results

Funded March 2022. Recruitment anticipated to commence by March 2024.

Discussion

Anticipated principal findings

Australia's capacity to meet its national palliative care standards have been challenged [10]. This project will examine the clinical and health economic impacts of FOCUSau and gauge its potential for sustainability . If shown to be effective, this intervention will improve the emotional wellbeing of patients with advanced cancer and their family carer, regardless of their location or current level of health care support. Empirical findings as described above will inform an implementation and sustainability strategy. The strategy will describe a pathway and recommended steps for longer-term systematic delivery of FOCUSau across Australia, linking where possible with existing nationally supported cancer and palliative care programs.

Comparison with prior research

Historically, much of the psychological and psychoeducational palliative care intervention research has been delivered in-person focusing on either the patient or their family carer(s) [21,23-25]. However, trials of dyadic interventions, which focus on the patient and family carer together, have shown favourable outcomes for both parties [18,20,21]. Furthermore, digital-health interventions offer an innovative modality and may provide considerable resource advantages to in-person interventions [26, 27]. Hence, our trial will advance knowledge in these areas.

Limitations

We acknowledge some of the limitations associated with our control arm; including that control participants will not have access to FOCUSau after the final data collection point. Unfortunately we do not have funding and resources required to support this. We will however report on the number of participants who withdraw because they have not been allocated to the intervention arm.

Conclusion

Advanced cancer is a 'family affair' significantly affecting the wellbeing of the person with cancer and their family [1]. We seek to determine the effectiveness and sustainability of a digital health intervention (FOCUSau) aimed at improving the wellbeing of patients with advanced cancer and their primary family carer.

Data availability: The data that support this study will be shared upon reasonable request to the corresponding author.

Conflicts of interest: The authors declare that they have no conflicts of interest.

Declaration of funding: This research is supported by funding from the Australian Government National Health and Medical Research Council (NHMRC).

Acknowledgements: We thank Alfreda Soetopo for her assistance in the manuscript submission preparation process.

Abbreviations

EoL: End of Life

QoL: Quality of Life

CST: Cancer Symptoms Trials group

CSRI: Client Services Receipt Inventory

CQOLC: Caregiver Quality of Life Index-Cancer

TDF: Theoretical Domains Framework

TFA: Theoretical Framework of Acceptability

EORTC: The European Organization for Research and Treatment of Cancer

ECOG: Eastern Cooperative Oncology Group

FS: Fixed Sequence

SD: Standard Deviation

References

1. Wang H, Yue H, Wang Z, Lu M, Feng D. The relationship between patient-family caregiver congruence/incongruence in acceptance of illness and family caregivers' anticipatory grief. Psychooncology; 2023 May;32(5):751-759. doi: 10.1002/pon.6121. PMID: 36890764.

2. Deloitte Access Economics. The economic value of informal care in Australia in 2015, Report for Carers Australia. Canberra: Deloitte Access Economics Pty Ltd; 2015.
3. Palliative Care Australia. National Palliative Care Standards. 5th edition. Canberra: PCA; 2018.
4. Australian Government Department of Health. National Palliative Care Strategy. Canberra; 2018.
5. Hudson P, Remedios C, Zordan R, et al. Guidelines for the psychosocial and bereavement support of family caregivers of palliative care patients. J Palliat Med; 2012 Jun;15(6):696-702. doi: 10.1089/jpm.2011.0466. PMID: 22385026.
6. World Health Organisation. National cancer control programmes: Policies and managerial guidelines. 2nd edition. Geneva: WHO; 2002.
7. Hudson P, Collins A, Boughey M, Philip J. Reframing palliative care to improve the quality of life of people diagnosed with a serious illness. Med J Aust; 2021 Nov 15;215(10):443-446. doi: 10.5694/mja2.51307. PMID: 34676567.
8. Collins A, McLachlan SA, Hill M, et al. A randomised phase II trial testing the acceptability and feasibility of a narrative approach to public health communication to increase community engagement with palliative care. Palliat Med; 2020 Sep;34(8):1108-1117. doi: 10.1177/0269216320932766. PMID: 32552310.
9. Berry LL, Castellani R, Stuart B. The Branding of Palliative Care. J Oncol Pract; 2016 Jan;12(1):48-50. doi: 10.1200/JOP.2015.008656. PMID: 26733621.
10. Swerissen H, Duckett SJ. What can we do to help Australians die the way they want to? Med J Aust; 2015 Jan 19;202(1):10-1. doi: 10.5694/mja14.01580. PMID: 25588426.
11. Kershaw T, Ellis KR, Yoon H, et al. The Interdependence of Advanced Cancer Patients' and Their Family Caregivers' Mental Health, Physical Health, and Self-Efficacy over Time. Ann Behav Med; 2015 Dec;49(6):901-11. doi: 10.1007/s12160-015-9743-y. PMID: 26489843.
12. Grande G, Rowland C, van den Berg B, Hanratty B. Psychological morbidity and general health among family caregivers during end-of-life cancer care: A retrospective census survey. Palliat Med; 2018 Dec;32(10):1605-1614. doi: 10.1177/0269216318793286. PMID: 30130458.
13. Ziegler L, Hill K, Neilly L, Bennett MI, Higginson IJ, Murray SA, Stark D; COMPASS Collaborative. Identifying psychological distress at key stages of the cancer illness trajectory: a systematic review of validated self-report measures. J Pain Symptom Manage; 2011 Mar;41(3):619-36. doi: 10.1016/j.jpainsymman.2010.06.024. PMID: 21310585.
14. Foreman LM, Hunt RW, Luke CG, Roder DM. Factors predictive of preferred place of death in the general population of South Australia. Palliat Med; 2006 Jun;20(4):447-53. doi: 10.1191/0269216306pm1149oa. PMID: 16875116.
15. Australian Institute of Health and Welfare. Palliative care services in Australia. Canberra: AIHW; 2020.
16. Candy B, Jones L, Drake R, et al. Interventions for supporting informal caregivers of patients in the

terminal phase of a disease. Cochrane Database Syst Rev; 2011 Jun 15;(6):CD007617. doi: 10.1002/14651858.CD007617.pub2. PMID: 21678368.

17. Harding R, List S, Epiphaniou E, Jones H. How can informal caregivers in cancer and palliative care be supported? An updated systematic literature review of interventions and their effectiveness. Palliat Med; 2012 Jan;26(1):7-22. doi: 10.1177/0269216311409613. PMID: 21737481.
18. Shaffer KM, Tigershtrom A, Badr H, et al. Dyadic Psychosocial eHealth Interventions: Systematic Scoping Review. J Med Internet Res; 2020 Mar 4;22(3):e15509. doi: 10.2196/15509. PMID: 32130143.
19. Boele FW, Given CW, Given BA, et al. Family caregivers' level of mastery predicts survival of patients with glioblastoma: A preliminary report. Cancer; 2017 Mar 1;123(5):832-840. doi: 10.1002/cncr.30428. PMID: 27787881.
20. Martire LM, Schulz R, Helgeson VS, et al. Review and meta-analysis of couple-oriented interventions for chronic illness. Ann Behav Med; 2010 Dec;40(3):325-42. doi: 10.1007/s12160-010-9216-2. PMID: 20697859.
21. Northouse LL, Katapodi MC, Song L, et al. Interventions with family caregivers of cancer patients: meta-analysis of randomized trials. CA Cancer J Clin; 2010 Sep-Oct;60(5):317-39. doi: 10.3322/caac.20081. PMID: 20709946.
22. Bakitas M, Lyons KD, Hegel MT, et al. The project ENABLE II randomized controlled trial to improve palliative care for rural patients with advanced cancer: baseline findings, methodological challenges, and solutions. Palliat Support Care; 2009 Mar;7(1):75-86. doi: 10.1017/S1478951509000108. PMID: 19619377.
23. Hudson P, Aranda S. The Melbourne Family Support Program: evidence-based strategies that prepare family caregivers for supporting palliative care patients. BMJ Support Palliat Care; 2014 Sep;4(3):231-7. doi: 10.1136/bmjspcare-2013-000500. PMID: 24644195.
24. Hudson P, Trauer T, Kelly B, et al. Reducing the psychological distress of family caregivers of home based palliative care patients: longer term effects from a randomised controlled trial. Psychooncology; 2015 Jan;24(1):19-24. doi: 10.1002/pon.3610. PMID: 25044819.
25. von Heymann-Horan A, Bidstrup P, Guldin MB, et al. Effect of home-based specialised palliative care and dyadic psychological intervention on caregiver anxiety and depression: a randomised controlled trial. Br J Cancer; 2018 Nov;119(11):1307-1315. doi: 10.1038/s41416-018-0193-8. PMID: 30425351.
26. Finucane AM, O'Donnell H, Lugton J, Gibson-Watt T, et al. Digital health interventions in palliative care: a systematic meta-review. NPJ Digit Med; 2021 Apr 6;4(1):64. doi: 10.1038/s41746-021-00430-7. PMID: 33824407.
27. Slev VN, Mistiaen P, Pasman HR, et al. Effects of eHealth for patients and informal caregivers confronted with cancer: A meta-review. Int J Med Inform; 2016 Mar;87:54-67. doi: 10.1016/j.ijmedinf.2015.12.013. PMID: 26806712.

28. Chi NC, Demiris G. A systematic review of telehealth tools and interventions to support family caregivers. J Telemed Telecare; 2015 Jan;21(1):37-44. doi: 10.1177/1357633X14562734. PMID: 25475220.
29. Widberg C, Wiklund B, Klarare A. Patients' experiences of eHealth in palliative care: an integrative review. BMC Palliat Care; 2020 Oct 14;19(1):158. doi: 10.1186/s12904-020-00667-1. PMID: 33054746.
30. Barak A, Hen L, Boniel-Nissim M, et al. A comprehensive review and a meta-analysis of the effectiveness of Internet-based psychotherapeutic interventions. 2008. In: Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews [Internet]. York (UK): Centre for Reviews and Dissemination (UK); 1995-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK76016/
31. Penedo FJ, Oswald LB, Kronenfeld JP, et al. The increasing value of eHealth in the delivery of patient-centred cancer care. Lancet Oncol; 2020 May;21(5):e240-e251. doi: 10.1016/S1470-2045(20)30021-8. PMID: 32359500.
32. Northouse LL, Mood DW, Schafenacker A, et al. Randomized clinical trial of a brief and extensive dyadic intervention for advanced cancer patients and their family caregivers. Psychooncology; 2013 Mar;22(3):555-63. doi: 10.1002/pon.3036. PMID: 22290823.
33. Northouse LL, Mood DW, Schafenacker A, Montie JE, Sandler HM, Forman JD, Hussain M, Pienta KJ, Smith DC, Kershaw T. Randomized clinical trial of a family intervention for prostate cancer patients and their spouses. Cancer; 2007 Dec 15;110(12):2809-18. doi: 10.1002/cncr.23114. PMID: 17999405.
34. Northouse L, Kershaw T, Mood D, Schafenacker A. Effects of a family intervention on the quality of life of women with recurrent breast cancer and their family caregivers. Psychooncology; 2005 Jun;14(6):478-91. doi: 10.1002/pon.871. PMID: 15599947.
35. Titler MG, Visovatti MA, Shuman C, et al. Effectiveness of implementing a dyadic psychoeducational intervention for cancer patients and family caregivers. Support Care Cancer; 2017 Nov;25(11):3395-3406. doi: 10.1007/s00520-017-3758-9. PMID: 28612157.
36. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M; Medical Research Council Guidance. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ; 2008 Sep 29;337:a1655. doi: 10.1136/bmj.a1655. PMID: 18824488.
37. Dockham B, Schafenacker A, Yoon H, et al. Implementation of a Psychoeducational Program for Cancer Survivors and Family Caregivers at a Cancer Support Community Affiliate: A Pilot Effectiveness Study. Cancer Nurs; 2016 May-Jun;39(3):169-80. doi: 10.1097/NCC.0000000000000311. PMID: 26496519.
38. Northouse L, Schafenacker A, Barr KL, et al. A tailored Web-based psychoeducational intervention for cancer patients and their family caregivers. Cancer Nurs; 2014 Sep-Oct;37(5):321-30. doi: 10.1097/NCC.0000000000000159. PMID: 24945270.

39. Matthys O, De Vleminck A, Dierickx S, et al. 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 Palliat Care; 2021 Dec 28;20(1):193. doi: 10.1186/s12904-021-00895-z. PMID: 34963453.
40. van der Wel M, van der Smissen D, Dierickx S, et al. Systematic translation and adaptation of the FOCUS program, a USA-based supportive intervention for persons with cancer and their family caregivers, for use in six European countries. Support Care Cancer; 2022 Dec;30(12):9763-9770. doi: 10.1007/s00520-022-07391-x. PMID: 36221035.
41. Van Goethem V, Dierickx S, Matthys O, et al. A self-management psychoeducational eHealth program to support and empower people with advanced cancer and their family caregivers: Development using the scrum methodology. Internet Interv; 2023 Aug 9;33:100659. doi: 10.1016/j.invent.2023.100659. PMID: 37593143.
42. Moore G, Campbell M, Copeland L, et al. Adapting interventions to new contexts-the ADAPT guidance. BMJ; 2021 Aug 3;374:n1679. doi: 10.1136/bmj.n1679. PMID: 34344699.
43. Roberts AE, Davenport TA, Wong T, et al. Evaluating the quality and safety of health-related apps and e-tools: Adapting the Mobile App Rating Scale and developing a quality assurance protocol. Internet Interv; 2021 Mar 17;24:100379. doi: 10.1016/j.invent.2021.100379. PMID: 33777705.
44. Sekhon M, Cartwright M, Francis JJ. Development of a theory-informed questionnaire to assess the acceptability of healthcare interventions. BMC Health Serv Res; 2022 Mar 1;22(1):279. doi: 10.1186/s12913-022-07577-3. PMID: 35232455.
45. Braun V, Clarke V. Using thematic analysis in psychology. Qualitative research in psychology; 2006;3(2):77-101. doi: 10.1191/1478088706qp063oa.
46. Ritchie J, Spencer, L. Qualitative data analysis for applied policy research. Analyzing Qualitative Data. London, UK: Routledge;1994.
47. Curran GM, Bauer M, Mittman B, et al. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. Med Care; 2012 Mar;50(3):217-26. doi: 10.1097/MLR.0b013e3182408812. PMID: 22310560.
48. Hübner U. What Are Complex eHealth Innovations and How Do You Measure Them? Position Paper. Methods Inf Med; 2015;54(4):319-27. doi: 10.3414/ME14-05-0001. PMID: 25510406.
49. Blandford A, Gibbs J, Newhouse N, et al. Seven lessons for interdisciplinary research on interactive digital health interventions. Digit Health; 2018 May 3;4:2055207618770325. doi: 10.1177/2055207618770325. PMID: 29942629.
50. World Health Organization. Monitoring and evaluating digital health interventions: a practical guide to conducting research and assessment. Geneva: WHO; 2016. ISBN: 978-92-4-151176-6.
51. Rankin NM, Butow PN, Hack TF, et al. An implementation science primer for psycho-oncology: translating robust evidence into practice. J Psychosoc Oncol Res Prac; 2019;1(3):e14. doi:

10.1097/OR9.0000000000000014.

52. Lazarus, Richard S, Folkman S. Stress, appraisal, and coping. New York, USA: Springer publishing company; 1984.
53. Hawkins RP, Kreuter M, Resnicow K, et al. Understanding tailoring in communicating about health. Health Educ Res; 2008 Jun;23(3):454-66. doi: 10.1093/her/cyn004. PMID: 18349033.
54. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst; 1993 Mar 3;85(5):365-76. doi: 10.1093/jnci/85.5.365. PMID: 8433390.
55. Jabbarian LJ, Groenvold M, Petersen MA, Christensen CA, Deliens L, van der Heide A, Kars MC, Miccinesi G, Payne S, Wilcock A, Korfage IJ; ACTION consortium. Assessing Emotional Functioning with Increased Power: Relative Validity of a Customized EORTC Short Form in the International ACTION Trial. Value Health; 2019 Jan;22(1):92-98. doi: 10.1016/j.jval.2018.07.002. PMID: 30661639.
56. Lewis FM. Family Home Visitation Study Final Report. National Cancer Institute, National Institutes of Health; 1996.
57. Groenvold M, Petersen MA, Aaronson NK, Arraras JI, Blazeby JM, Bottomley A, Fayers PM, de Graeff A, Hammerlid E, Kaasa S, Sprangers MA, Bjorner JB; EORTC Quality of Life Group. The development of the EORTC QLQ-C15-PAL: a shortened questionnaire for cancer patients in palliative care. Eur J Cancer; 2006 Jan;42(1):55-64. doi: 10.1016/j.ejca.2005.06.022. PMID: 16162404.
58. Weitzner MA, Jacobsen PB, Wagner H Jr, et al. The Caregiver Quality of Life Index-Cancer (CQOLC) scale: development and validation of an instrument to measure quality of life of the family caregiver of patients with cancer. Qual Life Res; 1999;8(1-2):55-63. doi: 10.1023/a:1026407010614. PMID: 10457738.
59. Tomich PL, Helgeson VS. Is finding something good in the bad always good? Benefit finding among women with breast cancer. Health Psychol; 2004 Jan;23(1):16-23. doi: 10.1037/0278-6133.23.1.16. PMID: 14756599.
60. Carver CS. You want to measure coping but your protocol's too long: consider the brief COPE. Int J Behav Med; 1997;4(1):92-100. doi: 10.1207/s15327558ijbm0401_6. PMID: 16250744.
61. Buunk BP, Berkhuysen MA, Sanderman R, Nieuwland W. Actieve betrokkenheid, beschermend bufferen en overbescherming. Meetinstrumenten voor de rol van de partner bij hartrevalidatie [The role of the partner in heart disease: Active engagement, protective buffering, and overprotection]. Gedrag & Gezondheid: Tijdschrift voor Psychologie en Gezondheid; 1996; 24(6), 304–313.
62. Buccheri G, Ferrigno D, Tamburini M. Karnofsky and ECOG performance status scoring in lung cancer: a prospective, longitudinal study of 536 patients from a single institution. Eur J Cancer; 1996 Jun;32A(7):1135-41. doi: 10.1016/0959-8049(95)00664-8. PMID: 8758243.

63. Chisholm D, Knapp MR, Knudsen HC, et al. Client Socio-Demographic and Service Receipt Inventory--European Version: development of an instrument for international research. EPSILON Study 5. European Psychiatric Services: Inputs Linked to Outcome Domains and Needs. Br J Psychiatry Suppl; 2000;(39):s28-33. doi: 10.1192/bjp.177.39.s28. PMID: 10945075.
64. Sekhon M, Cartwright M, Francis JJ. Development of a theory-informed questionnaire to assess the acceptability of healthcare interventions. BMC Health Serv Res; 2022 Mar 1;22(1):279. doi: 10.1186/s12913-022-07577-3. PMID: 35232455.
65. Cane J, O'Connor D, Michie S. Validation of the theoretical domains framework for use in behaviour change and implementation research. Implement Sci; 2012 Apr 24;7:37. doi: 10.1186/1748-5908-7-37. PMID: 22530986.
66. Northouse L, Schafenacker A, Barr KL, et al. A tailored Web-based psychoeducational intervention for cancer patients and their family caregivers. Cancer Nurs; 2014 Sep-Oct;37(5):321-30. doi: 10.1097/NCC.0000000000000159. PMID: 24945270.
67. Shaffer KM, Tigershtrom A, Badr H, Benvengo S, et al. Dyadic Psychosocial eHealth Interventions: Systematic Scoping Review. J Med Internet Res; 2020 Mar 4;22(3):e15509. doi: 10.2196/15509. PMID: 32130143.
68. Klaic M, Kapp S, Hudson P, et al. Implementability of healthcare interventions: an overview of reviews and development of a conceptual framework. Implement Sci; 2022 Jan 27;17(1):10. doi: 10.1186/s13012-021-01171-7. PMID: 35086538.
69. Sanetti LMH, Cook BG, Cook L. Treatment Fidelity: What it is and why it matters. Learning Disabilities Research & Practice; 2021; 36: 5-11. doi: 10.1111/ldrp.12238.
70. Lorencatto F, Gould NJ, McIntyre SA, et al. A multidimensional approach to assessing intervention fidelity in a process evaluation of audit and feedback interventions to reduce unnecessary blood transfusions: a study protocol. Implement Sci; 2016 Dec 12;11(1):163. doi: 10.1186/s13012-016-0528-x. PMID: 27955683.
71. Sekhon M, Cartwright M, Francis JJ. Acceptability of healthcare interventions: an overview of reviews and development of a theoretical framework. BMC Health Serv Res; 2017 Jan 26;17(1):88. doi: 10.1186/s12913-017-2031-8. PMID: 28126032.
72. Bellg AJ, Borrelli B, Resnick B, Hecht J, Minicucci DS, Ory M, Ogedegbe G, Orwig D, Ernst D, Czajkowski S; Treatment Fidelity Workgroup of the NIH Behavior Change Consortium. Enhancing treatment fidelity in health behavior change studies: best practices and recommendations from the NIH Behavior Change Consortium. Health Psychol; 2004 Sep;23(5):443-51. doi: 10.1037/0278-6133.23.5.443. PMID: 15367063.
73. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol; 2006; *3*(2):77–101. doi: 10.1191/1478088706qp063oa.
74. Gale NK, Heath G, Cameron E, et al. Using the framework method for the analysis of qualitative data

in multi-disciplinary health research. BMC Med Res Methodol; 2013 Sep 18;13:117. doi: 10.1186/1471-2288-13-117. PMID: 24047204.

75. Nowell LS, Norris JM, White DE, et al. Thematic Analysis: Striving to Meet the Trustworthiness Criteria. Int J Qualitative Methods; 2017;16(1):1-13. doi: 10.1177/1609406917733847.
76. Milat AJ, King L, Bauman AE, Redman S. The concept of scalability: increasing the scale and potential adoption of health promotion interventions into policy and practice. Health Promot Int; 2013 Sep;28(3):285-98. doi: 10.1093/heapro/dar097. Epub 2012 Jan 12. PMID: 22241853.
77. Shapiro M, Renly S, Maiorano A, et al. Digital Health at Enterprise Scale: Evaluation Framework for Selecting Patient-Facing Software in a Digital-First Health System. JMIR Form Res; 2023 Apr 7;7:e43009. doi: 10.2196/43009. PMID: 37027184.
78. Barwick M, Brown J, Petricca K, et al. The Implementation Playbook: study protocol for the development and feasibility evaluation of a digital tool for effective implementation of evidence-based innovations. Implement Sci Commun; 2023 Mar 7;4(1):21. doi: 10.1186/s43058-023-00402-w. PMID: 36882826.

Supplementary Files

Figures

Intervention overview.