Treating fear of cancer recurrence in primary care

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Colophon
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PhD thesis, Utrecht University, the Netherlands
ISBN: 978-90-393-7579-2
DOI: https://doi.org/10.33540/1871

Printed by Optima
Cover design by Erwin Timmerman

The research was funded by the Dutch Cancer Society (KWF).

Treating fear of cancer recurrence in primary care

Behandeling van angst voor terugkeer van kanker in de eerste lijn

(met een samenvatting in het Nederlands)

Proefschrift

ter verkrijging van de graad van doctor
aan de Universiteit Utrecht
op gezag van de
rector magnificus, prof.dr. H.R.B.M. Kummeling,
ingevolge het besluit van het college voor promoties
in het openbaar te verdedigen op

donderdag 19 oktober 2023 des middags te 2.15 uur

door

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geboren op 28 juli 1989
te Eindhoven

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General introduction

FEAR OF CANCER RECURRENCE

The number of cancer survivors is increasing due to earlier detection, improved treatments and longevity.[1,2] The Netherlands Comprehensive Cancer Organisation (IKNL) estimates that in the Netherlands, in 2032, there will be almost 780.000 people who have had a cancer diagnosis in the last ten years and are still alive.[3] Part of this group will have finished successful curative cancer treatment but will still be experiencing many physical and mental remnants. Mental health issues after cancer include fear of cancer recurrence (FCR), which is defined as 'the fear, worry or concern about cancer returning or progressing'.[4] Support for FCR has been listed as the most important unmet need of cancer survivors.[5] FCR leads to decreased quality of life[6,7] and increased healthcare costs.[8] While early detection and, if needed, referral for treatment can help patients manage their FCR and while therapeutic interventions can be cost-effective, healthcare providers often do not recognize FCR.[8,9]

A MODEL ON FEAR OF CANCER RECURRENCE

FCR is characterized by cognitions and emotions about cancer. Lee-Jones (1997) describes a model in which antecedents lead to FCR and FCR leads to consequences (see Figure 1). The antecedents are internal cues such as somatic stimuli that are interpreted as symptoms of recurrence, and external cues such as health care appointments and media items about cancer. These cues lead to FCR, which consists of cognitions, including the patient's perception of their risk of recurrence, and emotions, such as anxiety about cancer. FCR in turn leads to behavioural responses such as limited planning for the future, and psychological effects such as a misinterpretation of somatic symptoms.[10]

IMPACT OF FCR AND NEED FOR SUPPORT

Some people only experience FCR when it is triggered, for example, by medical appointments or loved ones receiving a cancer diagnosis.[11] However, others have continuous and intrusive thoughts about cancer, and experience great disruptions in their daily lives.[11] To cope with FCR, some try to take control by often checking their body for symptoms, searching online for information, and requesting medical check-ups. Others fearfully avoid all (potentially) cancer related activities and appointments.[11] While many people experience FCR, this does not always translate into a need or want for help.[12–14] Some do not experience the distress as severe enough to warrant intervention.[12] Others do not want to bother healthcare providers with emotional issues or consider seeking help a sign of failure or weakness. Also, some do not seek help, because their emotional needs are met by family and social networks.[15]

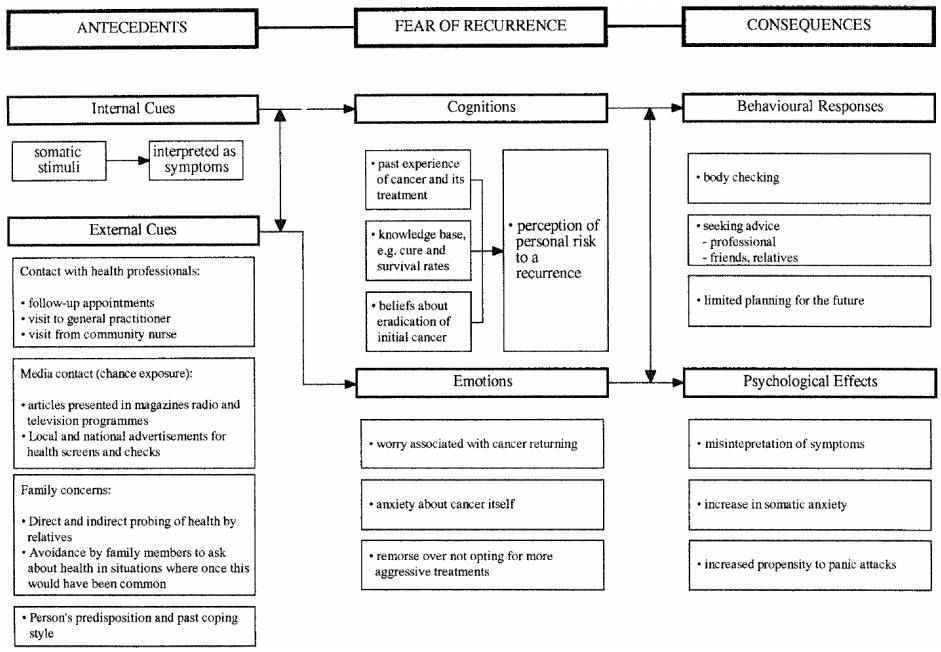

Figure 1. Model on fear of cancer recurrence by Lee-Jones (1997).

EXISTING PSYCHO-ONCOLOGICAL INTERVENTIONS

For those who do need help, many interventions for FCR have been developed. While there are some more basic psychoeducational, self-help and nurse or oncologist led interventions, most interventions are specialized psycho-oncological treatments.[16] They exist in many different formats (e.g., individual, group or couple) and many different settings (e.g., face-to-face, online, by phone, and blended). Most specialized interventions are based on traditional or contemporary cognitive behavioral therapy (CBT), including mindfulness-based CBT and acceptance and commitment therapy (ACT).[17] Many interventions have demonstrated effectiveness, though effect sizes are usually modest.[16,17]

STEPPED CARE TO PROVIDE CARE FOR ALL

Considering the high number of cancer patients and survivors, and the high prevalence of FCR, it is not possible to provide specialized psycho-oncological care to all. Therefore, in a Delphi study on research priorities for FCR, intervention research was nominated as the top priority, and stepped care and blended models with online elements were highlighted as important potential opportunities to increase accessibility.[18] In addition to being more scalable and less expensive, these low intensity interventions may also be more appealing for patients who want to stay in control and fear stigma.

Pradhan et al. (2021) recommend a four-step model, with psychoeducation as the first step, internet-delivered and self-help interventions as the second step, brief nurse-led interventions as the third step, and face-to-face psycho-oncologist delivered interventions as the fourth step.[16] An example of the first step, is a brief clinician-led intervention including normalization, prognostic information, education on recurrence symptoms, advice on managing worry and if needed, referral to a psycho-oncologist.[19] For the second step, four studies on online self-management interventions have been published. Three found small effects, one found no effect.[20–23] For the third step, nurse-led interventions, some initial studies have been done on interventions such as psychoeducation, discussing FCR, mindfulness and teaching coping strategies. These interventions show some potential, but the studies had low sample sizes and short follow-up times.[24]

A SELF-MANAGEMENT E-HEALTH INTERVENTION

Therapists and clients from the Helen Dowling Institute, an academic mental health institute that specializes in psycho-oncology, co-created an e-Health program for FCR that is based on CBT and the above-described model by Lee-Jones.[10] The program consists of three main modules with psychoeducation and CBT, and five optional modules. The optional modules are about rumination, avoidance, relaxing, reassurance and undertaking activities, and can be selected based on patients' individual needs. The program includes information, exercises and videos of other patients' experiences and is available 24/7. Online programs can increase the access to care and decrease costs. Patients do not need to take time off work or travel to their therapist and can work on the program at a time that is convenient for them, from the comfort of their own home.[25]

However, in a previous RCT, where the program was implemented as self-help, only 30 of the 130 respondents who were offered the program actively used it. 80 respondents logged in only once and 10 never logged in. No effect of the intervention was found, and professional support was recommended to enhance patient engagement.[22] Other studies have also shown that professional support increases engagement and effectiveness for e-Health interventions.[25]

THE ROLE OF THE GP IN CANCER CARE

Since cancer survivorship care is presently shifting from hospital care towards primary care, general practitioners (GP) may also play an increased role in providing care for FCR. Cancer survivors frequently favour their GP for psychosocial care and GPs consider this a fitting role.[26] GPs combine physical care with care for psychosocial issues and lifestyle behaviours,[27] commonly have a longstanding relationship with patients and often know

patients' family members and caregivers.[28] Also, their care is easily accessible, and patients experience less (self-)stigma when going to the GP, compared to going to a psychologist.[29] Moreover, the Dutch General Practitioner Association stated psychosocial and existential care are an essential part of GP care for cancer survivors.[28]

A PRIMARY CARE E-HEALTH INTERVENTION FOR FCR

Since 2014, GPs in the Netherlands can only refer patients to a psychologist if they fit the Diagnostic and Statistical Manual (DSM) of Mental Disorders criteria for a psychiatric disorder.[30] Therefore, almost all GPs employ mental health workers (MHW), who can help to provide mental health care.[31] MHWs' role is to provide care for mild psychological complaints in a timely manner, which can also prevent complaints from growing worse. They generally have five to seven sessions with patients and offer interventions such as (online) self-help programs, counselling, problem solving therapy and short CBT.[30,31] Thus, supporting patients with moderate FCR using a CBT-based e-Health program fits with their professional profile and competencies. Positioning the program in primary care instead of offering it as self-help can increase patient engagement and allow for clarification and support by the MHW. While some primary care healthcare providers feel they lack knowledge, skills and self-efficacy to provide care for FCR,[32] in prior research an e-Health intervention for cancer survivorship allowed healthcare providers who were not specialised in oncology to effectively support patients, and it reduced their workload.[33] A recent review also found that telehealth is a feasible modality for cancer survivorship care,[34] and a recent implementation study found that designing interventions that are specifically for FCR and not generally for fear facilitates implementation.[32]

AIM AND OUTLINE OF THIS THESIS

The overall aim of this thesis is to assess whether FCR can be effectively treated in primary care. In Chapter 2, we first assess the prevalence and severity of FCR for the general cancer population and for different subgroups since current estimates are wide ranging. Knowing the prevalence and severity of FCR helps to estimate the burden of FCR and to discern what types of interventions are required. Knowing which subgroups disproportionately experience FCR helps to target interventions to those most in need. However, not all patients with FCR want or require help. Therefore, in Chapter 3, we analyze the needs for different types of support, as well as the preferred providers and the extent to which these needs are currently being met. We include both formal and informal types of support. In Chapter 4, we present our protocol for a pragmatic RCT on the effectiveness of a face-to-face delivered primary care intervention for FCR. Unfortunately, we had to stop this study before the inclusion target was reached, in part due to the COVID-19 pandemic. In Chapter

5, we report lessons learned about the potential of the intervention and the advantages and disadvantages of offering it in primary care. In Chapter 6, we present the results of a second RCT, in which the intervention was offered online, with video calls replacing face-to-face sessions. In Chapter 7, we present the results of an interview study on patients' and MHWs' experience with the intervention and how they perceive its feasibility in daily practice. Finally, in Chapter 8, all results are summarized and discussed and implications for research and practice are presented.

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2

What is the prevalence of fear of cancer recurrence in cancer survivors and patients? A systematic review and individual participant data meta-analysis

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Published in Psycho-oncology in 2022.

ABSTRACT

Objective: Care for fear of cancer recurrence (FCR) is considered the most common unmet need among cancer survivors. Yet the prevalence of FCR and predisposing factors remain inconclusive. To support targeted care, we provide a comprehensive overview of the prevalence and severity of FCR among cancer survivors and patients, as measured using the short form of the validated Fear of Cancer Recurrence Inventory (FCRI-SF). We also report on associations between FCR and clinical and demographic characteristics.

Methods: This is a systematic review and individual participant data (IPD) meta-analysis on the prevalence of FCR. In the review, we included all studies that used the FCRI-SF with adult (≥18 years) cancer survivors and patients. Date of search: 7-02-2020. Risk of bias was assessed using the Joanna Briggs Institute critical appraisal tool.

Results: IPD were requested from 87 unique studies and provided for 46 studies comprising 11,226 participants from 13 countries. 9,311 respondents were included for the main analyses. On the FCRI-SF (range 0-36), 58.8% of respondents scored ≥13, 45.1% scored ≥16 and 19.2% scored ≥22. FCR decreased with age and women reported more FCR than men. FCR was found across cancer types and continents and for all time periods since cancer diagnosis.

Conclusions: FCR affects a considerable number of cancer survivors and patients. It is therefore important that healthcare providers discuss this issue with their patients and provide treatment when needed. Further research is needed to investigate how best to prevent and treat FCR and to identify other factors associated with FCR.

The protocol was prospectively registered (PROSPERO CRD42020142185).

Funding: This study was supported by the Dutch Cancer Society (KWF) grant number 10936.

Keywords: cancer, correlates, fear of recurrence, oncology, prevalence

BACKGROUND

Due to aging and improved diagnostic and treatment potential, the number of people living with and beyond cancer is rapidly increasing.[1] In 2018, the estimated number of cancer survivors diagnosed within the last five years was 43.8 million.[2] For this growing group, managing fear of cancer recurrence (FCR) has been reported as one of the most important unmet needs.[3–5] FCR is defined as "fear, worry, or concern relating to the possibility that cancer will come back or progress".[6] Low levels of FCR can be helpful by promoting treatment compliance and healthy lifestyle adaptations. However, at clinical levels, FCR can limit quality of life and daily functioning and require professional help.[7–12] A 2019 Delphi study conceptualized four features as key characteristics of *clinical* FCR: "(a) high levels of preoccupation; (b) high levels of worry; (c) that are persistent; and (d) hypervigilance to bodily symptoms".[13] It is important to address FCR, because FCR may also lead to increased healthcare costs[14] and for most patients, it does not decrease over time without intervention.[3,7,11,15,16] Furthermore, several effective interventions to treat FCR have been developed.[17]

In order to shape future healthcare provision, policy and research on FCR, it is crucial to know the prevalence and severity of FCR for the general cancer population and for different subgroups. This will help to estimate the burden of FCR and to target the type and intensity of interventions for those in need. Unfortunately, the precise prevalence of FCR remains unknown and estimates are wide ranging and inconclusive. For example, in a systematic review by Simard et al. (2013) studies found prevalences of 39-97% for any level of FCR, 22-87% for 'moderate to high' FCR and 0-15% for 'high' FCR.[3] Notably, part of this heterogeneity is caused by different studies using different scales. In the literature, the most commonly used measure of FCR is the Fear of Cancer Recurrence Inventory (FCRI).[18] Still, the comparability of studies is complicated by the use of different cut-off scores across studies, namely 13, 16 and 22.[10,19] Scoring ≥13 indicates the possibility of clinical level FCR, scoring ≥16 indicates the likely presence of clinical level FCR and scoring ≥22 indicates a clinical severity of FCR that needs specialized intervention.[10,19]

Several potential risk factors for FCR have been investigated. Predictive evidence is strongest for the presence of physical symptoms such as fatigue and pain,[3] sex, with women reporting higher levels of FCR than men[20], and age, with younger patients more likely to report FCR than older patients.[3,9,21] However, the results of a recent review showed that the strength of the latter association decreased over the last decade.[22] Associations with other factors such as sleep quality, cancer type, and time since cancer diagnosis or treatment have also been investigated but have yielded inconclusive results.[3,23]

A recent meta-analysis of FCRI found that 53.9% of cancer survivors and patients scored above the ≥13 cut-off, 43.3% above the ≥16 cut-off, and 30% above the ≥22 cut-off on the

FCRI severity subscale (FCRI-SF).[23] In this meta-analysis, only the cut-offs reported in the individual articles could be considered and studies reporting different cut-offs could not be analyzed together. For example, studies reporting only the ≥13 cut-off could not be analyzed together with studies reporting only the ≥22 cut-off. Also, the meta-analysis included studies that selected patients based on their level of FCR, and thus does not reflect the general cancer population. To obtain more precise estimates of the prevalence of FCR, we have conducted a systematic review and individual participant data (IPD) meta-analysis. In IPD analyses, researchers from each study are asked to share the original research data, so that these data can be combined and re-analyzed. Using IPD analyses, we could look at all cut-offs for all provided study data, unrestricted by the cut-offs reported by the authors of the individual studies. Also, we were able to conduct subgroup analyses that would not be possible with smaller sample sizes. Our main aim was to provide a comprehensive overview of the prevalence and severity of FCR among cancer survivors [no active cancer present] and patients [active cancer present] and to identify associations with clinical and demographic characteristics. In addition, we report the clinical and demographic characteristics of groups with different levels of FCR severity.

METHODS

A systematic review and IPD meta-analysis on the prevalence of FCR was conducted. The research plan was developed in collaboration with an international board of experts (the 'advisory board') who have specialized in psycho-oncology (AS, GH, NK, RZ, SL, SS, WL) and published in advance on the Open Science Framework* (OSF) and Prospero (CRD42020142185).

Selection of variables

Several tools to measure FCR[3,24] have been developed. The FCRI was selected to assess the main outcome because it has good psychometric properties, is widely used, and is available in ten different languages,[18,23,25–33] increasing sample diversity. The FCRI includes seven subscales: FCR severity, coping, functioning impairments, triggers, psychological distress, insight, and reassurance. The severity subscale (range 0-36) is widely used as a short form of the FCRI (FCRI-SF) and was also used as the primary outcome in this study, because the total score includes several aspects other than severity.[23] It contains nine items (range 0-4), e.g., "I am afraid of cancer recurrence", "I believe it is normal to be worried or anxious about the possibility of cancer recurrence" and "How much time per day do you spend thinking about the possibility of cancer recurrence?". Using the FCRI-SF allowed for the inclusion of studies that collected data using only this subscale and not

* https://osf.io/4rc35/

the total scale. If repeated measures were available, only baseline data were included. Since the different cut-offs represent different levels of FCR severity (see introduction), we examined all three cut-offs in this study.

In this study we distinguish between people who have active disease and those who no longer have active disease, by stratifying the results by these groups and calling them patients and survivors, respectively.

In collaboration with the advisory board and based on clinical experience and literature, we identified variables that we expected could correlate with FCR, would be clinically relevant, and for which we expected many studies to have collected data. The following variables were selected for inclusion in the study: age, sex, time since cancer diagnosis, cancer type, and continent where the study was conducted.

Eligibility criteria

Data from all participants from all studies that used the FCRI-SF from adult (≥18 years) cancer survivors and patients were eligible. Data from studies that selected patients based on the severity of their FCR were not included in the main outcome analyses, but were included for the analyses of the characteristics of groups with different levels of FCR.

Search and selection strategy

PubMed, MEDLINE, PsycINFO, Embase, EMcare, CINAHL and Scopus were searched on Feb 7, 2020, using the following terms:

- "Fear of cancer recurrence inventory"
- "FCRI" AND (fear OR worry OR concern OR anxiety)

Since the FCRI has only existed since 2009,[18] there was no time restriction. A forward search was done using all articles describing the development of a new translation of the FCRI. We expected that studies that use a questionnaire would always reference the article describing its development. Therefore, we expected this forward search would allow us to find all articles that used the FCRI.

Corresponding authors of eligible articles who were approached to share their data were also asked if they had additional published or unpublished datasets using the FCRI (e.g., from screening patients prior to including only those with a certain level of FCR in a study). These datasets were included if the data were of high quality (e.g., systematically obtained and recorded) and sufficient information was available about recruitment, sampling, and data collection method.

The records identified in the searches were screened based on their titles and abstracts. Potentially eligible records were full text screened. If upon reading the full article, there

was any doubt about whether the authors had collected data using the FCRI, authors were contacted. This includes protocol papers that stated they were intending to use the FCRI. Studies that included only part of the FCRI-SF were not included.

The screening was done by two independent reviewers (YL and NT), using Covidence, a software system for managing systematic reviews (www.covidence.org).

Quality assessment

To evaluate risk of bias, two researchers (YL and NT) independently assessed each study using the Joanna Briggs Institute Critical Appraisal Checklist for Studies Reporting Prevalence Data. Four out of nine domains were omitted due to lack of relevance for the present study. The domains that were used addressed the sample frame, the sampling method, the sample size, the description of subjects and setting and the response rate. For each domain, the researchers judged whether there was a risk of bias in answering the research question of the current study. Based on the available information in the published articles, they chose between "Yes", "No" and "Unclear". The risk of bias assessment is presented in Supplementary Materials 2A.

Domain 1 assessed the sample frames of the studies. Studies that excluded participants who score below one of the cut-offs on the FCRI-SF (e.g., RCTs on FCR interventions, requiring participants to have a certain level of FCR) do not reflect the general cancer population and were excluded for the analyses for the main outcome, due to a high risk of bias. Similarly, a study that excluded patients with sleeping disorders, which could correlate with FCR, was excluded for the main analyses. These studies, with a risk of bias on domain 1, were only used to describe the characteristics of groups with different levels of FCR (see Supplementary Materials 2D). In these analyses, comparisons are made within rather than across FCR severity groups, eliminating this risk of bias. For domain 3, sample sizes below 30 were considered a risk of bias. For domain 5, a response rate of less than 50% was considered a risk of bias. These cut-offs were selected in collaboration with the advisory board.

Collection of IPD

Corresponding authors of all eligible studies were contacted via e-mail and asked whether they would be willing to share their data. Every author was reminded at least twice, when there was no response after two weeks. If there was still no response another author was approached to request the data.

Authors who wished to share their data signed a data sharing agreement, which was created based on the example of the POLARIS study.[34] Authors received instructions on how to share data, including how to code the items. All received datasets were checked for

completeness, correctness and whether they fit the data format. If any uncertainties about the data remained (e.g., how data had been collected), authors were contacted to clarify these issues. Data that did not fit the required format (i.e., were coded differently), were adapted to the format by the reviewers.

Authors were asked to provide the following information: participants' eligibility criteria, recruitment methods, and definitions of survivors and patients used in the study. Authors were also asked to report any changes made to the original FCRI and whether times since diagnosis and end of curative treatment were obtained from medical record or from patient reporting. If available, authors were asked to share their study protocol. Finally, authors were asked to check their ethical protocols to ensure sharing individual data was permitted.

Statistical methods

All outcomes were predetermined in the protocol and published on PROSPERO and OSF. A one-stage approach was used for all analyses. All outcomes were reported separately for cancer survivors and patients. All analyses were performed in R.[35]

The primary study outcome was the prevalence of FCR. Prevalence of FCR per sex, age group (18-29, 30-44, 45-59, 60-74, ≥75), cancer type, time since cancer diagnosis (0-1 years, 2-5 years, 6-10 years, >10 years) and continent where the study was conducted were also reported. Prevalence estimates were reported as percentages of people scoring below, between, and above the various cut-offs on the FCRI-SF. Additionally, mean scores and confidence intervals were reported. When calculating mean scores, clustering effects per dataset were accounted for by adding a random intercept per study.[36]

Second, associations between FCR severity and sex, age, cancer type, time since cancer diagnosis and continent where the study took place were assessed using multilevel regression analysis with fixed effects for all variables and a random intercept per study.

Finally, the characteristics of respondents with different levels of FCR were described. The number and percentage of people within each FCR severity category (<13, 13-15, 16-21, ≥22) who have the characteristics measured in this study (e.g., age, sex) were reported. Studies that screened on level of FCR prior to inclusion were included only for these analyses.

In order to compare the results of our IPD analysis to the results of the studies that did not provide individual participant data, we performed an aggregate data analysis. Two independent reviewers (YL and a research assistant) extracted the mean FCRI-SF score and/or the percentage scoring ≥13, depending on what information was reported in the articles.

Missing data

If researchers had applied imputation, they were asked to provide the imputed datasets. Still, almost all received datasets had missing data. In the combined dataset used for the main analyses, there was a total of 2.8% missing data. We therefore applied multilevel imputation using *jomoImpute* to impute both sporadic and systematic missing data. Multilevel imputation has been shown to lead to better outcomes than complete case analysis and traditional multiple imputation.[37] It can also be applied to both linear and non-linear variables and even when some variables are entirely missing from some datasets.[37]

It was not possible to impute all variables for all participants at the same time. Therefore, for the prevalence and severity calculations, variables were imputed separately, to include as many participants as possible. Still, for some variables, the imputations did not converge and the unimputed data was used. For the multilevel regression analysis, data of survivors and patients were imputed separately, in order to impute as many variables as possible. As a result, participants without a known patient or survivor status, including two entire datasets, were excluded from these analyses. For patients, we imputed the categorical "time since cancer diagnosis" variable, since the imputation with the continuous variable did not converge. For survivors, neither the categorical nor the continuous time since cancer diagnosis variable converged. Therefore, participants without this variable could not be included in the analyses.

RESULTS

The database searches revealed 746 studies. After duplicates were removed, 280 abstracts were screened, and 203 papers were screened in full text, resulting in final inclusion of 154 papers (87 unique studies) (see Figure 1). There were 24 differences (.92 agreement) between reviewers during the abstract screening and 9 (.95 agreement) during the full text screening. All were easily resolved through discussion.

Authors of the 87 included studies were contacted to request participation in the IPD study and to provide data. Authors of 43 studies accepted and shared their datasets. In addition, 3 other unpublished datasets were provided by these authors. In total, data from 46 independent studies (11,226 participants)[15,16,18,25-29,32,38–72] were included in the IPD meta-analysis. No important issues were identified in checking IPD.

For the remaining 44 studies, no data could be included. Three studies did not collect data using the FCRI. Reasons for not including the other 41 were: the author did not respond (n=12), the author did not follow-up after initial contact (n=8), the university did not give permission (n=7), the ethics committee did not give permission (n=5), the data were not yet published (n=5), the authors did not have time to participate (n=3), and there were no

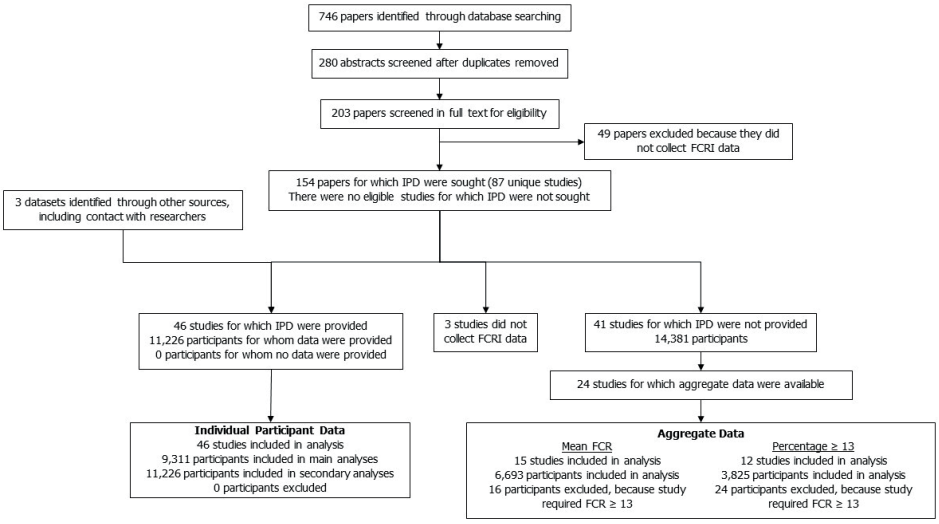


Figure 1. Flowchart of studies identified, screened, and included with individual participant data (IPD) or aggregate data.

contact details on the article (n=1). Notably, the data were requested during the COVID-19 pandemic, which may have impacted authors' opportunities to share data.

For 24 studies for which IPD was not available, aggregate data could be obtained from the articles. Fifteen studies reported data on the mean FCR score (29,65–78) and 12 studies reported data on the percentage scoring ≥ 13 (65,68,70,74,78–85). The other studies reported neither outcome.

Quality assessment

The outcomes of the risk of bias assessment for both the IPD and the aggregate data analyses are presented in Supplementary Materials 2B. For the studies that provided IPD, there were 14 differences (.94 agreement) in risk of bias ratings between reviewers. All were easily resolved through discussion.

For the studies that did not select participants on FCR severity, the overall risk of bias was low (Supplementary Materials 2B, Figure 1). There were some concerns about the sampling method (domain 2) and the response rate (domain 5). Risk of bias on domain 2 was mostly due to studies' main topic being FCR, which could lead to selection bias. People who experience FCR may be more likely to participate in studies on FCR than people who do not experience FCR, because the topic interests them, though it is also possible that patients with high FCR may be reluctant to join these studies as they may want to avoid the topic. The risk of bias assessment did not lead to exclusion of any studies.

Prevalence of FCR

Overall, in the IPD analysis (n=9,311), 58.8% of participants scored ≥13, 45.1% scored ≥16 and 19.2% scored ≥22 on the FCRI-SF. The distributions were similar for survivors and patients (see Table 1).

Table 1. The prevalence of FCR for survivors and patients according to cut-offs on the FCRI-SF, using imputed data.

	< 13	13-15	16-21	≥22
Cancer survivors n (%)	2960 (41.1)	946 (13.2)	1867 (26.0)	1417 (19.7)
Cancer patients n (%)	878 (41.4)	325 (15.3)	547 (25.8)	371 (17.5)
Total	3838 (41.2)	1271 (13.7)	2414 (25.9)	1788 (19.2)

The percentages of the subgroups that scored below, between and above the different FCRI-SF cut-off scores are presented in Table 2. Survivors and patients follow a similar pattern. For survivors, 46% of men scored ≥13 and 12% scored ≥22, compared with 64% and 28% of women. In the youngest age category (18-29 years) 88% of survivors scored ≥13 and 48% scored ≥22, compared with 37% and 9% in the highest age category (≥75 years), respectively. Some differences between cancer types were observed. For example, for prostate cancer 37% of survivors scored ≥13, for endometrial cancer 39% and for colorectal cancer 50% compared with 82% for thyroid cancer and 80% for leukemia & non-Hodgkin lymphoma. For time since cancer diagnosis, in all categories approximately 60% of survivors scored ≥13 and approximately 20% scored ≥22. There were also no major differences between the continents, though respondents from studies conducted in Asia scored somewhat lower.

Mean FCR severity scores

The mean FCR severity score for all participants (n=9,311) was 14.8 (95%CI 13.7-16.0). Mean FCR scores stratified by clinical and demographic characteristics are presented in Table 3. The FCRI-SF scores in this table may be considered normative scores. Mean FCR severity scores and main characteristics per study are presented in Supplementary Materials 2C. On average, patients scored two points higher than survivors, and women scored approximately two points higher than men. FCR severity scores were lower for higher age groups, with the youngest group (18-29) scoring 16.9 and 17.0 and the oldest group (≥75) scoring 10.9 and 12.6 for survivors and patients respectively. Looking at cancer types, all mean scores ranged between 11.2 and 16.8, with the highest mean scores for lung cancer and melanoma. FCR severity scores were similar across different time periods since cancer diagnosis. For patients, the mean FCR severity scores were slightly higher (1.1 points) for respondents with longer times since cancer diagnosis, while for survivors, FCR severity scores were slightly lower (1.3 points) for respondents with longer times since cancer diag-

nosis. Comparing the continents, respondents from studies carried out in Australia scored highest, followed by respondents from studies in North America, Europe and finally Asia.

Table 2. The prevalence of FCR according to FCRI-SF cut-offs, stratified by clinical and demographic characteristics.

	Survivors n (%)				**Patients n (%)**			
	< 13	**13-15**	**16-21**	**≥22**	**< 13**	**13-15**	**16-21**	**≥22**
Sex								
Men	1133 (54)	271 (13)	446 (21)	259 (12)	343 (51)	103 (15)	153 (23)	79 (12)
Women	1828 (36)	675 (13)	1421 (28)	1158 (23)	535 (37)	222 (15)	394 (27)	291 (20)
Age groups								
18-29 years	22 (12)	12 (6)	54 (29)	95 (52)	5 (20)	3 (13)	4 (16)	13 (51)
30-44 years	160 (17)	106 (11)	269 (29)	398 (43)	68 (26)	36 (14)	75 (28)	85 (32)
45-59 years	770 (33)	349 (15)	735 (32)	475 (20)	288 (36)	136 (17)	231 (29)	152 (19)
60-74 years	1522 (51)	383 (13)	684 (23)	382 (13)	419 (48)	133 (15)	207 (24)	106 (12)
≥75 years	486 (63)	96 (12)	125 (16)	67 (9)	98 (61)	17 (11)	30 (19)	15 (10)
Cancer type								
Melanoma	89 (31)	42 (15)	90 (31)	66 (23)				
Lung cancer	56 (32)	16 (9)	35 (20)	67 (38)	35 (31)	18 (16)	38 (34)	22 (20)
Breast cancer	1332 (37)	497 (14)	1005 (28)	778 (22)	351 (40)	143 (16)	245 (28)	140 (16)
Thyroid cancer	3 (8)	6 (15)	8 (19)	23 (59)				
Colorectal cancer	335 (50)	88 (13)	148 (22)	105 (16)	203 (52)	49 (13)	91 (23)	48 (12)
Endometrial cancer	123 (61)	24 (12)	34 (17)	22 (11)	15 (38)	9 (23)	8 (21)	8 (19)
Leukaemia & non-Hodgkin lymphoma	15 (20)	10 (13)	25 (33)	27 (35)				
Prostate cancer	745 (63)	145 (12)	201 (17)	83 (7)	158 (54)	49 (17)	57 (20)	27 (9)
Other cancer types	115 (27)	43 (10)	138 (32)	133 (31)	111 (29)	55 (14)	100 (26)	114 (30)
Time since cancer diagnosis								
0-1 years	1053 (41)	355 (14)	669 (26)	501 (19)	487 (44)	162 (15)	285 (26)	171 (15)
2-5 years	1287 (41)	409 (13)	817 (26)	617 (20)	274 (39)	120 (17)	175 (25)	141 (20)
6-10 years	426 (41)	131 (13)	273 (26)	204 (20)	83 (38)	29 (13)	59 (27)	46 (21)
>10 years	194 (44)	51 (11)	109 (24)	91 (21)	33 (37)	14 (15)	28 (30)	17 (18)
Continent where study was conducted								
Asia	451 (49)	116 (13)	235 (26)	112 (12)	251 (40)	87 (14)	166 (26)	127 (20)
Australia	174 (34)	78 (15)	156 (30)	111 (21)				
Europe	1115 (41)	380 (14)	758 (28)	480 (18)	96 (46)	27 (13)	55 (26)	29 (14)
North America	1221 (40)	372 (12)	718 (24)	713 (24)	531 (41)	212 (16)	326 (25)	215 (17)

Groups with less than 10 participants were omitted. All data were imputed, except the cancer type variable, since its imputation did not converge.

Table 3. Mean FCR severity scores stratified by clinical and demographic characteristics.

	Survivors		Patients	
	n	Mean (CI)	n	Mean (CI)
Total	7190	14.3 (13.0-15.5)	2121	16.2 (15.6-16.8)
Sex				
Men	2108	13.0 (11.8-14.1)	678	14.6 (13.8-15.4)
Women	5082	15.1 (14.6-15.5)	1443	16.3 (14.2-18.5)
Age groups				
18-29 years	183	16.9 (15.2-18.7)	25	17.0 (13.6-20.4)
30-44 years	933	16.8 (15.4-18.3)	264	17.9 (9.6-26.3)
45-59 years	2329	15.5 (13.9-17)	807	16.9 (8.6-25.3)
60-74 years	2970	13.2 (11.6-14.7)	865	14.8 (6.5-23.1)
≥75 years	775	10.9 (9.3-12.6)	161	12.6 (4-21.2)
Cancer type				
Melanoma	302	16.2 (13.5-18.9)		
Lung cancer	175	15.5 (14.4-16.7)	114	16.8 (13-20.5)
Breast cancer	3675	15.0 (13.8-16.2)	883	15.5 (14.7-16.2)
Thyroid cancer	40	14.2 (11.8-16.6)		
Colorectal cancer	697	14.1 (13.4-14.9)	395	15.2 (12.2-18.3)
Endometrial cancer	247	12.0 (9.8-14.3)	40	16.3 (7.1-25.5)
Leukaemia & non-Hodgkin lymphoma	77	11.4 (9.6-13.1)		
Prostate cancer	1191	11.2 (10.6-11.9)	293	12.6 (10-15.2)
Other cancer types	452	13.9 (13-14.9)	381	16.7 (13.1-20.3)
Time since cancer diagnosis				
0-1 years since diagnosis	2577	14.7 (13.1-16.4)	1105	15.8 (14.5-17.1)
2-5 years since diagnosis	3130	14.1 (12.2-16)	710	16.3 (11.5-21)
6-10 years since diagnosis	1034	14.2 (11.8-16.5)	218	16 (10.4-21.7)
>10 years since diagnosis	445	13.4 (9.9-16.9)	92	16.9 (9.3-24.4)
Continent where study was conducted				
Asia	915	13.0 (8.3-17.8)	631	14.3 (3.4-25.2)
Australia	519	15.4 (11.4-19.4)		
Europe	2733	14.0 (10.7-17.3)	206	15.7 (6.1-25.2)
North America	3023	15.0 (12.8-17.3)	1284	17.0 (16.4-17.6)

All data was imputed, except the Cancer type variable, since its imputation did not converge.

Associations with FCR severity

We assessed the statistical significance of the associations between FCR severity and the included variables using multilevel regression analyses, whereby all variables were analyzed in the same model. The reference categories were men, breast cancer and North America. Separate models were made for survivors and patients.

For survivors, statistically significant associations were found between FCR severity and age (β=-0.16, p<.001), sex (β=1.18, p<0.01), endometrial cancer (β=-3.02, p<0.01), leukemia and non-Hodgkin lymphoma (β=-2.77, p<0.05) and prostate cancer (β=-1.36, p<0.05). For continent where the study was conducted, there was only a significant association with Asia (β=-2.78, p<0.05). There were no significant associations with time since cancer diagnosis. The explained variance (R^2) of the model with all the factors was .19.

For patients, there were significant associations between FCR severity and age (β=-0.10, p<.001), sex (β=1.38, p=0.01), colorectal cancer (β=1.58, p<0.05), lung cancer (β=3.02, p<0.001), and the group of "other cancer types" (β=4.06, p<0.001). There were no significant associations with time since cancer diagnosis and continent where the study was conducted. The explained variance (R^2) of the model with all the factors was .14.

Characteristics of groups according to FCRI-SF cut-off scores

To inform those who wish to address a specific FCR severity group – for example, when designing an intervention for the group scoring above one of the cut-offs – we present the characteristics of each FCR severity group in Supplementary Materials 2D. For this analysis, 12 additional studies were included, namely those who selected respondents based on the severity of their FCR.

The two highest FCR severity groups (scoring 16-21 and ≥22 on the FCRI-SF) had the following characteristics: approximately three-quarters of respondents were women; approximately three-quarters were aged between 45 and 74 years; approximately 60% of survivors and 45% of patients had breast cancer; and about 90% of patients and 80% of survivors had been diagnosed with cancer within the past 5 years.

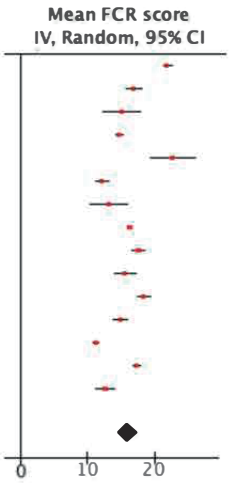
Aggregate data analysis

To compare the results of the data we collected in our IPD analysis with the studies that did not provide data, we conducted an aggregate data analysis. In the aggregate data analysis, we included all studies that did not provide data, that did not select participants based on their level of FCR and that reported data on a) mean FCR severity score, and/or b) percentage of participants scoring ≥ 13. The combined mean FCR score was 16.1 (14.4-17.7), compared with 14.3 for survivors and 16.2 for patients in the IPD analysis. The percentage of participants scoring ≥13 was 50.6% in the aggregate data analysis, which was 8.2% lower than the percentage in the IPD analysis.

Table 5. Aggregate data analysis of a) mean FCR severity scores and b) percentage of respondents scoring ≥ 13.

a)

Study or Subgroup	Mean FCR score	SE	Mean FCR score IV, Random, 95% CI
Bateni 2019	21.94	0.33	21.94 [21.29, 22.59]
Dieng 2016	17	0.6	17.00 [15.82, 18.18]
Dodds 2015	15.14	1.42	15.14 [12.36, 17.92]
Galica 2018	14.78	0.24	14.78 [14.31, 15.25]
Galica 2020	22.8	1.68	22.80 [19.51, 26.09]
Hong 2020	12.21	0.5	12.21 [11.23, 13.19]
Kasparian 2016	13.28	1.43	13.28 [10.48, 16.08]
Leclair 2019	16.38	0.16	16.38 [16.07, 16.69]
Merckaert 2017	17.66	0.52	17.66 [16.64, 18.68]
Nelson 2018	15.67	0.88	15.67 [13.95, 17.39]
Peng 2019	18.39	0.5	18.39 [17.41, 19.37]
Petzel 2012	14.9	0.51	14.90 [13.90, 15.90]
Shin 2020	11.2	0.2	11.20 [10.81, 11.59]
Tesson 2017	17.4	0.3	17.40 [16.81, 17.99]
Walburg 2019	12.7	0.71	12.70 [11.31, 14.09]
Total (95% CI)			**16.05 [14.39, 17.71]**



b)

Author (publication year)	n	% scoring ≥ 13
Costa, D. S. J., et al. (2016)	286	72
Dieng, M., et al. (2016)	164	68
Galica, J., et al. (2020)	15	93
Herman, S., et al. (2014)	242	85
Kasparian, N. A., et al. (2016)	19	32
Peng, L., et al. (2019)	207	77
Petzel, M. Q. B., et al. (2012)	224	34
Shun, S. C., et al. (2018)	97	55
Smith, T. G., et al. (2019)	2107	39
Thewes, B., et al. (2012)	218	70
Van Liew, J. R., et al. (2014)	138	60
Walburg, V., et al. (2019)	108	44

DISCUSSION

Main findings

In this sizeable international IPD meta-analysis, we found that more than half (59%) of cancer survivors and patients report at least a moderate level of FCR (FCRI-SF ≥13) and that about 1 in 5 (19%) experience a high level of FCR (FCRI-SF ≥22), indicative of a need for specialized intervention. There were no major differences between survivors and patients in the prevalence of FCR. FCR was consistently more prevalent among women and younger respondents. While FCR affects survivors and patients across cancer types, on average,

participants with lung cancer and melanoma reported the highest scores and participants with prostate cancer reported the lowest scores; although it is important to note that not all cancer types were represented. FCR is also experienced across continents and at all time points since cancer diagnosis. Our IPD results are comparable to the results of our aggregate data analysis and to a recent meta-analysis which found 53.9% scored ≥13, 43.3% ≥16 and 30% ≥22.[23] The higher percentage scoring ≥22 in the meta-analysis is most likely due to a difference in inclusion criteria. In the present study, studies that selected patients based on their level of FCR were excluded, while in the recent meta-analysis these studies were included.

In the regression analyses, significant associations were found between FCR severity and age and sex for both survivors and patients, with younger patients and women reporting higher FCR levels. This is consistent with earlier findings.[3,9,20,21] Regarding cancer types, with breast cancer as the reference category, patients with lung cancer and colorectal cancer reported significantly higher levels of FCR, and survivors with endometrial cancer, prostate cancer, and leukemia and non-Hodgkin lymphoma reported significantly lower levels of FCR. Thus, some observed differences in prevalence between cancer types are not reflected by significant associations. In these cases, the difference in prevalence may be explained by other variables (e.g., age). Also, for some cancer types, the number of participants was relatively low, and there could be sampling bias. No significant associations were found for time since cancer diagnosis, which is in line with previous research,[7] suggesting that without intervention or treatment, FCR likely persists over time. For survivors, FCR was somewhat lower for respondents from Asia. While we have no clear explanation for this, it could be due to cultural differences in the experience or self-reporting of FCR.

We also explored the characteristics of respondents *within* each FCR severity group, to inform people who aim to target a specific group. The two highest FCR severity groups (16-21 and ≥22) had the following characteristics: most respondents were aged between 45-74 years, most were women, most were within five years since diagnosis, and about half had breast cancer. Notably, these results are affected by the characteristics of the participants in the included studies.

Study limitations

A major strength of the present study is the large amount of data included in the analyses; 46 datasets including data from 11,226 respondents from 13 countries. There were also 41 studies with 14,381 respondents that did not provide data. 24 of these studies could be included in the aggregate data analysis which found similar results to the IPD analysis.

Some limitations should also be noted, for instance the underrepresentation of some groups. There were no studies from South America or Africa and very few from low and

middle-income countries (LMICs). Also, survivors and patients aged ≥70 years were underrepresented. In our sample, 23% of survivors were aged ≥70 years and only 3% were aged ≥80 years, while for example in the USA, 49% of cancer survivors are aged ≥70 years and 21% are aged ≥80 years.[95] Underrepresentation of the elderly is a common issue in cancer research.[96] Considering that the prevalence of FCR is low in this age group, caution needs to be taken when extrapolating our findings on prevalence of FCR to the cancer population as a whole.

Another limitation relates to the use of FCRI-SF scores as a measure of FCR: FCRI-SF scores do not reflect all key characteristics of clinical FCR,[13] since hyper-alertness to bodily symptoms is not included.[23]

Finally, the severity of one's FCR may affect interest in participating in studies on FCR. In one FCR intervention study that did not select on FCR levels, it was found that older patients and patients with less FCR were less likely to participate.[64] On the other hand, patients who use avoidance to cope with high FCR may be less likely to participate.

Clinical implications

As we have shown, FCR is a highly prevalent concern, affecting more than half of cancer survivors and patients. Consequently, this is an issue that needs to be addressed by healthcare providers and policy makers. We recommend providing brief psychoeducation about FCR to all cancer survivors and patients, to normalize FCR and help individuals seek support when they need it, even if they are no longer undergoing hospital-based treatment or surveillance. Due to the high prevalence of FCR, psychoeducation for all may be more effective than screening. An example of a brief psychoeducational program is a recently piloted intervention including normalization, prognostic information, recurrence symptoms education, advice on managing worry and if FCR was high, referral to a psycho-oncologist.[97] Since FCR exists at all times since cancer diagnosis, we also recommend discussing FCR on multiple occasions.

Also, the best way to address FCR still needs to be investigated. Additional research is needed to identify which patients desire support and how to tailor interventions to different levels of FCR and to individual needs and preferences.[17] While current interventions are often face-to-face and specialist led,[17] accessible, low-resource programs (e.g., online or group therapy) may be fitting for the group with moderate FCR (FCRI-SF scores between 13 and 22) and can be more easily scaled.

Implications for future research

We have identified several medical and demographic factors that are associated with fear, but in agreement with previous research, these factors only explain a limited proportion of

the variance in FCR severity.[98] Therefore, there may be other important factors. We recommend investigating the role of other factors, such as cancer stage, type of treatment and psychosocial factors, including prior and current psychiatric disorders. Also, we recommend investigating the prevalence of FCR in understudied cancer types, such as thyroid cancer and hematological cancers, understudied regions of the world, including South America, Africa and LMICs, and understudied groups, such as racial and ethnic minority groups. Furthermore, to increase comparability between studies, we recommend for researchers to report proportions above both the 13 and 22 cut-offs, when reporting FCRI-SF data.

Finally, since FCR is a multidimensional construct and since these dimensions are captured by the FCRI, future research could explore more deeply what the characteristics of this fear are and how different aspects of the fear relate to each other, including the role of triggers, coping styles, and social circumstances. Differences between patient groups or even individual patients could be explored, in order to target interventions and help people suffering from FCR better.

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3

Patient reported needs for coping with worry or fear about cancer recurrence and the extent to which they are being met, a survey study

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Published in Journal of Cancer Survivorsip in 2022.

ABSTRACT

Purpose: Many cancer patients and survivors experience fear or worry about cancer recurrence (FCR). Evidence suggests support for FCR is their largest unmet need. We aimed to assess which types of support are needed, which providers are preferred and to what extent patients' needs are being met.

Methods: Together with the Dutch Federation of Cancer Patient Organizations (NFK) a purpose-designed questionnaire was distributed online via e-mail, newsletters, and social media. All questions were multiple choice or Likert scales, except for an open-ended question about the preferred provider of care.

Results: Out of 5,323 respondents, 4,511 had experienced FCR and were included. Among them, 94% indicated a need for support. The required types of support that were reported the most were talking about FCR (69%), enjoyable activities for distraction (56%) and psychological help or counselling (40%). On average, younger respondents and women wanted more support than older respondents and men. 85% of respondents received at least one type of support they wanted. Practical tips about FCR and additional medical check-ups were most often missed. Social contacts provided an important part of support, especially with talking and distracting activities. For other types of support, respondents usually preferred professionals.

Conclusions: Almost all patients who experience FCR have a need for support. Even though most receive some support, several gaps remain.

Implications for cancer survivors: Many report an unmet need for psychological help or practical tips about FCR. We recommend for healthcare providers to discuss FCR with patients and inform them about the support available .

Keywords: fear of cancer recurrence, needs, oncology, cancer survivorship

INTRODUCTION

Due to longevity and improved treatments, the number of cancer patients and survivors is increasing.[1] In an individual participant data meta-analysis of 46 studies, 58.9% of cancer patients and survivors experienced fear of cancer recurrence (FCR).[2] FCR is defined as 'fear, worry, or concern relating to the possibility that cancer will come back or progress'.[3] In several studies, FCR is listed as the most common problem and the largest unmet need.[4–7] Whilst effective programs and treatments exist,[8] it is unclear whether these match patient needs and whether they always reach patients.

To add to the complexity, not all patients who experience FCR want or require help[9-11] and the association between measured distress and subjective need for psychological help is limited.[12] In one study, only 36% of distressed patients had a desire for help[13], in another study 49%.[14] In a review of 53 studies (n=12,323), nearly half of cancer patients and survivors who were offered a psychological intervention did not accept it. Notably, patients who were identified in screening as being distressed were less likely to accept interventions than other patients.[15] In addition, in another study, one fourth of those who in screening did not score high on distress did want help.[10] Also, some patients only experience FCR when it is triggered, e.g. by medical check-ups, and not the rest of the time.[16,17] Therefore, screening alone may not be enough to identify patients in need of help.[10,15]

Ideally, patients receive the type and intensity of care that matches their needs and that prevents a larger care need in the future. Studies have shown there is a need for help for FCR [6] by asking patients to rate items such as, "I need help to manage my concerns about the cancer coming back".[18] However, they do not specify what kind of help is needed, nor who can best provide this help. Most intervention studies focus on high intensity, psychological care,[19] whilst some patients may be helped by low intensity support or a supportive social network. Exploring alternatives to specialized care can help to provide appropriate care to more patients, especially considering that the implementation of psychological interventions is complex and costly.[20,21]

We aimed to explore the variety of patient needs for both professional and non-professional support for FCR. We aimed to assess which types of support are needed, which providers are preferred, and to what extent patients' needs are currently being met.

METHODS

In December 2021, the Dutch Federation of Cancer Patient Organisations (NFK in Dutch) distributed a questionnaire about FCR. NFK is an umbrella organisation uniting 19 cancer patient organisations in the Netherlands.

Eligibility criteria

The questionnaire was open to all adult (≥ 18 years) cancer patients and survivors. However, patients were excluded from the analyses if they never experienced FCR.

For most of the results section, only the respondents who had FCR at the time of the questionnaire were included, since this population best reflects the population in potential need of FCR support, without recall bias influencing outcomes. In the sections 'Treatment phase in which FCR was experienced' and 'Support received', respondents who *previously* had FCR were also included. As these sections describe the development of FCR over time and the effect of receiving support, including these participants contributes towards a more complete picture.

Data collection

A questionnaire was developed by a working group with members from NFK, patient representatives and experts in the fields of primary care and psycho-oncology from the Julius Centre for Health Sciences and Primary Care and from the Helen Dowling Institute, an academic mental health institute specialised in cancer-related psychological problems. After the working group specified the objectives, NFK designed a first draft of the questionnaire, which was further improved by the group. To limit the length of the questionnaire, it was decided not to use validated measures for FCR. Instead, a single item rating the level of FCR from 1-10 was used. The questionnaire was introduced by stating that cancer can lead to worry or fear and that the researchers want to learn more about this, in order to improve care for those with FCR. It was also stated that any adult who currently or previously had cancer could participate, regardless of whether they have experienced FCR or not. The questionnaire was distributed online between November 30 and December 14, 2021, via e-mail, newsletters, and social media by NFK, affiliated cancer organizations, the Dutch Cancer Society, the website kanker.nl, the Helen Dowling Institute and several hospitals. The questionnaire was also sent to NFK's patient panel, which regularly fills out questionnaires. Respondents participated anonymously in the survey.

The following background information was collected in the survey: gender, age, education status, heredity of cancer, family situation, treatment status, cancer status, cancer type, time since diagnosis and general fearfulness before cancer, as reported by the respondent.

Regarding their FCR, respondents filled out questions about the stages in which they experienced FCR and about the content, triggers, and consequences of their FCR. FCR was always phrased as 'worry or fear about cancer recurrence'. Concerning need for support, respondents answered questions about the type of support that was needed, the preferred provider, whether they received the support and, if so, whether it helped. All questions were closed-ended (multiple choice or Likert scales), including, where relevant,

an 'other' category. The only exception is the question about who respondents would like to receive support from, which was open-ended. The full questionnaire can be found in Supplementary Materials 3A.

Data analysis

We report descriptive statistics, including means and percentages. The type of support that was needed was also calculated for different subgroups, based on age, gender, family situation, general level of fear, treatment phase, expressions of FCR and consequences of FCR. We also compared the need for support between subgroups (e.g., men vs. women). Due to the large percentage of respondents requiring help, we calculated the mean percentage across support types. As statistical significance is easily reached with our large sample size (including for clinically irrelevant differences) and since we aim to reflect clinical relevance and applicability, we report percentages and did not perform statistical testing.

The open-ended question about who respondents would like to receive support from was answered separately for each type of support. Based on the answers, the responses were grouped into three categories: professionals, social contacts and other. Professionals consisted of the following sub-categories: general practitioners, specialists, nurses, psychological care, and other professional caregivers. There were myriad types of 'other professional caregivers' including social workers, physiotherapists, dieticians, spiritual counsellors and haptotherapists. Social contacts consisted of partners, family and friends, and other contacts. Other consisted of (online) tools, patient organizations, and fellow patients.

No imputation was applied. All analyses were done in R 3.6.3.[22]

RESULTS

Out of 5,323 respondents, 812 (15%) had never experienced FCR and were excluded. Of the remaining 4,511 respondents, 3,178 (70%) had FCR at the time of the questionnaire and were included for all analyses. 1,333 (30%) respondents previously had FCR, but not at the time of the questionnaire. These respondents were included only for the sections FCR and treatment phase' and 'Support received'.

Demographics

The sample of patients who had FCR at the time of the questionnaire consisted of 2,331 (73%) women and 845 (27%) men. The average age was 59 (SD ±11). Two thirds had completed treatment at the time of the survey and three quarters had a partner. For further demographic and medical information, see Table 1.

Table 1: Demographic and medical information of respondents who had FCR at the time of the questionnaire.

	n (%)
Gender	
Men	845 (27)
Women	2331 (73)
Other	2 (0)
Education status	
No education	8 (0)
Practical education	434 (14)
Secondary education	1130 (36)
Higher education	1550 (49)
Other	11 (0)
Family situation	
Living together	1494 (47)
Living together with children	946 (31)
Living alone	496 (16)
Living alone with children	180 (6)
Cancer type	
Breast cancer	1754 (33)
Haematological and lymphatic cancers	840 (16)
Prostate cancer	716 (14)
Colorectal cancer	606 (11)
Urogynaecological cancer	492 (9)
Lung cancer	183 (3)
Skin cancer	141 (3)
Stomach/oesophageal cancer	113 (2)
Other	478 (9)
Hereditary cancer	
Yes	129 (4)
No, but common in family	498 (16)
No, not that I'm aware of	2551 (80)
Treatment status	
Currently in treatment	1041 (33)
Treatment not yet started	47 (1)
Wait-and-see	159 (5)
Treatment completed, but still check-ups	1590 (50)
Treatment completed, no more check-ups	341 (11)
Cancer status	
No cancer anymore	1726 (54)
Curable cancer	265 (8)
Incurable cancer	986 (31)
Do not know	201 (6)

Table 1: Demographic and medical information of respondents who had FCR at the time of the questionnaire. (*continued*)

	n (%)
Time since diagnosis	
0-2 years	1263 (40)
3-5 years	850 (27)
6-10 years	619 (20)
10+ years	421 (13)
General fearfulness before cancer (1-10)	
1-3	2156 (68)
4-5	437 (14)
6-7	347 (11)
8-10	238 (8)

Fear of cancer recurrence

FCR and treatment phase

Of the participants who had FCR at the time of the questionnaire, 2,028 (64%) had had FCR since the diagnosis and for 1,150 (36%) it started at a later stage.

The percentage of respondents reporting high FCR (8-10 on a scale of 10) is highest around diagnosis (60%) and decreases with each following phase. The percentage experiencing low FCR (1-3 on scale of 10) was 10% around diagnosis, 9% between diagnosis and treatment, 12% during treatment, 16% shortly after the end of treatment and 23% longer than one year after treatment. Figure 1 shows the development of FCR severity in the different treatment phases.

Triggers for FCR

The most reported triggers were medical examinations, such as blood tests or scans (68%), physical symptoms or being ill (63%) and thinking about the future (51%). The remaining triggers, in order from most to least reported, were reading or talking about chances of recurrence or death (43%), healthcare appointments in general (28%), hearing about cancer from people around me (27%) and physical self-examination (15%). Only 2% of respondents stated there were no specific triggers for their FCR.

Content of FCR

When asked what people are afraid of, all topics included in the multiple-choice question were selected by at least 75%. These topics were: consequences of cancer or treatment for partner (reported by 98%) and for self (97%), having to go through treatment again (95%), incurable metastases and dying (93%), recurrence in a different area (92%), consequences of cancer or treatment for children (83%) and for others (80%) and recurrence in the same area (75%). The average amount of FCR experienced was rated around 6.5 on a scale of

ten for all topics except dying, which was rated 7.3, and incurable metastases, which was rated 5.1.

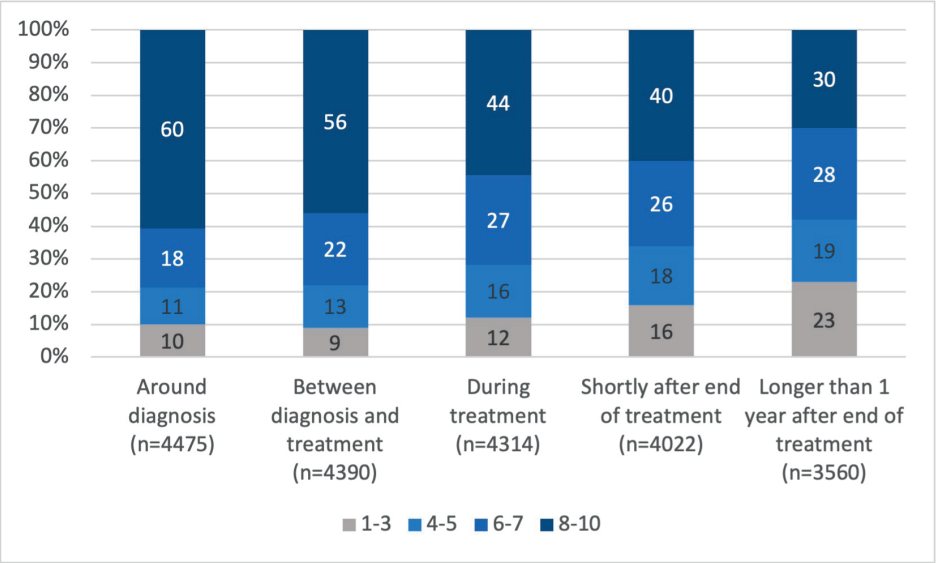

Figure 1: Overview of the percentage of respondents that experienced different levels of FCR in different treatment phases. N.B. the different totals are due to some patients not yet having started or completed treatment at the time of the questionnaire.

Expressions of FCR

The most reported expressions of FCR were rumination (67%), nervousness (55%) and poor sleeping (53%). In addition, some respondents experience sadness (35%), inability to concentrate (35%), irritability (33%), listlessness (21%), physical complaints such as headaches (20%), a changed eating pattern (18%), increased heartrate (15%), tingling in hands or feet (12%), panic attacks (12%) or other consequences (8%). On average, respondents report 3.8 (SD=2.2) of these expressions; 2.6% report none.

Consequences of FCR

The most reported consequences of FCR are difficulties with sex or intimacy (55%), less enjoyment of things previously enjoyed (52%), fewer social activities (46%), inability to do work or volunteer work (45%), difficulties with daily activities (42%) and inability to do hobbies (42%). In addition, some have tensions within the family (24%), relationship problems (18%) and a less healthy lifestyle (10%). On average, respondents have 2.9 (SD=2.2) of these consequences; 18% have none.

The average negative influence of FCR on quality of life was rated 6.2 (SD=2.3) on a scale of ten.

Patient preferences for type of support

Needed types of support and preferred providers

The percentages of respondents who need different support types are presented in Table 2. The types of support that are most often needed are talking about FCR (69%), enjoyable activities for distraction (56%), and psychological help or coaching (40%). In addition, about one third report a need for practical tips about managing FCR (36%) and information about FCR (30%). Only 6% has no need for support. For talking about FCR and enjoyable activities for distraction, respondents mostly prefer social contacts (68% and 77% respectively) although 41% also want to talk to professionals. For the other types of support, respondents mostly prefer professionals (see Table 2).

Table 2: Numbers and percentages of respondents who want to receive different types of support, and, within those groups, numbers and percentages of those who want to receive it from professionals, social contacts and others. These groups are defined in the methods section.

	Total (%)	professionals (%)*	social contacts (%)*	other (%)*
Talking about FCR	2185 (69)	872 (41)	1440 (68)	257 (12)
Enjoyable activities for distraction	1785 (56)	32 (2)	1296 (77)	22 (1)
Psychological help or coaching	1285 (40)	1062 (86)	50 (4)	32 (3)
Practical tips about managing FCR for self	1144 (36)	790 (75)	70 (7)	124 (12)
Information about FCR	960 (30)	753 (84)	31 (3)	90 (10)
Additional medical check-ups	695 (22)	539 (82)	13 (2)	1 (0)
Practical tips about managing FCR for environment	521 (16)	332 (72)	43 (9)	49 (11)
Lifestyle support	476 (15)	331 (74)	43 (1)	14 (3)
Medication	462 (15)	308 (71)	4 (1)	0 (0)
No need for support	204 (6)	-	-	-
Other	267 (8)	-	-	-

*The percentages do not add up to 100%, because respondents could list multiple providers and some also did not list any.

In the following paragraph, all percentages are proportions of the group that wants a certain type of support. Most respondents who want to talk, want to talk to family (44%) or their partner (38%). Some want to talk to fellow patients (12%), a specialist (11%), their GP (10%) or a psychological care provider (9%). Respondents prefer receiving psychological help or coaching from psychological care professionals (55%) and some from other caregivers (19%) or their GP (8%). Respondents prefer receiving practical tips about managing FCR from psychological care professionals (21%), specialists (11%), other caregivers (11%) or fellow patients (8%). Respondents prefer receiving information about FCR from specialists (45%) or in some cases a nurse (13%) or GP (12%). For additional medical check-ups, most respondents prefer seeing a specialist (55%) and some a GP (12%) or nurse (7%).

Respondents prefer receiving support for a healthy lifestyle from other professional caregivers (50%) or psychological care professionals (14%). The preferred provider of medication is most often the GP (46%).

Differences between subgroups

The number and percentage of respondents who need the different support types are presented per age group, gender, family situation, level of general fearfulness before cancer, treatment phase, FCR expressions and FCR consequences in Supplementary Materials 3B.

Younger respondents report a greater need for support. For example, averaging across the different support types, 18% more of the 20-40 age group than the 70+ age group needs support. The difference is especially great for psychological help or coaching, which is needed by 64% of the 20-40 group compared to 20% of the 70+ group.

On average, more women than men need support. The difference is greatest for psychological help or coaching and for enjoyable activities for distraction. Only the need for practical tips for the environment is the same in both groups. Notably, part of the difference between the genders is explained by the younger age of the women than the men in our sample.

The difference in care needs between respondents with different family situations, treatment phases and levels of general fearfulness are small (see Supplementary Materials 3B). Respondents with more expressions of FCR, report a greater need for all types of support. Also, respondents with more consequences of FCR report a greater need for all types of support except distracting activities. There are few differences between the type of expressions or consequences and the type of support needed. More of those with panic attacks need psychological help or coaching (61% vs 38%), medication (32% vs 12%) and/or practical tips about managing FCR for self (53% vs 36%) or their environment (25% vs 15%). Also, more of those who have relationship problems need psychological help or coaching (60% vs 37%).

Notably, age, family situation and treatment phase at the time of the questionnaire may not always have been the same as when the care need was experienced.

Support received

Among those who experienced FCR at the time of the questionnaire or previously, 85% of respondents received at least one type of support they needed. If support was received, it usually helped (91%). Table 3 shows whether the different types of support were received and helped. Overall, most needs for enjoyable activities for distraction (88%), talking (82%), medication (78%) and psychological help or coaching (69%) were fulfilled and

helped. Practical tips about managing FCR for both self (41%) and respondents' environment (49%) and additional medical check-ups (45%) were often missed.

Table 3: Numbers and percentages of respondents who need different support types who did and did not receive them and for whom this did or did not help.

	Did not receive support	Received support, and this helped	Received support, but this did not help
Talking about FCR	342 (11)	2459 (82)	207 (7)
Enjoyable activities for distraction	204 (9)	2083 (88)	68 (3)
Psychological help or coaching	340 (21)	1096 (69)	156 (10)
Practical tips about managing FCR for self	573 (41)	697 (50)	111 (8)
Information about FCR	389 (31)	765 (61)	100 (8)
Additional medical check-ups	387 (45)	410 (48)	60 (7)
Practical tips about managing FCR for environment	318 (49)	292 (45)	38 (6)
Lifestyle support	218 (35)	341 (55)	61 (10)
Medication	80 (14)	446 (78)	47 (8)

DISCUSSION

Most patients with FCR need support. FCR is most common around diagnosis and becomes less prevalent with every following phase. Nonetheless, more than 1 year after treatment ended, 58% of those who experienced FCR at some point in their cancer journey still scored 6 or higher on a scale of ten. 94% of respondents with FCR want support. The kinds of support that are most needed are talking about FCR, enjoyable activities for distraction and psychological help or coaching. The first two support types, patients mostly want from social contacts, though 41% also want to talk to professionals. The remaining support types, patients want from professionals. In accordance with other studies, younger respondents and women on average were found to need more support.[10,23,24] They also experience a higher level of FCR.[2] Notably, since respondents could select more than one preferred support type, higher percentages needing support could be partly explained by a greater diversity in preferred types of support rather than a higher need for support. Comparing care needs between different family situations, treatment phases, levels of general fearfulness, FCR expressions and FCR consequences, we found that most differences are small. One exception is the need for psychological help or coaching. More of the respondents with children, panic attacks or relationship problems and more of those scoring 4-7 on general fearfulness expressed a need for this. More of those with panic attacks also need medication and/or practical tips. It is remarkable that more of those scoring 4-7 than 8-10 on general fearfulness need psychological help. This may have to do with those scoring higher already having received help or avoiding help.

85% of respondents received at least one type of support they needed. Especially talking and distracting activities were often received. Support that was received, usually also helped. Practical tips and additional medical check-ups were often missed.

Study limitations

This study has several limitations. Firstly, it is a survey study in which respondents answered questions about their needs. Yet, they may not know exactly what different types of support entail and what would help them the most. What they answer may also not be fully aligned with the type of support they would accept and seek out in practice. In addition, it may have been difficult for respondents to distinguish between the impact of the FCR and the impact of the cancer and its treatment. For example, poor sleeping, relationship difficulties and being unable to work can be caused by both FCR and cancer (treatments).

Secondly, the respondents may not have been entirely representative of all patients with FCR. The survey was distributed by a cancer patient organisation. People who are affiliated with cancer patient organizations may be more (pro)active than average, may experience more needs, and may also be more able to find support. In addition, in our sample there was an overrepresentation of women, some cancer types and people with higher education. These characteristics may affect the need for support, as well as the ability to find it.

Finally, the questionnaire was distributed during the COVID-19 pandemic. The pandemic may have made people more fearful. In addition, some healthcare appointments and treatments were postponed, and others were replaced by phone calls. This may have made people less confident they were receiving the best possible care and could increase FCR.

Clinical implications

Almost all cancer patients who experience FCR want some type of support. Fortunately, most respondents already received at least one type of support, and this support usually also helped. Social contacts provide an important part of this support. Talking about FCR and distracting activities are the most reported needs with most respondents preferring to receive these from social contacts. Other studies have also shown the importance of the social network, especially for social and psychological aspects.[25]

However, professional help is still needed. First, in our study, information about FCR, help with lifestyle and practical tips about FCR were often missed, and most preferred to receive these from professionals. Different patients preferred different types of professionals: some preferred psychological care professionals, others preferred medical specialists, nurses, GPs, or other caregivers. Professionals need to be supported to improve the

availability of these types of support. They can, for example, discuss these topics during consults or provide a brochure or website. Second, patients would like additional medical check-ups. Interestingly, medical examinations are also the most common trigger for FCR. We therefore recommend to discuss with patients whether additional check-ups would have clinical benefits and/or help to combat anxiety, or whether alternative strategies might be more helpful. Ankersmid et al. (2022) recommend shared decision-making about surveillance schedules to adapt them to patients' individual needs, preferences, and risks and to increase patients' comprehension and support of these schedules.[26]

Finally, whilst in our study four-fifths of those who wanted psychological help or coaching received it, one fifth did not. In another study, 41% did not receive it.[27] Therefore, it is recommended to increase the effort to make sure that patients know the available opportunities for psychological care in case they need and want it. Especially patients with children, panic attacks or relationship problems may need this help. Most respondents preferred to receive this type of help from a psychological care provider, some from another care provider. Stigma and accessibility might be reasons why patients prefer other care providers.[28] Notably, some patients may benefit from psychological care, but may not seek it. In one study, it was found that only 36% of distressed patients established contact with the psychosocial care team, although the team proactively reached out.[29] In another study, it was found that patients prefer to hear about psychological support from their oncologist and were more likely to follow their recommendation.[27,30] Sometimes, psychoeducation about risks and management opportunities may increase a desire for help[9] and can decrease stigmatization.[2,31]

CONCLUSION

Whilst this study shows a great need for support for FCR, it is encouraging that many respondents already found (part of) the support they needed. Room for improvement among professionals consists mostly of the provision of practical tips and information about FCR, shared decision making about the number of medical check-ups and increasing awareness about the availability and potential benefits of psychological help or coaching. Considering the variety of needs between patients and the fluctuations of FCR over time, we recommend healthcare providers to discuss FCR and the opportunities for support with all patients. We also recommend additional research on and implementation of low intensity types of support such as information and tips. These types of support are needed by many patients and are more economical and feasible to provide to large numbers of patients than specialized psychological care. Lastly, in order to match patients with the most suitable type of support, we recommend qualitative research to clarify what

people hope to obtain from different support types, and research on the effectiveness of different support types in meeting these needs.

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4

Study protocol of the BLANKET-trial: a cluster randomised controlled trial on the (cost-) effectiveness of a primary care intervention for fear of cancer recurrence in cancer survivors

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Published in BMJ Open in 2019.

ABSTRACT

Introduction: Many successfully treated cancer patients suffer from fear of cancer recurrence (FCR), affecting their quality of life and their physical, emotional, cognitive, and social functioning. Effective psychological interventions for FCR exist, but are not widely available, as they are typically offered by specialised psycho-oncology professionals and institutes. Concurrently, the role of primary care in cancer and survivorship care is increasing. Therefore, there could be a role for general practitioners (GP) and mental health workers (MHW) working in primary care in supporting patients with FCR. In the current study the effectiveness of a primary care delivered FCR intervention will be evaluated.

Methods and analysis: A two-armed cluster-randomised trial will be conducted. The primary outcome will be FCR severity; secondary outcomes will be FCR-related distress, healthcare uptake and healthcare costs. Primary care practices in the Netherlands will be invited to participate in the study. Participating practices will be stratified by size and socio-economic status and randomized. In the control arm, practices will provide care as usual. In the intervention arm, practices will offer the cognitive behavioural FCR intervention that is being studied, which consists of an intake with the GP and five sessions with the MHW. Patients who have finished successful curative treatment for cancer between 3 months and 10 years ago will be invited to participate in the study by invitation letter from their GPs. Participating patients fill out questionnaires at baseline, after three months and after twelve months. Data on healthcare use is collected from their electronic health records (EHR). Qualitative interviews are held at T1 with patients and practitioners in the intervention group.

Ethics and dissemination: The Medical Research Ethics Committee Utrecht provided approval for the study. Results will be dispersed through peer-reviewed publications and scientific presentations.

Trial registration: NL7573 in the Netherlands Trial Register on 25-02-2019.

Keywords: fear of cancer recurrence, primary care, psycho oncology, mental health worker

STRENGTHS AND LIMITATIONS OF THIS STUDY

- A robust, pragmatic trial design will be implemented in general practices, reflecting daily care.
- Quantitative and qualitative data are combined to provide comprehensive results.
- The intervention and trial were designed in close cooperation with patients and healthcare workers.
- A cluster randomised design, randomising at practice level, was required, since practitioners who have been trained on the intervention are unlikely to be able to provide usual care in the same way as before training.
- Patients are actively invited to participate in the study, making them less representative of the patients who currently seek care for FCR.

INTRODUCTION

Advances in the medical field have caused the number of cancer survivors to rise steadily in the past decades.[1] With an increasing number of survivors, there is also an increasing need for survivorship care.[2] A systematic review showed that fatigue, depression and anxiety are commonly reported in the ten years after primary cancer treatment.[3] Fear of cancer recurrence (FCR) is a more prevalent concern than any physical issue.[2] In a study about unmet needs after breast cancer, FCR was the most reported need in all age groups (38.2%), despite a relatively good prognosis.[4]

FCR has been defined as "fear, worry, or concern relating to the possibility that cancer will come back or progress".[5] A review by Simard (2013) found that an average of 73% of cancer survivors experience FCR, 49% experience a moderate to high level of FCR and 7% experience a high level of FCR.[6] FCR is a multidimensional construct, as demonstrated by the subscales of the Fear of Cancer Recurrence Inventory (FCRI): triggers, severity, psychological distress, coping strategies, functioning impairments, insight and reassurance.[7] FCR exists on a scale from normal to clinical.[8] In a 2-day colloquium with a group of experts and patient advocates, five preliminary categories of potential characteristics of clinical FCR were identified using the Delphi method. These are: preoccupation with cancer return or progression, unhelpful coping strategies, impairments in daily functioning, great level of distress and limited ability to make plans.[5]

Many studies have explored factors that correlate with FCR development, with mixed results. The evidence for correlations between FCR and age, gender and physical symptoms is strongest, whereby younger patients, female patients and patients with more symptoms experience more FCR.[6] In contrast, social support, optimism, having detailed information and being conscientious correlate with having less FCR.[6,9,10] Notably, associations between

FCR and psychological factors (e.g. metacognitions) are generally stronger than associations between FCR and demographic factors.[11] FCR can persist for many years after the end of cancer treatment.[6,12] There are also triggers that can temporarily increase FCR, including: medical appointments, having unexplainable symptoms and hearing about cancer in the media.[13]

The impact of FCR varies. Having some FCR can be protective, if it leads to treatment compliance and healthy lifestyle adaptations. However, severe FCR can significantly decrease quality of life.[14] Maladaptive coping styles include overuse of primary care for common acute symptoms, which can inadvertently augment fears and cause unnecessary healthcare costs,[15] but also avoidance of social and healthcare appointments, risking delayed diagnosis of cancer recurrence. On average, healthcare uptake is increased for people with high FCR.[16]

A Danish study found that patients discussed social or psychological aspects of cancer, including FCR, more with family and friends than with their GP, because they thought it was not the GP's mandate to address these concerns.[17] In a Dutch study, 75% of patients' physical problems after having received a cancer diagnosis were discussed with GPs, compared to only one third of emotional and social problems.[18] When the need for psychosocial care is recognised, this positively affects quality of life, appreciation of care, and communication with care providers.[19] Therefore, it seems of added value if GPs assess the presence of FCR and refer to additional care when needed.[20]

Treating FCR is different from treating other anxiety disorders, because FCR is not irrational, since the threat is actual and significant.[21] Currently, there are different treatment options for FCR, which can be applied in a stepped care approach. The first level involves psychoeducation, normalisation, and self-management. Next, cognitive behavioural therapy (CBT), therapies focusing on acceptance[22] and pharmacological treatment[23] can be applied. In recent years, several trials have shown the effectiveness of new FCR interventions,[24,25] including mindfulness programs,[26–28] psychoeducation,[29] cognitive behavioural therapy interventions,[30–32] an intervention based on metacognitive therapy[33] and a gratitude intervention.[34] The SWORD study found that blended treatment with a specialized psychologist and an online FCR program reduced FCR significantly more than usual care.[32]

Specialised psychological care for cancer is typically provided in hospitals and specialized institutes. Unfortunately, travel distance, limited energy of ex-cancer patients and waiting lists counteract accessibility.[35] Also, most cancer survivors do not require intensive specialised psychotherapy, but rather accessible psychological care. Online treatment is easily accessible and allows patients to obtain care when they feel fit enough and for a manageable duration. However, evidence for the effectiveness of completely self-guided

interventions among cancer patients with psychological distress is lacking. Some level of therapist involvement can help encourage engagement and promote adherence.[36]

Concurrently, cancer care and survivorship care are increasingly being provided in primary care, because of patient preference, increasing numbers of cancer patients and rising healthcare costs.[1] Primary care is comprehensive, longitudinal and integrated, provided by teams of different professionals,[1] increasingly including mental health professionals.[37] Primary care providers generally have a longstanding relation with the patient.[38,39] Patients view primary care staff as trusted professionals[40] and prefer coming to primary care for anxiety issues, because of practical reasons and stigma.[41] General practitioners want to provide psychosocial support to cancer patients and feel they are well-positioned,[42,43] but they face capacity challenges[44,45] and report a need for training on cancer survivorship,[46,47] in particular on treating psychological problems.[44] Involving and training auxiliary staff, such as primary care mental health workers (MHW, in Dutch POH-GGZ), in survivorship care, may help to overcome both capacity challenges and the need for improved expertise in primary care. [47]

The BLANKET study was designed to assess the effectiveness of a primary care delivered, blended care intervention for FCR, in reducing patients' severity of FCR, compared to usual care. Since this is a pragmatic trial, we include all patients who want care for FCR at their GP practice.

We hypothesise that
1. the FCR intervention will reduce FCR severity,
2. the FCR intervention will reduce FCR-related distress,
3. healthcare consumption of patients who have received the FCR intervention will be reduced,
4. the FCR intervention will be considered desirable and of added value by patients and practitioners.

The primary outcome is FCR severity. Secondary outcomes are FCR-related distress, FCR-related healthcare use, FCR-related health costs, and satisfaction of patients and practitioners with support provided by trained MHWs and GPs.

METHODS

Study design

The BLANKET study is a two-armed cluster randomised clinical trial, in which the general practice is the unit of randomisation.

Study procedure

Participating practices will identify all of their patients who have successfully completed curative cancer treatment between three months and ten years ago and will send them an invitation letter by mail. Patients are asked to participate if they desire support for FCR. After providing informed consent, patients are asked to fill out an online baseline questionnaire. Patients also fill out questionnaires 3 months and 12 months after baseline. At the end of the first questionnaire, they are urged to make an appointment with their GP about support for FCR. During this consultation, the GPs in the intervention group refer the patients to the MHW for the intervention, while GPs in the control group provide usual care.

Eligibility

Clusters of collaborating GPs and MHWs in the Netherlands who are willing to receive training and to implement it will be recruited. In the Dutch setting, almost all general practices employ MHWs[48]. Both a GP and an MHW need to agree to participate for the practice to be eligible to join the study.

Patients are eligible if they: (1) are registered at a general practice that is participating in the study, (2) are 18 years or older, (3) have finished successful curative cancer treatment between 3 months and 10 years ago, (4) desire support for FCR, and (5) have sufficient Dutch reading and writing skills to receive the intervention and complete the questionnaires. If patients have a cancer recurrence during the study, no more data will be collected. GPs select patients who can be invited for the study. GPs exclude vulnerable patients (e.g., severe psychiatric morbidity), who would be confused by the letter or unable to participate in the study.

Since this is a pragmatic real-world trial, we include all patients who want care for FCR at their GP practice. We chose not to screen for level of FCR as an inclusion criterion, because this would not reflect daily practice. This intervention could also be relevant for patients with non-clinical levels of FCR who are nonetheless limited by FCR in daily life. We will train the MHW to refer patients who require specialized psychological care.

Recruitment

The aim is to include 244 patients during 1,5 years. Patients are recruited using an invitation letter sent by patients' own GPs. All of the patients of participating practices, who are 18 years or older and have finished curative cancer treatment between 3 months and 10 years ago will receive the letter. To spread the workload for the practitioners, invitation will be done in rounds, starting with patients who most recently finished cancer treatment.

Randomisation

Randomisation is done at practice level. GPs and MHWs will know in which group they have been placed. Patients will not. Clusters are formed, in which all GPs and MHWs working in the same building are grouped together, to decrease the risk of contamination. Minimisation is applied for size of the practice and the socio-economic status (SES) of the neighbourhood they are located in, to ensure balance between study arms (patients and professionals). For practice size, there are three categories: small (1-3 GPs), middle-sized (4-6 GPs) or large (7 GPs or more). For SES, the list of disadvantaged areas by postal code made by the Dutch government for general practices is used. Practices will be assigned to the intervention or the control group, using the number generator at Research Randomizer (randomizer.org). An external data manager will generate the numbers. Practices are randomised in two blocks. The inclusion rate from the first block will help to confirm how many more practices are needed for the second block.

Intervention

GPs and MHWs in the intervention group will provide an intervention specifically designed for FCR, with online modules, which focus on normalisation, psychoeducation, and self-management.[49] The modules were developed at the Helen Dowling Institute based on CBT, clinical experience, and input from patients, and are currently being used by specialised psychologists for blended treatment. The intervention consists of three CBT modules, which include psychoeducation on FCR, and five optional modules on rumination, avoidance, relaxing, reassuring and undertaking activities. The FCRI is used to determine which optional modules are most important for each patient. Patients can also choose additional modules.

GPs in the intervention group will receive a 1-hour online training. MHWs in the intervention group will receive two 2-hour training sessions by an experienced clinical psychologist, including role plays with an actor playing a patient. The trainings will be about FCR and how to provide the intervention. In between sessions the MHWs will practice using the online modules, both as a patient and as a practitioner. In providing the intervention, the GP's role is to assess the need for care during an intake and to refer to the MHW. The MHW's role is to assign and discuss the modules with the patients during five contact moments. MHWs will openly listen to the patients' experiences, normalize fears, apply CBT, and discuss what was gained from the modules. Any related questions and issues that came up will also be discussed. GPs and MHWs in the control group will provide usual care.

Usual care

Patients in the control group receive usual care. In the literature, little is known about the usual care that GPs provide for FCR. Therefore, usual care will be mapped in this study, in relation to the severity of FCR.

Outcomes

Participants will provide data using online self-report questionnaires hosted by ResearchOnline.com. Participants will receive an invitational e-mail with a link to complete the questionnaires online. These links will be sent at baseline (T0), after three months, once the intervention in the intervention group is completed (T1), and one year after the baseline (T2). Participants who do not respond receive reminders. If participants prefer to fill out the questionnaires on paper, this will be arranged. If patients do not fill out the questionnaires, they are sent reminders.

The primary outcome is the severity of FCR after 3 months, comparing the FCR intervention with usual care. To measure this, the severity scale (SF) of the Dutch version of the Fear of Cancer Recurrence Inventory (FCRI-NL) will be used.

The secondary outcomes are the development from baseline to T1 to T2 of severity of FCR, FCR-related distress, FCR-related healthcare use and FCR-related health costs; and the desirability and added value of the intervention.

Covariates

If the intervention is found to be effective, relations between the outcomes and the following variables will be explored, to identify groups of patients for whom the intervention might be more or less effective.

At the patient level: age, gender, level of education, coping style, severity of anxiety and depression, somatic complaints, severity of FCR at the start of the study, FCR-related distress at the start of the study, psychiatric history, previous health care use, additional care used by patients (e.g., alternative care), time since the cancer diagnosis, time since the end of the curative cancer treatment, and cancer type.

At the practice level: general practice size and SES status of practice.

At the MHW level: number of years of work experience and educational background of the MHW.

Data collection

Patients will fill out the FCRI-NL. It contains 43 items, measuring seven subscales. The severity, distress and coping subscales will be used to measure FCR severity, distress, and

coping. The FCRI was translated into Dutch and validated by van Helmondt, van der Lee & de Vries.[50] While for the FCRI, it is recommended to use the total score of all subscales to obtain a score for FCR,[7] this multi-dimensional structure was not replicated in the validation of the FCRI-NL. Instead, the individual subscales provide important information and are recommended to be used separately.[50]

The 4DKL will be used to provide data on general distress, depression, anxiety, and somatic complaints. The 4DKL is a 50-item questionnaire that measures four dimensions: distress, depression, anxiety, and somatic complaints. The list is already used in some GP practices and is therefore practically applicable.

Patients will also be surveyed about their educational level, current daily activity (e.g., work), reasons for participating in the study, additional care used that is not in the electronic health records (EHR) including alternative care, and other factors that they think might have influenced their FCR.

In order to collect data on patients' cancer type, treatment and healthcare use, data will be obtained from patients' EHR. Data will be collected on number of GP visits related to cancer, FCR and neither, number of sessions with MHW and number of referrals for physical care and for psychological care. GP visits will only be considered FCR-related if FCR is specifically mentioned. Some patients may not mention FCR but have increased healthcare uptake due to hyper-vigilance. If that is the case, we expect the number of cancer-related visits to decrease if FCR decreases. At baseline, data on healthcare use per year since the end of curative cancer treatment will also be obtained, to exploratively compare usual care in our control group with usual care in the years prior to the study. FCR-related health costs will be calculated based on the healthcare use.

The desirability and added value of the intervention will be evaluated using custom-made, non-validated questionnaires and semi-structured interviews with a selection of patients and practitioners at T1. The interviews will explore which aspects of the support are effective, unnecessary, practical, or pleasant and why. They will also explore whether the GP and MHW are considered to be the right practitioners to provide this type of care and what changes with regard to FCR are most desirable and sought after. Varied groups will be purposively sampled. For patients, in terms of age, time since diagnosis, severity of FCR at T0, and severity of FCR at T1; for practitioners in terms of professional background and years of work experience.

Additional information about data collection, data management, monitoring and dissemination of results can be found in the trial master file.

Sample size calculation

When determining the required group size for finding a relevant difference between the groups, we used a difference in means of 3 and a standard deviation of 7 on the FCRI severity scale. The difference in means was based on expert opinion. The standard deviation was based on the FCRI-NL validation study by van Helmondt et al. (2017), which found an SD of 7 on the severity scale.[50] Using an alpha of 0.05 and beta of 0.8, we calculated a required sample size of 86 participants in both groups for sufficient power. Because multiple patients are treated by the same MHW, there might be a cluster effect. Based on an average of 15 inclusions per MHW and an intraclass correlation coefficient (ICC) of 0.01, an inflation factor of 1.14 has been applied. This leads to a group size of 98 patients per arm. Because the clusters (number of patients per MHW) will probably not all have the same size, an inflation factor of 10% is applied, leading to a group size of 108. We also assume a dropout of 12% of patients. That is why we aim to include 122 patients in each group.

Statistical analysis

The primary outcome will be expressed as difference in the mean (with 95% CI and p-value) of the severity scale of the FCRI-NL scale between intervention and control group at T1.

This will be analysed with a linear mixed model. A random intercept will be included to correct for inclusion per MHW. We will include residual covariances in order to correct for repeated measurement in each patient.

The analyses will be conducted in two steps. First, an analysis will be performed with time, treatment, and a time by treatment interaction. Second, a correction for baseline measurement of the outcome will be added to the first model.

The validity of the models will be assessed with residual analyses.[51]

A similar approach will be used to analyse secondary outcomes and covariates. Where applicable, a generalised linear model will be used to analyse dichotomous and count outcomes (for binomial and Poisson distributions respectively).

Healthcare utilisation is analysed using multilevel analyses. The number of visits to the GP between T1 and T2 is compared between the intervention group and the control group. Shifts in type of visits – physical vs. psychological – will also be explored. The healthcare uptake in the control group between T1 and T2 will also be compared to the period before the baseline measurement to assess whether healthcare uptake has changed since participating in the study.

The costs of healthcare are compared between the control group and the intervention group for the period between T0-T1, T1-T2 and T0-T2, whereby T0-T2 is most important

since it combines the costs of the intervention and the potential change in costs in the 9 months after the intervention. Healthcare costs are calculated based on healthcare utilisation, according to the method of the *Guidelines for carrying out economic evaluations in health care.*[52]

For the outcomes for which the intervention is found to be effective, the effect of the covariates on the outcomes will be explored.

First, intention to treat (ITT) analyses will be done. Then, per-protocol analyses will be carried out to estimate the effectiveness of the intervention if executed per protocol. During the analyses, the assessor will be blinded about the groups.

The validity of study results may be challenged by missing values, either at baseline or missing outcomes at follow-up. Multiple imputation will be used to address missing values at baseline for relevant variables. For missing outcomes, correction for relevant prognostic factors will be considered to ensure the validity of the results.[53]

The desirability and feasibility of the intervention according to patients and practitioners will be measured qualitatively. Semi-structured interviews will be held. These will be transcribed, and then coded by two independent researchers. Differences in coding will be discussed until consensus is reached. Important themes will be identified, using the data as the starting point.

Patient and public involvement

When developing the intervention, patients provided input on desired content and appearance, e.g., preference for short texts. Once implemented, the intervention was further adapted based on patient feedback.

When developing the study, patients provided input on the general idea. They also provided feedback on the recruitment process and in particular on the invitation letter to patients. Based on their input, the study and the letter were adapted.

DISCUSSION

With an increased number of cancer survivors, there is an increased need for survivorship care. Providing survivorship care in primary care may improve access and reduce the pressure on specialised institutions. In this study, the effectiveness of a primary care FCR intervention will be compared to usual care. An evaluation of healthcare consumption and costs will assess whether this can also decrease healthcare uptake and costs. To our knowledge, this is the first trial assessing the effectiveness of a primary care FCR intervention. In addition, it is one of few pragmatic trials on FCR interventions.

Heterogeneity of usual care

To assess whether this intervention is more effective than what is currently being offered, we chose to compare with usual care. No clear guidelines are available for GPs for FCR, so usual care may be quite diverse. Therefore, we will register usual care during the study.

Recruitment

Because prior research shows that patients often do not mention FCR to their GP, we chose to actively invite patients to participate in the study. The disadvantage of this choice is that we are activating our participants, making them less representative of the patients who currently seek care for FCR. However, we want to know whether this intervention can help patients with FCR, if they choose to seek care.

Usual care

We recognise that the usual care measured in this study might not fully reflect actual usual care, since we have activated the patient population and made the general practices more aware of this issue. To assess the effect of this activation, we compare the healthcare use in the control group with retrospective healthcare use. Also, practices who agree to participate in the study might have increased interest and expertise in FCR. To assess this, we ask them about any education on FCR or related topics they have received.

Randomisation level

We chose to randomise practices and not patients to prevent contamination. Practitioners who have been trained will have increased knowledge and awareness and will no longer provide usual care the way they did before training. Also, patients at the same practice might discuss the intervention they receive and notice the differences. Patients are unaware of the randomisation, to prevent patients in the control group from being disappointed and less motivated.

Trial status

Invitation of primary care practices has started in October 2018. The first patient was included on April 15, 2019. Final results are expected in 2020.

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5

Need for a primary care based intervention for fear of cancer recurrence: conclusions from the BLANKET-trial

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Published in Journal for Psychosocial Oncology Research and Practice in 2022.

ABSTRACT

Background: More than half of cancer survivors experience fear of cancer recurrence (FCR). There has been a call for easily accessible, inexpensive interventions for moderate FCR to complement existing specialized care. In the randomised BLANKET-trial, we investigated the effectiveness of a short, primary care intervention for FCR. We report on the potential of the intervention and the suitability of primary care to offer this intervention.

Methods: The BLANKET-trial is a cluster randomized controlled trial with change in FCR severity (severity subscale of the Fear of Cancer Recurrence Inventory (FCRI)) as its main outcome. Participating general practitioners invited all patients who completed successful curative cancer treatment between 3 months and 10 years ago. We report effect measures, outcome of our recruitment strategy, intervention uptake, reasons not to participate and experiences with the intervention.

Results: 62 of 1368 (4.5%) invited cancer survivors participated. Main reported reasons not to participate were not experiencing FCR and not wanting help. Due to the low participation, we could not robustly evaluate the intervention's effectiveness. Indicatively, in the intention-to-treat analysis, FCR severity decreased from T0-T1 by 2.7 points (SD=4.7) in the intervention group (n=27) and 1.8 points (SD=3.6) in the control group (n=18). In the per-protocol analysis, the decreases were 3.5 points (SD=4.5) and 0.7 points (SD=2.7), respectively.

Conclusions: Although the prevalence of FCR and the need for help for FCR are high according to literature, the uptake of our primary care based intervention proved low. While the intervention shows potential, alternative delivery routes need to be explored, due to the low number of patients who need help for FCR per primary care practice. We recommend additional research on the impact of FCR, on which patients require and desire help, and on what kind of intervention and setting are fitting for what patients.

Keywords: blended healthcare, cancer, e-Health, fear of cancer recurrence, mental health worker, oncology, primary care, RCT

INTRODUCTION

With improved cancer treatments, the number of cancer survivors and the number of people facing challenges during cancer survivorship are increasing.[1] Over half of cancer survivors experience fear of cancer recurrence (FCR),[2] which has been labelled their most important unmet need.[3,4] FCR can lead to decreased quality of life[5] and increased health-care costs[6] and for most people, FCR does not dissolve over time without intervention.[7] Several effective interventions to treat FCR have been developed. Most include aspects of cognitive behavioural therapy (CBT)[8] and are provided by specialised psychologists.[9] However, for patients with low levels of FCR, low intensity interventions may be sufficient and preferred.[9]

Primary care may be well-positioned to provide this type of care. It offers accessible care,[11] that includes both physical and psychosocial aspects.[12] Primary care is also increasingly involved in cancer survivorship, and cancer survivors frequently favour their general practitioner (GP) for psychosocial care.[13] In the Netherlands, most primary care practices employ mental health workers (MHW), who provide low threshold psychological care.

Therefore, we designed a blended, low intensity, primary care intervention for cancer survivors with FCR. In the BLANKET-trial, we aimed to evaluate the effectiveness of this intervention in reducing patients' FCR in a real-world setting. We present the results of the trial, as well as lessons we learned due to challenges with recruitment and uptake.

MATERIALS AND METHODS

Design

The BLANKET-trial is a two-armed cluster randomised controlled trial, comparing our intervention to usual care. The intervention consists of an intake with the GP, five sessions with an MHW and an online CBT-based program. The GP practice is the unit of randomisation. Outcomes are measured at patient level. For full details see the protocol paper.[14]

Participants

Eligible patients had finished successful curative cancer treatment between 3 months and 10 years ago, were registered at a participating GP practice, were ≥ 18 years, desired support for FCR and had sufficient Dutch reading and writing abilities. The required sample size was 244 patients.

Recruitment

Sixty-two GPs and 21 MHWs from 20 GP practices participated in the study. They identified all registered patients who met the eligibility criteria and invited them by letter, except

patients with severe comorbidity (e.g., severe psychiatric morbidity). Patients who wished to participate provided informed consent by mail. After completing the first questionnaire, patients in both groups were asked to go to their GP for a consult on FCR. Because the study took place in a real-world setting, we chose not to screen on FCR severity, to reflect daily primary care practice. Besides, the intervention also targets patients with moderate FCR, so screening for clinical level FCR would not identify our target group.

Outcomes and data collection

Data was collected at baseline, after 4 months (T1) and after 12 months (T2). The primary outcome was the difference between the groups in FCR severity at T1, measured by the validated Dutch version of the severity subscale of the FCRI (FCRI-SF).[15] Both intention-to-treat analyses and per-protocol analyses were conducted. In the per-protocol analyses, only those who went to their GP (control group) and those who received the intervention from the MHW (intervention group) were included.

Due to the initial low response, we inquired reasons for non-participation in the second phase of inclusion. A form to indicate reasons for non-participation was included with the 256 remaining invitation letters. GPs who had already sent their invitations were asked to call 3-5 invited patients and ask them for their reasons not to participate.

RESULTS

Participation

1368 invitation letters were sent between April 1, 2019, and September 1, 2020. 62 patients (4.5%) joined the study, 36 in the intervention and 26 in the control group. On average, one patient per GP participated. See Figure 1 for a flowchart on trial participation. 30 GPs recorded the reasons for not inviting patients that fit the criteria. They omitted 110 (21%) out of 521 patients. Of them, 77% was considered too vulnerable (e.g., due to Alzheimer) and 14% did not speak sufficient Dutch. We received 88 non-participation surveys (34% of those invited) and 26 patients were approached by phone. Their main reasons not to participate were not experiencing FCR (76% and 69%) and feeling no need for support (38% and 12%). We suspect no impact of COVID-19 on participation, as the large majority of letters was sent before the pandemic.

Demographic characteristics

The mean age of the participants was 62.9 years and 56% were women. Most had breast cancer (36%) or colorectal cancer (29%). More demographic characteristics are presented in Supplementary Materials 4A.

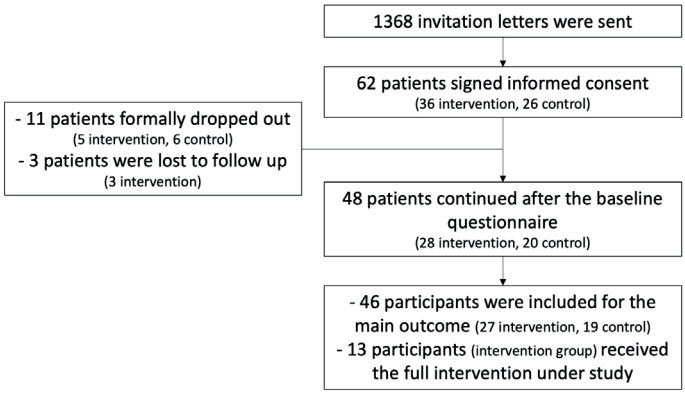

Figure 1: Flowchart on trial participation and data collection.

Intervention uptake

19 (83%†) participants in the intervention group and 14 (70%) in the control group went to the GP. In the intervention group, 14 (74%) went to the MHW with an average of four sessions, compared to three (21%) in the control group with an average of five sessions.

Main outcomes

In the intention-to-treat analysis, FCR severity decreased from T0-T1 by 2.7 points (SD=4.7) in the intervention group and 1.8 points (SD=3.6) in the control group (see Table 1). In the per-protocol analysis, the decreases were 3.5 points (SD=4.5) and 0.7 points (SD=2.7), respectively.

Table 1: Mean FCR severity scores and FCR severity reduction in the intervention and control group (intention-to-treat analysis).

	Intervention group		**Control group**	
	n	mean (SD)	n	mean (SD)
FCR severity T0	33	17.7 (7.5)	24	17.1 (7.1)
FCR severity T1	27	15.1 (7.2)	19	16.2 (6.4)
FCR severity T2	25	13.1 (6.5)	18	14.3 (7.0)
FCR severity reduction T0-T1	27	2.7 (4.7)	19	1.8 (3.6)
FCR severity reduction T0-T2	25	3.6 (5.8)	17	3.2 (3.8)

† Due to the COVID-19 pandemic, data could only be collected from the GP practices of 43 participants.

Experiences with the intervention

Mean patient satisfaction was higher in the intervention (n=10) than in the control group (n=7) (3.5 vs. 3 on a scale of 5). Both groups considered the care practical (3.6 and 3.5 / 5) and neither considered it burdensome (1.6 and 1.8 / 5). The intervention group was more likely to recommend the care (3.9 vs. 3.2 / 5). MHWs (n=12) in both groups rate the expected reduction in fear 3 on a scale of 5. 78% of MHWs in the intervention group plan to continue providing this intervention.

DISCUSSION

Although reviews show that more than half of cancer patients experience FCR[2] and that care for FCR is the largest unmet need for survivors,[3] only 4.5% of invited patients participated in our study. The main reported reasons not to participate were not experiencing FCR and not needing support for FCR. Although the number of participants was too low for a valid effect estimate, the results of the trial suggest that the intervention has potential: FCR decreased more in the intervention than in the control group and practitioners and patients were positive about the intervention.

We consider four reasons for patients' low interest in this primary care FCR intervention. First, it could indicate a low prevalence of FCR, but a recent review (n=7,190) shows over half of survivors experience at least moderate FCR.[2] Second, it may indicate less need for help than earlier research suggests. Patients who experience FCR do not always desire or require help[16] and some patients only experience FCR when triggered, e.g., around medical check-ups.[17] Thus, for some, the impact on daily life may not be enough to seek help. Third, it is possible that this type of intervention was not appealing to some patients, who may prefer self-help,[18] support from friends and family[19] or treatment from a different healthcare provider (e.g., at the hospital). Some patients may have also wished to avoid the confrontation with cancer. Finally, we may have used a suboptimal way of inviting patients. If the intervention would have been offered in person by the GP, the response may have been greater.

Future research

Despite the low response, we still believe there is a need for easily accessible, inexpensive interventions for FCR. More research is needed on the impact of FCR, on which patients require and desire help, and on what kind of intervention and setting are fitting for what patients.

For future FCR research and interventions, we also recommend addressing the barriers for participation that arose in our study, e.g., by not using invitation letters. Invitation letters may easily be forgotten and may come at a time when patients are not interested,

especially since FCR may fluctuate over time.[20] In addition, some may not participate due to avoidance. Finally, some patients may feel more addressed by the words 'worry' and 'concern' than 'fear'. Based on above findings and patient feedback we have adapted our recruitment strategy and intervention and are now assessing the effectiveness of an online FCR intervention, with video calls replacing face-to-face visits.

Clinical implications

In all, our results suggest that there is a group of people who can benefit from this primary care based intervention, but that this group is much smaller than previously expected. Therefore, offering it in all general practices is probably not (cost-) effective. Alternative delivery routes, i.e., joint provision within groups of practices or online in video calls, need to be explored.

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6

A guided online primary care intervention for fear of cancer recurrence versus waiting list: a randomised controlled trial

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Submitted.

ABSTRACT

Background: Fear of Cancer Recurrence (FCR) is highly prevalent among cancer survivors and leads to decreased quality of life and increased healthcare costs. We assessed the effectiveness of a guided online primary care intervention for FCR, compared to waiting list.

Methods: In this RCT, participants were recruited online and randomised 1:1. All adults who finished successful curative cancer treatment between three months and ten years ago, wanted support for FCR, and had sufficient Dutch skills were eligible. The intervention consisted of a ten-week online program with three to five 30-minute video calling sessions with a trained mental health worker. The online program was based on cognitive behavioural therapy. After 6 months, the control group received the same intervention. Neither participants nor healthcare providers could be blinded due to the use of a waiting list control group. The primary outcome was the difference between the groups in the change in FCR severity from baseline (T0) to six months (T2), measured online with the short form of the Fear of Cancer Recurrence Inventory. All participants who filled out at least one questionnaire were included in the analyses. The trial was prospectively registered in the Netherlands Trial Register on 25-02-2019 with number NL7573.

Findings: Between July 14, 2020, and September 8, 2021, 173 participants were enrolled and randomised to the intervention (n=86) or control group (n=87). 85 (intervention) and 82 (control) participants were included in the analyses, 131 women and 36 men. In the intention-to-treat analysis, FCR severity dropped 2.1 points more in the intervention group (2.7 points (SD=3.9) vs. 0.6 points (SD=3.6), $t(154) = 3.4$, $p=0.0007$, Cohen's $d=0.56$).

Interpretation: This easily accessible and relatively inexpensive intervention effectively reduces FCR and can potentially replace or precede existing more intensive psychological treatments, improving patients' access to care.

Funding: Dutch Cancer Society.

RESEARCH IN CONTEXT

Evidence before this study

On March 2, 2020, we searched PubMed for research articles on *primary care* interventions for fear of cancer recurrence (FCR) and found one study, on an interprofessional primary care training for FCR. We also searched PubMed for reviews on FCR interventions in general. A review on (specialized) psychological interventions for FCR found that many interventions were developed and that they showed small but robust effects ($g = 0.33$). A review on non-mental health practitioner led interventions concluded that research on those interventions was lacking. Also, there was a call for accessible, inexpensive interventions to complement existing specialized psychological treatments.

Added value of this study

We have shown that a brief, online, cognitive behavioural program that is supported by three to five video calling sessions with a mental health worker working in primary care effectively reduces the severity of FCR and improves general mental well-being. This effect remains at ten months follow-up.

Implications of all the available evidence

This accessible and inexpensive primary care intervention can complement existing more intensive psychological treatments and can provide a solution for the large number of cancer survivors with FCR for whom specialized care is not available due to resource constraints. For some patients this intervention will be sufficient, for others it can serve as the first step in a longer treatment trajectory.

INTRODUCTION

The number of cancer survivors is rising due to earlier detection, improved treatments and longevity.[1] After successful cancer treatment, more than half of survivors experience FCR,[2] which has been defined as "fear, worry, or concern relating to the possibility that cancer will come back or progress".[3] Survivors with FCR experience decreased quality of life[4] and incur increased healthcare costs.[5] Without treatment, for most people, FCR does not disappear.[6] A recent study found that 94% of respondents with FCR needed some type of support and 40% needed psychological care or coaching.[7] Many specialised psychological interventions for FCR have been developed, with different formats (e.g., individual and group) and in different settings (e.g. face to face, online, by phone, and blended). Many have been demonstrated to decrease FCR.[8]

However, due to the large number of cancer survivors, the high prevalence of FCR, and the increasing healthcare costs, it is impossible to provide specialised mental healthcare to all cancer survivors.[9] There is a need for less complex psychological interventions that can be provided in easily accessible and low resource formats.[10] Many patients probably do not require specialised psychological care for FCR and may prefer more basic care.[11] Web-based and blended treatments can play an important role in this need.[12]

Cancer survivorship care is presently shifting from recurrence surveillance to holistic patient care. As a result, it fits better in primary than in hospital care, because a general practitioner (GP) can integrate it with care for psychosocial issues, lifestyle behaviours, and comorbidity.[13] Many cancer survivors also prefer receiving psychosocial care from their GP[14] and appreciate the integrated, easily accessible support that GP practices are able to provide.[15] In the Netherlands, almost all GP practices employ mental health workers (MHW) who provide accessible mental health care for moderate psychological and psychosocial issues. Their care does not require a formal diagnosis, is covered by standard health insurance, and often includes brief cognitive behavioural therapy (CBT) and the use of e-Health programs.[16]

Therefore, in this study, we assessed the effectiveness of an online primary care intervention for FCR that consists of an online program and three to five video calling sessions with an MHW working in primary care. This study is the sequel of the original BLANKET-trial[17] in which the intervention was executed face-to-face in primary care practices. Due to the COVID-19 pandemic, we adapted our intervention to a fully online version using video calling.

METHODS

Study design

We performed a randomised controlled trial with waiting list comparison. The intervention was delivered online by eight MHWs who normally work in different primary care practices in the Netherlands, and who were specifically employed and trained to provide the intervention. The Medical Research Ethics Committee (METC) Utrecht reviewed and approved the study.

Participants

All adult (≥ 18 years) cancer survivors were eligible, if they a) finished successful curative cancer treatment between three months and ten years ago, b) wanted support for FCR, and c) had sufficient Dutch reading and writing skills. This includes patients who had follow-up cancer appointments or were undergoing adjuvant hormone therapy. Since this is a pragmatic trial aiming to reflect daily practice and to develop a broadly applicable

intervention for all who want support for FCR, we included all cancer types and performed no screening on clinical level FCR. Cancer survivors were recruited online via social media, cancer patient organizations, and existing cancer cohorts. The COVID-19 pandemic caused delayed patient inclusion, leading to resource constraints. We therefore chose to stop inclusion before the intended sample size was reached since we expected to be close enough to our sample size target for robust conclusions.

Randomisation and masking

Participants were the unit of randomization. An external data manager generated a random allocation sequence using Research Randomizer (randomizer.org). After informed consent was signed, participants were allocated by the research team 1:1 according to the sequence. After participants filled out the baseline questionnaire, the research team informed participants about their group. The intervention group then started the intervention. The control group started the intervention six months later (after T2) and was free to use other care in the meantime. Since we aimed to assess the effect of all aspects of the intervention (the included information, the online program, and the sessions), we had a waiting list control group and did not use one of these aspects as an active control condition. Neither the participants nor the MHWs could be blinded because of the waiting list design.

Procedures

The intervention was designed by healthcare professionals, researchers and patients at the Helen Dowling Institute, an academic mental health institute specialising in psycho-oncology. It is based on CBT and the model on FCR by Lee-Jones (1997).[18] It consists of an online program [19] and three to five 30-minute video calling sessions with an MHW over a period of ten weeks. The program includes information, videos, and exercises and is available on-demand so that patients can access it whenever they need or want to, even after the intervention ends. The program consists of three main modules for all - which contain psychoeducation about FCR, the basic principles of CBT, and exercises to learn to recognize fear - and five optional modules - on rumination, avoidance, relaxing, reassuring and undertaking activities -, which can be selected based on patients' individual needs. Participants' GPs were informed about their patients' participation in the study. And if the participants gave permission, the MHWs also called the GPs to discuss the participants' medical and psychiatric history in light of the FCR intervention.

To assess implementer fidelity, one session was audio recorded and analysed for each MHW. A score form was used on which the scorer could mark whether each technique (e.g., psychoeducation) was applied when applicable in the session. MHWs also filled out a form

for each participant, including the number of sessions, the included modules, and their own satisfaction with the outcome.

Participants filled out questionnaires online at baseline (T0) and four (T1), six (T2) and ten (T3) months after baseline. The control group filled out additional questionnaires after twelve (T4) and sixteen (T5) months. Table 1 presents an overview of when participants filled out which questionnaires. The questionnaires used in this study were the Dutch version of the Fear of Cancer Recurrence Inventory (FCRI-NL),[20] the Four-Dimensional Symptom Questionnaire (4DSQ)[21] and a custom-made questionnaire about the feasibility and acceptability of the intervention, which contained both Likert scales and open-ended questions. Participants also filled out questions about demographic characteristics, cancer history, and healthcare uptake, including complementary care.

The FCRI-NL

The FCRI is the most commonly used measure for FCR[2] and contains 43 items and seven subscales: triggers, severity, distress, coping strategies, functioning impairments, insight, and reassurance. The FCR severity subscale is also known as the short form of the FCRI (FCRI-SF) and was used in this study to measure the primary outcome FCR severity. The distress subscale was used to measure FCR-related distress. In the literature, three possible cut-off scores for clinical FCR for the FCRI-SF are reported: 13, 16, and 22 points (maximum score is 36 points). [22,23] We report all cut-offs.

The 4DSQ

The 4DSQ (in Dutch: 4DKL) has 50 questions on four dimensions: anxiety, depression, distress, and somatic complaints.[21] The questionnaire is often used in Dutch GP practices as part of mental health assessments.

Outcomes

The primary outcome was the difference in change in FCR severity from T0 to T2 between the intervention and control group. Secondary outcomes were the effect of the intervention over time from T0-T2 on FCR severity, FCR-related distress, and general anxiety, distress, depression, and somatic complaints. In addition, we assessed the perceived feasibility and acceptability of the intervention according to participants. Since the control group received the intervention after T2, it was not possible to include T3 in the linear models that compare the control group with the intervention group. We do report follow-up measurements for the control group after 14 and 16 months, so that the T2-T5 measurements of the control group are comparable with the T0-T3 measurements of the intervention group (see Table 3).

Table 1. Overview of the questionnaires that were filled out at each time point. FCRI = Fear of Cancer Recurrence Inventory. 4DSQ = Four-Dimensional Symptom Questionnaire. FCRI-SF = severity subscale of the Fear of Cancer Recurrence Inventory.

	Time	Questionnaires
T0	Baseline	■ FCRI (NL) ■ 4DSQ ■ Questionnaire about demographics, cancer history and healthcare uptake
T1	4 months	■ FCRI-SF (NL) ■ Questionnaire about healthcare uptake ■ *Only intervention group:* Questionnaire about the feasibility and acceptability of the intervention
T2	6 months	■ FCRI (NL) ■ 4DSQ ■ Questionnaire about healthcare uptake
T3	10 months	■ FCRI (NL) ■ 4DSQ ■ Questionnaire about healthcare uptake ■ *Only control group:* Questionnaire about the about the feasibility and acceptability of the intervention
T4 (only control group)	12 months	■ FCRI (NL) ■ 4DSQ ■ Questionnaire about healthcare uptake
T5 (only control group)	16 months	■ FCRI (NL) ■ 4DSQ ■ Questionnaire about healthcare uptake

Statistical analysis

To calculate the sample size, a relevant between group difference in means of 3.0 points and an SD of 7.0 points on the FCRI-SF were used (alpha = 0.05, beta = 0.8).[20] Since there is no established minimal clinically important difference in the literature, we selected 3.0 points based on clinical expertise and the improvements in other FCR interventions (see Discussion). A 12% increase for expected dropout of participants was added. Consequently, the aim was to include 192 participants, 96 per group.

Mean scores and SDs for all time points were reported for the FCRI-SF, the FCR distress subscale and the 4DSQ scales. In addition, the number of respondents who scored above the cut-offs for the FCRI-SF and the 4DSQ scales and the number who improved at least three points on the FCRI-SF were reported.

The statistical significance of the between group difference for the primary outcome was assessed using a t-test. To assess the effect of the intervention on FCR severity over time, we used a likelihood-ratio test to compare a) a linear mixed model with a random intercept per participant and fixed effects for baseline FCRI-SF score, group, time (months) and an

interaction effect of group*time, to b) the same model without the interaction effect. Since the second model was not inferior to the first, we used the second model.

Furthermore, we assessed the effect of the intervention on FCR severity for different subgroups. Subgroups were based on age, sex, education, the baseline scores of FCR severity, FCR-related distress, and general anxiety, depression, distress, and somatic complaints. We also assessed whether there was a correlation between the effect of the intervention and the number of healthcare visits per month between T0 and T1 to GPs, MHWs, medical specialists, psychological care, and complementary care. In addition, we assessed whether there was a difference between the MHWs, their educational background or their work experience (years). Finally, we assessed whether there was a difference in the effect of the intervention for the control group, which was waitlisted first, and the intervention group, which started immediately.

To assess the effectiveness of the intervention for the subgroups we used likelihood ratio testing. For each potential effect modifier, we compared a) the above defined model for FCR severity with an additional fixed effect of the effect modifier, to b) the same model with an interaction effect of group*[effect modifier]. To assess differences between MHWs, their educational background and their work experience (years), we compared within the intervention group a) the above defined model for FCR severity without the fixed effect for group, to b) the same models with fixed effects for the aforementioned variables. To assess differences between being waitlisted or not, we created a dataset in which for the control group T0 and T1 were excluded, and T2-T5 became T0-T3. We then compared a) the above defined model for FCR severity to b) a model with an interaction effect of group*time.

To assess the effect of the intervention on FCR-related distress and the 4DSQ scales, we used linear models with fixed effects for the respective baseline scores and group.

We also performed a per-protocol analysis for those who completed at least half the intervention, to determine their mean FCRI-SF scores, the number and percentage who improved at least three points, the difference in change from T0-T2 between intervention and control groups, the mixed model for FCR severity and the difference between subgroups.

Finally, we report the results of the survey on participant experience and the forms the MHWs filled out at the end of each treatment.

All analyses were done in R studio v2022.02.2.[24] Multilevel imputation with the *mice* and *jomoImpute* packages was applied to impute missing data on the outcome variables.[25]

Due to the negligible risk status of the trial, no data safety monitoring board was established.

The trial was prospectively registered in the Netherlands Trial Register on 25-02-2019 with number NL7573.

RESULTS

Between July 14, 2020, and September 8, 2021, 173 people consented to participate; 86 were randomised to the intervention group and 87 to the control group. Six participants (one in the intervention group and five in the control group) were unreachable and therefore lost to follow-up before filling out the baseline questionnaire, resulting in 85 participants in the intervention group and 82 in the control group that could be analysed. See Figure 1 for more details on participants' participation in the study.

Table 2 presents demographic and medical information of the intention-to-treat population at baseline. Additional information can be found in Supplementary Materials 5A.

Eighty-one (95%) participants in the intervention group were referred to an MHW. Three patients dropped out and 1 was hospitalised. 69 (81%) completed at least half of the intervention by T2. The participants had a median number of 5 (1) sessions with the MHW over a span of 10 (5) weeks. Ninety-seven percent completed the main modules, 86% completed at least one optional module and 74% three or more. The module on rumination was used the most (79%), followed by the modules on relaxing (64%), avoidance (63%), reassuring (58%), and undertaking activities (52%). The MHWs rated their satisfaction with the outcome on average 4.0/5, with a score of 3 or higher for 96% of participants[‡]. In the intervention group, two participants were referred to a psychologist and three others were already seeing a psychologist. In the implementer fidelity assessment, all were found to implement the intervention as instructed.

In the intention to treat analysis, from T0 to T2, FCR severity dropped 2.1 points more in the intervention group (delta 2.7 points, SD=3.9) than in the control group (delta 0.6 points, SD=3.6), $t(154) = 3.4$, $p=0.0007$, Cohen's $d=0.56$. See Table 3 for all mean scores per time point on the FCRI-SF, the FCRI distress scale, and the 4DSQ scales.

As can be seen in Table 3, all measurements on the FCRI-SF, the FCRI distress scale, and the 4DSQ scales demonstrated a greater improvement in the intervention group than in the control group between T0 and T2. This includes the number of participants scoring below the cut-off values on both the FCRI-SF and all subscales of the DSQ. The improvement in the intervention group remained stable at T3. After T2, when the control group received the intervention, a similar improvement in the outcomes for the control group was demonstrated. In Figure 2 the change in FCR severity over time is presented.

‡ 1 = not at all, 2 = slightly, 3 = moderately, 4 = very, 5 = extremely

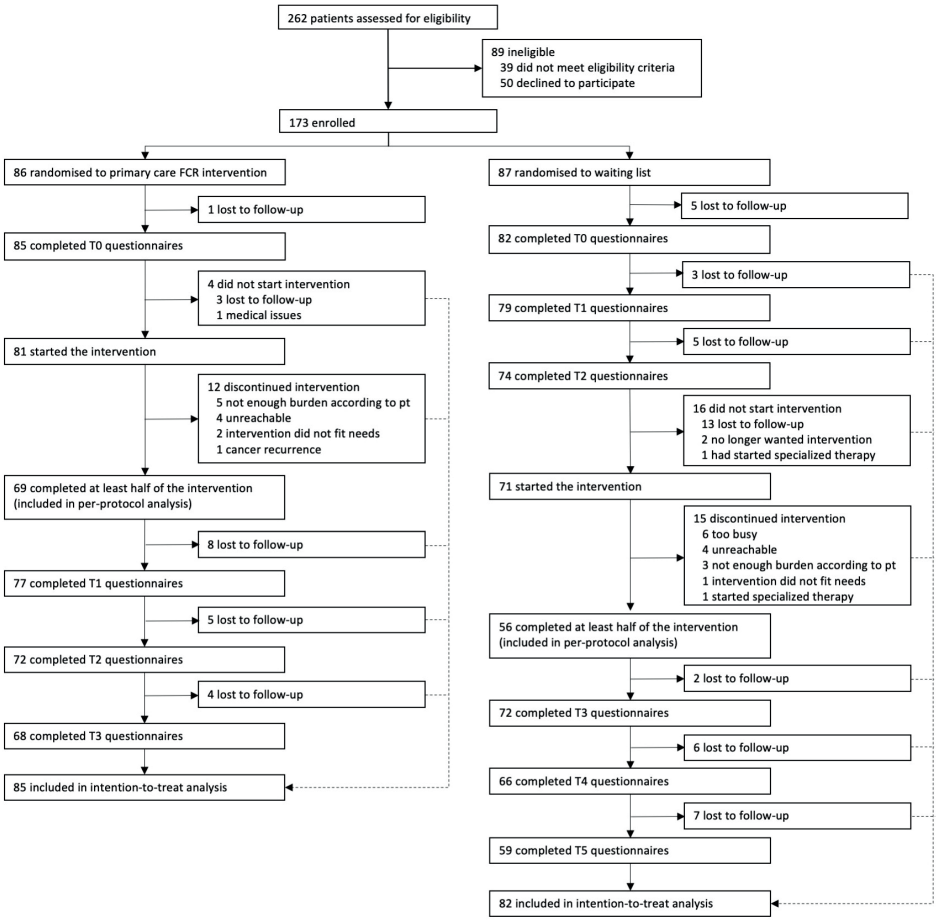

Figure 1. Trial file.

The log likelihood comparison with and without the group*time (months) interaction effect showed no difference (X^2 = 2.28, p =.13) demonstrating that the effect at T1 remained stable at T2. Using the model without the interaction effect to compare the effect of the intervention on FCR severity over time between the groups, we found that FCR decreased significantly more in the intervention group (β = 2.28 (95% CI 1.08 to 3.47), p =.0002 for the fixed effect of group). In the linear models to assess the effect of the intervention on FCR-related distress and the 4DSQ scores, we found the group term was significant for all outcomes, whereby the scores decreased more in the intervention group than in the control group. See Table 4 for β-values, 95% confidence intervals and p-values for the group term for each analysis.

Table 2. Demographic and medical information of the participants at baseline.

	Primary care FCR intervention n= 85	**Waiting list n= 82**
Age (years)	51.9 (27-73)	54.7 (30-72)
Time since primary cancer diagnosis (years)	3.2 (0-21)	3.7 (1-27)
Time since the end of curative cancer treatment (years)	2.0 (0-8)	1.8 (0-10)
FCR severity at baseline	21.7 (7-31)	23.6 (11-33)
Sex		
Women	64 (75%)	67 (82%)
Men	21 (25%)	15 (18%)
Education		
Primary education	3 (4%)	5 (7%)
High school	13 (16%)	14 (19%)
Higher education (non-academic)	53 (66%)	39 (52%)
Academic education	9 (11%)	16 (21%)
Other	2 (3%)	1 (1%)
Employment status		
Employed or self-employed	44 (55%)	37 (49%)
Retired	12 (15%)	18 (24%)
Incapacitated for work	15 (19%)	11 (15%)
Unemployed	2 (3%)	2 (3%)
Other	7 (9%)	7 (9%)
Previous diagnosis anxiety or depression	21 (25%)	28 (34%)

In the likelihood ratio tests to assess the effectiveness of the intervention for different subgroups, no significant differences were found. Also, no differences in outcome were found between different MHWs, their educational backgrounds or their work experience (years). There was also no difference in effect between the group that was waitlisted before receiving the intervention and the group that was not. In Supplementary Materials 5B, we present β-values, 95% confidence intervals, std. errors, t-values, and p-values for all tested variables.

In the per-protocol analysis, we included the 69 participants who had completed at least half of the intervention by T2. This group scored 22.1 (SD = 5.1) at T0, 19.6 (SD = 5.0) at T1, and 18.8 (SD = 5.3) at T2 on the FCRI-SF. By T1, 29 (43%) had improved at least 3 points and by T2, 37 (53%). Comparing the change from T0-T2, FCR severity dropped 2.8 points more in the intervention group than in the control group, $t(122) = 4.3$, $p < 0.0001$. In the mixed model for FCR severity, the β-value for the group term was 2.77 (95%CI 1.75 to 3.80), $p < .0001$. There were no differences between subgroups.

Table 3. Mean scores and number of participants scoring above the cut-offs on the FCRI-SF, the FCRI distress and the 4DSQ scales.

	Primary care FCR intervention				Control group during waitlist			Control group after intervention		
	n=85				n=82					
	T0*	T1	T2	T3	T0	T1	T2 / T0**	T3 / T1	T4 / T2	T5 / T3
FCRI-SF (max 36)	21.7 (5.3)	19.4 (5.3)	19.0 (5.5)	19.0 (5.9)	23.6 (4.9)	22.5 (4.8)	23.1 (4.7)	20.9 (4.9)	20.9 (5.2)	21.0 (5.4)
FCRI distress (max 16)	7.4 (3.4)	-	5.4 (3.3)	6.0 (3.5)	8.3 (3.1)	-	7.6 (3.6)	6.6 (3.5)	6.5 (3.6)	6.9 (3.4)
Anxiety (max 24)	3.8 (3.4)		2.5 (3.1)	2.2 (3)	5.2 (4.5)		4.8 (4.8)	3.4 (4.1)	3.6 (4.2)	3.6 (5)
Depression (max 12)	1.7 (2.5)		1.1 (1.9)	1 (1.9)	2 (2.9)		2.1 (2.8)	1.6 (2.3)	1.5 (2.3)	1.7 (2.6)
Distress (max 32)	15.9 (7.2)		12.1 (8.3)	12 (8.5)	15.1 (7.5)		14.8 (8.5)	12.9 (9.3)	12.3 (9.3)	12.9 (9.7)
Somatic complaints (max 32)	11.1 (6.3)		8.3 (6)	8.9 (6.3)	10.7 (6.3)		10.7 (7.2)	9.2 (6.6)	9.3 (6.9)	9.6 (7.7)
Improvement FCRI-SF ≥3 pts		35 (41%)	40 (47%)	38 (45%)		21 (25%)	22 (27%)	40 (49%)	38 (47%)	43 (53%)
FCRI-SF ≥22	45 (53%)	30 (35%)	26 (30%)	30 (35%)	52 (63%)	43 (53%)	49 (60%)	39 (47%)	40 (49%)	35 (42%)
FCRI-SF ≥16	72 (85%)	65 (76%)	62 (74%)	59 (69%)	78 (95%)	75 (91%)	78 (95%)	72 (88%)	69 (84%)	70 (85%)
FCRI-SF ≥13	81 (95%)	74 (87%)	74 (87%)	75 (89%)	81 (99%)	82 (100%)	80 (97%)	80 (98%)	78 (95%)	79 (96%)
4DSQ anxiety ≥3	36 (43%)		27 (32%)	26 (31%)	47 (58%)		46 (57%)	34 (41%)	32 (39%)	30 (36%)
4DSQ depression ≥2	20 (24%)		15 (17%)	12 (14%)	22 (27%)		26 (31%)	23 (28%)	21 (26%)	23 (28%)
4DSQ distress ≥10	68 (80%)		47 (56%)	46 (55%)	55 (68%)		58 (71%)	43 (53%)	44 (54%)	46 (56%)
4DSQ somatic complaints ≥10	45 (52%)		29 (34%)	32 (38%)	40 (49%)		40 (49%)	33 (41%)	30 (37%)	34 (42%)

* T0-T5 measurements were taken after 0, 2, 4, 6, 10, 12 and 16 months.

** The control group was offered the intervention after filling out the T2 questionnaires. Hence, the T2-T5 measurements for the control group can be compared to the T0-T3 measurements of the intervention group.

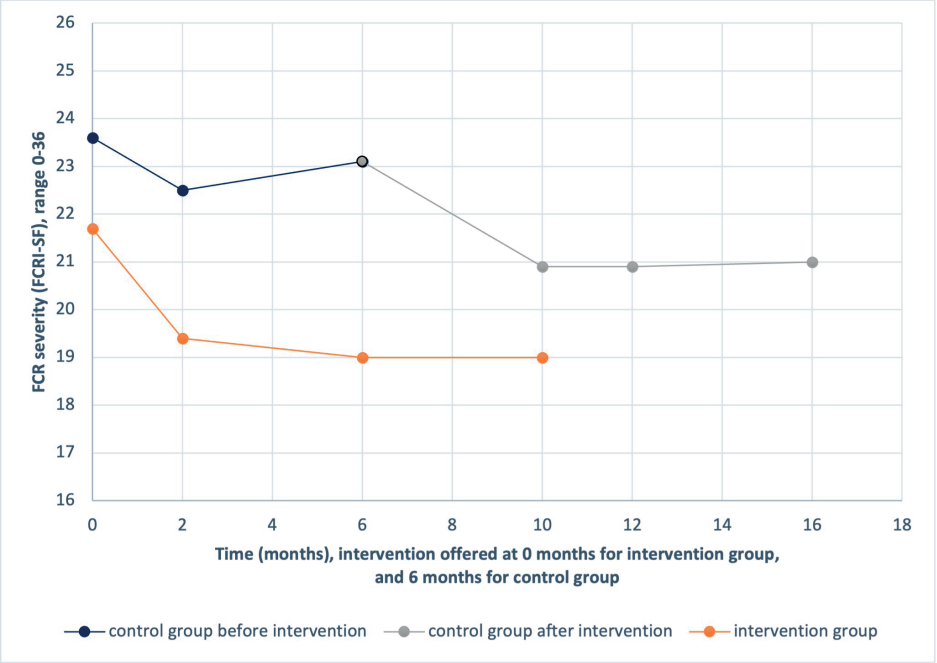

Figure 2. Graph of FCR severity over time, comparing the control group and the intervention group. The intervention group was offered the intervention at 0 months and the control group at 6 months.

Table 4. β-values, 95% confidence intervals, and p-values for the fixed effect of group in the models to assess the effect of the intervention over time.

	β	95% CI	p
FCR severity	2.28	1.08-3.47	0.0002
FCR-related distress	1.61	0.40-2.82	0.011
4DSQ anxiety	1.58	0.63-2.51	0.0012
4DSQ depression	0.68	1.25-0.11	0.021
4DSQ distress	3.52	1.63-5.40	0.0004
4DSQ somatic complaints	2.59	1.01-4.18	0.0016

In the survey on feasibility and acceptability, 89% of the intervention group considered it the right approach, 90% found it practical, and 91% were content with the outcome (all scoring 3 (=”moderately”), 4 (=”very”) or 5 (=”extremely”) on a scale of 5). 90% would recommend the intervention. Others emphasised it would not be the right fit for everyone, e.g., those who are not independent or self-disciplined enough to participate in such a program. 79% appreciated the program being completely online. Still, in response to our open question, over one third said to prefer face-to-face sessions to have deep, personal conversations. Regarding the best provider for this intervention, some respondents

stressed that it is most important that the provider has expertise in psycho-oncology. A more elaborate analysis of the survey is presented in Supplementary Materials 5C.

DISCUSSION

Our results demonstrate that an online primary care intervention for FCR effectively reduces FCR among participants and that this effect remains at the 10 months follow-up. A decrease in FCR severity was found in the intervention group, while FCR persisted at baseline level in the control group during the waitlist period. After being offered the intervention, the control group experienced a similar decrease in FCR, which also remained at the 10 months follow-up. In addition, FCR-related distress, and general anxiety, depression, distress, and somatic complaints improved following the same pattern as FCR severity, showing that this intervention not only affects FCR but also general mental well-being. The intervention seemed to work equally well for all subgroups and was not associated with the individual competence of the MHW, though the trial was not powered for these analyses. Participants were generally positive about the intervention, considered it not burdensome, and most would recommend it to others. While many stressed the benefits of it being offered online, such as flexibility in scheduling appointments and reduced travel time, over one third of the participants would prefer face-to-face contact. Without the COVID-19 pandemic and related measures, this number may be even higher.

The intervention was designed for patients with moderate FCR, who generally do not require specialised treatment. Yet, in our study, 53% of the intervention group started with high FCR (FCRI-SF ≥22), experienced a significant decrease, and was satisfied with the intervention. Also, although FCR severity decreased and participants were generally satisfied with the outcome, at T2, many participants still scored above the 13 (87%) and 16 cut-offs (78%). Considering that the scores on the 4DSQ significantly improved and that patients were satisfied with the intervention, this could indicate that although many participants still experience some FCR after the intervention, the fear is better manageable and its burden on their mental well-being has decreased.

A strength of the study is that it was conducted in a realistic clinical setting. Also, in addition to FCR, general mental well-being and participant experience were assessed. Stopping inclusion before reaching the initially intended sample size could be considered a weakness. However, even with a smaller sample, an effect could be confirmed. Another weakness is that we used self-referral, which could limit the representativeness of the participants.

To date, most FCR interventions are psychologist-led and offered in a mental healthcare setting.[8] Ours is the first to evaluate the impact of a psychological intervention in primary

care. So far, there have been five studies on FCR interventions led by non-mental health specialists, with mixed results. Four were nurse-led and one was an interprofessional primary care training on identifying and discussing FCR.[11] Two were found to be effective, one was not, and two did not measure FCR as an outcome.[11] Furthermore, results for four *self-management* FCR interventions have been published: Smile, iConquerFear and FoRtitude were found to be effective post-intervention, while CAREST was not.[26–29] Comparing our results with those of other interventions who used the same outcome measure, we conclude that high intensity specialised interventions scored the same or somewhat better, e.g. ConquerFear 2.3 points difference in FCR reduction,[30] ACT 2.3 points[31] and SWORD 4.0 points;[32] and low intensity interventions scored the same or somewhat worse than our intervention, e.g. a psychoeducational intervention 2.1 points[33] and Smile Smartphone psychotherapy 1.7 points.[29]

Our online intervention for FCR can meet the need for accessible, inexpensive interventions for FCR, and complements existing specialised care. For many patients, our short intervention could be sufficient or a good starting point, especially if there are waiting lists. However, for other patients (e.g., those with childhood trauma or other complex needs) it may be better to start with specialised care from the beginning.

The intervention fits well with the role of MHWs in primary care practices. Since the intervention can be offered online, providers can serve many patients in a wide region. If the intervention is implemented in a single GP practice, there may be financial and organizational barriers, because the number of patients per practice who need this intervention is relatively low,[17] and this may limit practices' willingness to invest in this type of care. If a group of practices employs an MHW or the scope of the intervention is broadened – to a more general psychological cancer survivorship intervention or to patients with fear of recurrence for other diseases -, it may help to overcome these barriers. Alternatively, it may be possible for trained nurses in hospitals to offer this intervention. As mentioned above, some nurse-led FCR interventions have already been found effective and can possibly be integrated with our approach.[11]

Further research is needed to determine what type and intensity of care to offer to which patients. Finally, additional research could optimise the use of online treatments by helping to distinguish which types of patients are served best online and by identifying specific components that patients prefer not to receive online.[12]

In conclusion, our online primary care intervention for FCR reduces FCR among participants and improves general mental well-being. This accessible and relatively inexpensive intervention can potentially replace or precede existing more intensive psychological treatments and can provide a solution for the large number of cancer survivors with FCR for whom specialized care is not available due to resource constraints.

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7

A qualitative study on the feasibility and acceptability of a primary care intervention for fear of cancer recurrence

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Submitted.

ABSTRACT

Purpose: The majority of cancer survivors experience fear of cancer recurrence (FCR). There has been a call for easily accessible, inexpensive interventions for moderate FCR to complement existing specialized care. Recently, the BLANKET trial demonstrated the effectiveness of a short primary care intervention. This study aimed to assess the feasibility and acceptability of this intervention from the perspectives of patients and mental health workers (MHW).

Methods: The intervention consists of an e-Health program based on cognitive behavioral therapy, combined with 3-5 online or face-to-face sessions with a primary care based MHW. After trial participation, 9 patients and 13 MHWs participated in a semi-structured interview. Interview transcripts were analyzed using the thematic analysis approach.

Results: Patients and MHWs appreciated the online program for having recognizable content, being adaptable, and stimulating self-management. They experienced the combination of an online program and sessions with an MHW as a valuable mix that transfers knowledge in an efficient manner, provides opportunities for in-depth conversations, and allows patients to take the lead in their own recovery. The program appeared less suitable for patients lacking certain digital or language skills and those who considered the content too familiar or simplistic. Both patients and MHWs considered the primary care setting very suitable for the intervention, as it closely fits general practitioners' holistic perspective including both physical and psychosocial complaints.

Conclusion: The program is considered feasible and acceptable and has previously been shown effective in reducing FCR. Therefore, we recommend implementing it in practice.

Keywords: fear of cancer recurrence, primary care, qualitative research, cognitive behavioral therapy, feasibility, acceptability

INTRODUCTION

More than half of cancer survivors experience fear of cancer recurrence (FCR),[1] which has been defined as "fear, worry, or concern relating to the possibility that cancer will come back or progress".[2] FCR can lead to decreased quality of life and increased healthcare costs.[3,4] FCR causes preoccupation, worry, hypervigilance to bodily symptoms[5] and/or avoidance of worry by circumventing potential triggers, such as medical appointments.[6] Almost all cancer survivors who experience FCR need support and for 40% this includes psychological care.[7] Several effective interventions have been developed, mostly consisting of specialized psychological treatments.[8]

However, many patients with FCR may not need intensive psychological treatment. Stepped care models, in which care is provided based on FCR severity, have been recommended, since cancer services lack psychosocial staff to treat all patients and some patients may prefer low intensity types of support (e.g. nurse-led).[9] Because general practices have an increasing role in survivorship care and are used to providing easily accessible care for moderate psychosocial complaints, they may be the right actor to provide these low intensity types of support for FCR. Cancer survivors frequently favor their general practitioner (GP) for psychosocial care and GPs also consider this a role that fits their position.[10]

Therefore, we developed a primary care intervention for cancer survivors with FCR. It consists of an e-Health program and three to five 30-minute sessions with a primary care based mental health worker (MHW). To evaluate this intervention, we conducted two RCTs known as the BLANKET study. In the first RCT, sessions with the MHW were held face-to-face at patients' own primary care practice.[11] However, the number of participating patients per practice was low and due to the COVID-19 pandemic, no new practices could be included. Therefore, inclusion was stopped before the required sample size was reached.[12] Considering that patients do not need GP involvement to opt for our intervention, we started a second RCT based on self-referral recruitment. The sessions were provided via video calling by MHWs specifically employed for the study, who were not part of participants' regular primary care team. The intervention was found to be effective in decreasing FCR and in improving general mental well-being (Luigjes-Huizer, et al., manuscript submitted).

As a final step towards clinical implementation, we aimed to qualitatively assess the intervention's feasibility and acceptability, based on patients' and MHWs' perspectives. We wanted to know how patients and MHWs experienced the intervention. In addition, since meta-analyses have shown that guidance usually increases interventions' effectiveness,[13,14] we aimed to investigate the role of the MHW. Finally, we aimed to investigate perceptions on primary care as the setting for this intervention.

METHODS

Design

In this qualitative study, we conducted semi-structured interviews with patients and MHWs who had participated in one of the two RCTs of the BLANKET study.[12]

Study population and recruitment

The study population of both RCTs consisted of adult cancer survivors who a) finished successful curative cancer treatment between 3 months and 10 years ago, b) wanted support for FCR, and c) had sufficient Dutch reading and writing skills. In the first trial, survivors were recruited by letter via participating GP practices. In the second trial, they were recruited online via social media, cancer patient organizations, and existing cancer cohorts. In the patient information letter they received, they were already informed they might be approached for the interview study.

After trial participation, patients and MHWs were contacted via e-mail and/or phone to recruit them for the interview study. Written informed consent for recording and analyzing the interviews was taken prior to the interviews. MHWs from both trials were interviewed. Unfortunately, due to time and resource constraints only patients from the first trial were interviewed, not from the second trial. In that regard, we were unable to purposively sample our participants.

The intervention

The primary care intervention was designed at the Helen Dowling Institute, an academic mental health institute specializing in psycho-oncology. It includes an e-Health program with three CBT-modules and five optional modules on rumination, avoidance, relaxing, re-assurance and undertaking activities, which can be selected based on patients' individual needs. The program includes information, exercises, and videos with experiences of other patients, and is available 24/7. Patients also have three to five 30-minute sessions with a trained MHW.

Data collection

The semi-structured interviews were conducted by YL and AR, who have been professionally trained in qualitative research. Interview guides were used. They were designed by the research team and improved after three interviews. The guides contained questions about expectations, experiences, positive and negative aspects, practical concerns, the primary care setting, and an overall appraisal (see Supplementary Materials 6A). Neither interviewer knew the interviewees before study participation. Interviewees were aware that the research was being conducted to improve the care for patients with FCR and was

part of a PhD dissertation. No one else was present during the interviews. Interviews were audio-recorded and transcribed verbatim. In addition, brief notes were taken by the interviewers. As the content of the interviews was rather straightforward, no member checks were carried out.

Qualitative data analysis

The transcripts were analyzed using inductive thematic analysis. We used the phases outlined by Braun and Clarke to structure data analysis.[15] In the first and second within-case analysis phases, two researchers (YL with RW or AR) independently familiarized themselves with the transcripts and conducted initial open coding of the interviews using MAXQDA software.[16] Subsequently, they discussed the codes until reaching consensus. This led to a coding scheme on which the analysis of the following interviews was based. After the first five interviews of each group (patients, MHWs from trial 1, and MHWs from trial 2) were analyzed, YL coded the remaining interviews. After all interviews were analyzed, two researchers (YL with RW or AR) organized the codes into potential topics according to the third cross-case analysis phase, which were checked with the interview data in the fourth phase. During the fifth phase, the multidisciplinary research team (ML, CH, SD, MS and YL) organized two meetings and grouped the codes and topics into themes. In the sixth and final phase, the manuscript was written.

Research team

Six of the eight authors are women. YL is a health scientist, epidemiologist, and PhD candidate. MS is a behavioral scientist and senior researcher in psycho-oncology. SD is an epidemiologist and PhD candidate. RW is a behavioral scientist and junior researcher in psycho-oncology. AR is a Psychology MSc student and a research assistant. NW is professor of general practice with 25 years' experience as GP. CH is MD, epidemiologist, and assistant professor of general practice. ML is professor in medical psychology, and a healthcare psychologist with extensive experience in treating FCR.

RESULTS

Participants

Nine out of thirteen participants who received the intervention in the first trial, were approached and interviewed. The remaining participants were not selected, because they were treated by the same MHWs as other interviewees. Participants from the second trial could not be interviewed due to time and resource constraints. Six out of eight MHWs from the first trial and seven out of eight MHWs from the second trial were interviewed. The remaining MHWs declined to participate, because of limited experience with the interven-

tion, a preference not to be audio recorded, and a lack of time. All interviews took place between December 2019 and November 2021. Patients were interviewed at the location of their preference (patient's residence (n=6), the Helen Dowling Institute (n=2) or by phone (n=1)) and lasted approximately one hour. The interviews with the MHWs lasted 45 minutes and were conducted at the GP practice (n=2), via phone (n=4), and via video calling (n=7). In table 1, sociodemographic and clinical characteristics of the patients are presented, which are comparable to the whole sample. In table 2, sociodemographic and professional characteristics of the MHWs are presented.

Table 1. Sociodemographic and clinical characteristics of the 9 patients.

	Patients (n=9)
	mean (range)
Age (years)	59.2 (39-76)
Time since diagnosis (years)	4.9 (1-9)
Time since end of treatment (years)	4.8 (1-9)
FCR at baseline (FCRI-SF*, range 0-36)	22.3 (19-26)
	n (%)
Gender	
Men	4 (44)
Women	5 (56)
Cancer type	
Breast cancer	4 (44)
Respiratory system	2 (22)
Hematological	1 (11)
Colorectal	1 (11)
Liposarcoma	1 (11)

*FCRI-SF = Fear of Cancer Recurrence Inventory, short form.

Feasibility and acceptability of a primary care FCR intervention

The analysis of the interview data resulted in five main themes: 1) *treatment content*; 2) *treatment support*; 3) *treatment format*; 4) *patient characteristics*; and 5) *primary care setting*. Quotes belonging to each theme are presented in Table 3.

Overall, both patients and MHWs appreciated the program. While some patients still experienced fear after participation, they were better able to manage it. Patients described that the intervention helped them find new coping strategies, process their emotions, and learn to involve their support system when needed.

Table 2. Sociodemographic and professional characteristics of the 13 MHWs of trial 1 and 2

	MHW 1-6, trial 1 (n=6)	**MHW 7-13, trial 2 (n=7)**
	mean (range)	mean (range)
Age (years)	43.3 (26-56)	52 (24-65)
Working experience (years)	n.a.	18.9 (0-30)
Number of patients seen	2 (1-3)	20.4 (4-46)
	n (%)	n (%)
Gender		
Men	0 (0)	1 (14)
Women	6 (100)	6 (86)
Educational background		
Psychology	4 (67)	2 (29)
(Social psychiatric) nursing	2 (33)	3 (43)
Social work		1 (14)
Other		1 (14)

Theme 1. Treatment content

1.1 Focusing on cancer

Both patients and MHWs valued the content of the intervention. MHWs explained that in daily practice, they already had modules to treat fear. However, patients and MHWs appreciated that this program was specifically focused on cancer related fear, including videoclips of other patients sharing their experiences. Patients recognized themselves in these experiences and felt supported.

1.2 Stimulating self-management

Doing the program confronted patients with their FCR, which they experienced as difficult yet helpful. They described how the program helped them to reflect on their thoughts and feelings, and to apply the learned coping strategies when needed.

1.3 Fitting the intervention to patients' needs

MHWs indicated that the intervention is useful for different types of people because it can be flexibly adapted to each individual patient. Different optional modules suited different patients. Also, MHWs described that the number and depth of the conversations differed between patients, matching their needs.

Theme 2. Treatment support

2.1. Open communication

MHWs created a safe environment for patients to share their stories and express their thoughts and feelings. Patients appreciated being heard. MHWs and patients emphasized the importance of establishing a good relation for the sessions to be supportive.

2.2 Facilitating role

MHWs and patients described how the MHWs clarified and elaborated on the topics in the program. For example, they probed patients how to best apply what they learned in daily life. Also, MHWs encouraged patients to do the exercises and to keep going.

2.3 Prior experience with cancer

Both patients and MHWs indicated it was very helpful that the MHWs had prior knowledge on cancer, its treatment, and its psychological consequences. This helped them to acknowledge and normalize patients' experiences and prevented them from being scared or shocked by patients' stories. Some patients shared that, prior to this study, they had encountered an MHW in daily practice that was unequipped to treat FCR.

2.4 Including the support system

While it was not a standard aspect of the intervention, patients and MHWs also highlighted the benefit of MHWs considering the patient's support system. When the patient has a partner, he or she can comfort the patient after emotional sessions. Partners can also help the patient manage FCR in daily life. If there was no partner, MHWs discussed whether patients were comfortable doing the online program without support at home and helped patients to identify people to contact if needed.

Theme 3. Treatment format

3.1 Treatment format: online program and sessions with MHW

Patients and MHWs considered the *combination* of an online program and (face-to-face) sessions with an MHW of added value. The online program was continuously accessible and allowed patients to work at their preferred pace and time. The sessions with the MHW provided space for patients to share their stories and feel supported (see Theme 2. Treatment support). Patients indicated that without sessions, the program would feel too impersonal, and it would be difficult to engage with this sensitive topic, whilst only having sessions would take too much time for both MHWs and patients.

3.2 Online sessions with MHW

Online and face-to-face sessions each have pros and cons. MHWs indicated that online sessions take less time, fit more easily between other activities, can be offered to patients

who live far away, do not involve a risk of COVID-19 contamination, and can even continue when patients feel sick. MHWs learn about patients' home situation and patients feel more human and less like patients. MHWs expressed that they were able to build a relation with patients using video calling, as they do in face-to-face sessions. A disadvantage of online sessions is that video calling sometimes falters due to bad internet connections and that for some, especially older, patients it was unfamiliar and somewhat stressful. Also, when distressing events occurred (e.g., patients developing metastases), online contact could feel quite distant and some MHWs considered it insufficient to support patients the way they wanted. Importantly, some patients also strongly prefer face-to-face sessions.

3.3 Face-to-face sessions with MHW

The main benefit of face-to-face sessions is the increased depth of conversation. Also, there are no distractions from the home situation (e.g., children), and MHWs noticed that being required to travel to sessions ensured patients' motivation for treatment. Some MHWs considered face-to-face sessions more appropriate for the sensitive subject, and some found it easier to motivate patients who avoid as a coping strategy during face-to-face sessions. Some MHWs also indicated that lonely patients feel more supported by face-to-face contact. MHWs suggest a combination of online and face-to-face sessions may be ideal, e.g., having the first and last sessions face-to-face and the others online.

Theme 4. Patient characteristics

While MHWs considered the intervention useful for many different patients, there were also patients for whom it seemed less suitable.

4.1 Lacking digital and language skills

To benefit fully from the program, digital and language skills are required. A few patients had trouble with the online modules. Also, some patients had trouble expressing themselves and writing down what they felt.

4.2 Prior knowledge

While for some the content was too challenging, for others it was too simplistic or familiar, decreasing their willingness to do the program. The MHWs adjusted how quickly they went through the modules, but this was not enough to engage some participants.

4.3 Lack of time or motivation

MHWs reported that despite their support, a few patients lacked time or motivation to engage with the online modules in between sessions. Some patients described having only moderate fears and felt the program and the time it requires was therefore out of

proportion. Yet, others felt that, despite having moderate fears, it made a positive and important difference in their lives.

Theme 5. Primary care setting

5.1 GPs provide holistic and accessible care

Our intervention was situated in the primary care setting. MHWs and patients indicated this was fitting because GPs can easily check in with patients, especially when hospital care has ended. GP care is accessible and nearby patients' homes, and many patients have longstanding relationships with their GPs, which provide a safe space to discuss FCR. MHWs explained that when patients often present with physical symptoms and no physical issues are found, GPs can discuss a potential relation with FCR and, if relevant, offer psychological care. They also described that compared to hospital or specialized psychological care, GP care helps patients to feel more normal and less like patients, which patients prefer, and which is helpful for their recovery.

5.2 Barriers in discussing FCR with GPs

GPs have limited time and see many patients. Relatively few of them suffer from FCR. Some MHWs explained that considering the large number of topics GPs provide care for, they may not prioritize FCR. Some patients described they barely know their GP or do not have a positive relationship and would therefore not feel comfortable sharing this sensitive topic. In general, many patients would not mention FCR to their GP and appreciate it if the GP proactively discusses it. However, since this often does not happen, MHWs stressed the importance of informing patients about FCR, so that they can seek help when they cannot manage FCR on their own.

5.3 Fit with MHW role in GP practices

MHWs indicated that within the GP practice, the intervention fits well with the role and expertise of MHWs, who offer short-term, accessible interventions, including CBT and e-Health programs.

In our study, all MHWs were trained. They found it helpful to practice listening and being present without immediately trying to solve patients' problems. This helped MHWs to manage their feelings of powerlessness. The information about (the influence of) cancer was also new and helpful. Some MHWs stated MHWs do not require specific training to provide this intervention, especially if the topic is already touched upon in their education. Other MHWs posited that the topic is very intense and that some MHWs lack CBT skills. They therefore recommend specialized training. Moreover, if MHWs regularly provide the intervention, it helps them to offer It smoothly.

Table 3. Quotes about the feasibility and acceptability of a primary care FCR intervention

1. Treatment content 1.1 Focusing on cancer "Everything she [the patient] read in there, she recognized, and she felt the same things. She received a bit of reassurance, a bit of confirmation that what she was doing, was okay. And also like, it's not strange that when you see a commercial, that it can trigger fear. The goal is not to completely let that disappear, that you're not allowed to be fearful anymore." MHW 1, female, age 26. 1.2 Stimulating self-management "I remember sitting here and opening the program and that it really moved me. That it made me really sad. And those were the moments you start thinking about it again. A sort of learning moment. And not even that I really benefitted from what was being said, simply that it forced me to look at myself." patient 1, male, 43. 1.3 Fitting the intervention to patients' needs "There's not just one thing that helps, all those different modules can be helpful. I always say, read through the program and get out of it what is of benefit to you. And that really differs." MHW 12, female, age 61.
2. Treatment support 2.1 Open communication "Those were some very good conversations. Very nice for me to talk about things that I normally don't express." patient 6, male, age 71. 2.2 Facilitating role "I ask, 'Oh yes, and how was that?' Then I try to adapt to what comes next. And then I always ask, "did you also work with the modules? And how did that go? And how could that help you in this situation?" MHW 4, female, age 46. 2.3 Prior experience with cancer "I just like it better when I have a good sounding board. In the sense that people really know what they are talking about. And of course, the general practitioner also has that, but the general practitioner cannot talk to you for half a year, for half an hour." patient 9, female, age 54. 2.4 Including the support system "What I noticed so far is that partners are often involved. That is also what I advise, involve your partner or a good friend. So that when things are difficult, you have someone that you can call. I always try to check whether the support system is sufficient to do that." MHW 3, female, age 47.
3. Treatment format 3.1 Treatment format: online program and sessions with MHW "But if you only have those exercises, then you are just doing that on your own. [...] And you already feel incredibly alone, and then you also need to do those exercises. While you're really scared." patient 1, male, age 43. "When we look at those long waiting lists, I think that working online can definitely be a plus for people to start working on it by themselves. That way, help can be offered to them sooner, but it is also nice for us because it takes some pressure off your schedule." MHW 3, female, age 47. 3.2 Online sessions with MHW "Despite only having sessions via video calling, you do build a connection with each other. And yes, it doesn't really matter whether you see each other physically or not." MHW 7, female, age 65. 3.3 Face-to-face sessions with MHW "A conversation with someone you can look directly in the eyes, is of course the very best." patient 8, female, age 54.

Table 3. Quotes about the feasibility and acceptability of a primary care FCR intervention (*continued*)

4. Patient characteristics 4.1 Lacking digital and language skills "Language can be quite hard. That's why those videoclips are so good, because it [rest of the program] is quite focused on language. That is a disadvantage, I think. So then, such a thought record [a type of exercise] can be quite difficult. So if I didn't want that for people, then I only worked with the basic modules." MHW 11, female, age 51.
4.2 Prior knowledge and wanting more depth "You cannot offer a course on different levels; this is of course for everybody. […] You often have to maintain a basic skill level. But when you don't have that level [when your level is higher], it starts to become annoying after a while. It becomes too explanatory, too stimulating, too emphasized, especially too emphasized." patient 2, female, 76.
4.3 Lack of time or motivation "She quit. She was not motivated. She had a neighbor who said, 'you should do this, too, it's very good for you'. It turns out that's not the right motivation." MHW 7, female, 65.
5. Primary care setting 5.1 GPs provide holistic and accessible care "A three-month oncological revalidation program is much more intense, with much more personal attention and context, but if that barrier is too high for people, this can really help. Not everyone wants to travel to such a program or is mobile enough. Or people can find it too much and too intrusive, then this might help much more." patient 3, female, age 39.
5.2 Barriers in discussing FCR with GPs "I really hope this gets implemented at the GPs. I really think it is very valuable. And at the same time, I hope GPs get a bit more financial space because that's the other side. GPs get more and more responsibilities, right? And always [require] more resources so to say. It is not our problem, but of course they should also get some financing. Like, who will do what? But I think this is a very valuable type of care, that does not have to cost that much." MHW 12, female, age 61.
5.3 Fit with MHW role in GP practices "You work with people who had a life-threatening illness, you need to offer CBT, and you need to know some things about psychopathology. So I think these three things really need to come together. I don't think this can be done by just anyone. For that, the target group has been through too much already". MHW 9, female, age 40.

DISCUSSION

In this study, we have shown that our primary care intervention for FCR, which was previously found to be effective in reducing FCR (Luigjes-Huizer, et al., manuscript submitted), is also positively valued by patients and MHWs. The intervention helped patients learn how to manage their fear. The online program was appreciated for being recognizable, adaptable and time efficient, and stimulating self-management. The sessions with the MHWs engaged patients, motivated them to continue, provided a safe space to share stories, and helped them to include or broaden their support system. A prior RCT found that our e-Health program was ineffective without support,[17] in line with previous studies,[13,14] but combined with sessions with an MHW it *was* effective, and also feasible and acceptable. The program appeared less suitable for patients lacking digital or language skills and for

those who considered the content too simplistic. Both patients and MHWs considered the intervention very suitable for the primary care setting, since it fits in GPs' holistic perspective that considers both physical and psychosocial complaints, and matches with MHWs' role of offering accessible short-term interventions. Online and face-to-face sessions each have advantages and disadvantages. Ideally, the patient can combine both as preferred.

Strengths and limitations

A strength of our study is that we interviewed both patients and MHWs. A limitation is that we were unable to include patients from the second trial. Consequently, we miss the patient perspective on receiving the intervention via video calling. Fortunately, we were able to include MHWs who gave some information about the patient perspective, but data saturation likely was not reached on this topic. Prior research on video calling during the COVID-19 pandemic has shown that, while patients experience somewhat more distance and somewhat less personal contact online, they are pleasantly surprised about the quality of the therapeutic relationship and feel more at ease at home.[18]

Implications for clinical practice and research

Because of the intervention's previously demonstrated effectiveness, its acceptability, and the good fit with primary care, we recommend implementing it there. However, there are practical barriers. There are few patients with FCR per GP practice, making it difficult for MHWs to build expertise and possibly limiting the investments practices are willing to make to provide this care. Therefore, MHWs need to learn about FCR as part of their regular professional training and the online program needs to be easily accessible (e.g., included in widely used e-Health platforms), so that MHWs can easily implement it when they encounter a patient with FCR. Additional training can be offered for MHWs who feel uncomfortable with the topic or who want to specialize in this topic.

It is also important that the available care reaches patients. A recent feasibility study identified lack of FCR awareness among patients and inadequate detection and referral by healthcare providers as barriers for FCR interventions.[19] Since patients often do not take initiative to discuss FCR with their doctor, it is helpful if healthcare providers proactively tell patients that they may experience FCR, and that care is available. Therefore, increased awareness among GPs is needed. Also, future research could investigate the best phase and ways to inform patients about FCR and the available care options.

For some patients, this intervention seemed less suitable. This includes, for example, patients who lacked adequate digital skills, had trouble writing about their thoughts and feelings or who considered the content too simplistic or familiar. By adjusting the program to patients' needs and preferences, MHWs can increase its suitability and utility. They can, for example, provide the program on paper, do the first exercises together, or encourage

patients to *apply* the already familiar strategies in daily life. Still, it is recommended to discuss beforehand with patients whether the intervention matches their needs. Also, research is needed on factors that predict which patients require professional help and what kind of help works best for whom. Finally, making interventions less language-dependent, e.g., by adding more videos, could improve their usability.[19]

Conclusions

Patients and MHWs appreciate our primary care FCR intervention, which combines an online program with (online) sessions with an MHW and was previously shown to reduce FCR severity. We recommend implementing it in primary care, by making it available on all existing e-Health platforms for MHWs, including it in general education for MHWs and ensuring all patients and healthcare providers receive information about FCR and the available care types.

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8

General discussion

This thesis explores the opportunities for treating fear of cancer recurrence (FCR) in primary care. In addition, the prevalence of FCR and patients' need for help for FCR were researched. In this chapter, the main findings are summarized and reflected upon. In addition, strengths and limitations, implications for clinical practice and recommendations for future research are presented.

MAIN FINDINGS OF THIS THESIS

In Chapter 2, an individual participant data meta-analysis on the prevalence of FCR showed that a substantial percentage of cancer patients and survivors experience FCR: 58.8% experience at least moderate FCR (≥13 on the short form of the Fear of Cancer Recurrence Inventory (FCRI-SF)) and 19.2% experience high FCR (≥22), indicative of a need for specialized treatment. FCR was found in all tested subgroups – based on age, gender, cancer type, continent where the study was conducted and time since diagnosis – and somewhat more for women and younger participants. In Chapter 3, a survey study on needs for coping with FCR showed that 94% of those who experienced FCR need help. Part of these needs can be fulfilled by informal support networks, e.g., by talking or doing enjoyable activities for distraction, but for other needs professional help is required. Fortunately, 85% of respondents with a need already received at least one type of support. The main gaps were for practical tips, medical check-ups and psychological help or coaching.

To support patients with moderate FCR, we developed the first FCR intervention for primary care. This intervention consists of an online cognitive behavioral therapy (CBT) based program and three to five sessions with a trained mental health worker (MHW), and was designed to be easily accessible and inexpensive and to replace or precede existing specialized care for patients with moderate FCR. In a pragmatic trial to evaluate this intervention's feasibility and cost-effectiveness, the intervention was provided in general practices, by patients' own general practitioners (GP) and MHWs. The protocol for this trial is presented in Chapter 4 and the results are presented in Chapter 5. Despite the high prevalence of FCR and the need for help for FCR, only 62 (4.5%) of the invited cancer survivors participated in the trial. With these low numbers, we could not robustly evaluate the intervention's (cost-)effectiveness. However, with a decrease of 3.5 points on the FCRI-SF in the intervention group and 0.7 points in the control group (per protocol analysis), it showed potential. Due to the COVID-19 pandemic, it was not possible to recruit additional GP practices for the trial. Therefore, a second trial was started, in which the face-to-face sessions were replaced by video calling sessions. The results of this trial (n=173) are described in Chapter 6. The intervention was found to significantly reduce FCR among participants: 2.7 points (SD=3.9) on the FCRI-SF in the intervention group and 0.6 points (SD=3.6) in the control group, $t(152) = 3.4$, $p < 0.001$ (intention to treat analysis).

In addition, general anxiety, depression, distress, and somatic complaints were significantly reduced. These reductions remained at 10 months follow-up. This intervention was found to be effective for a broad group of patients and independent of individual MHWs' competences. Also, in a survey, almost all participants reported they considered the intervention practical and the right approach and were content with the outcome. Finally, we performed interviews with patients and MHWs about the acceptability and feasibility of the intervention (Chapter 7). These interviews confirmed that the intervention was appreciated by both patients and MHWs. The combination of an online program and sessions with an MHW provided opportunities for patients to be heard and to ask questions in the sessions, and to deepen their understanding and to practice at home. The flexibility in the intervention, including optional modules on different topics, allowed for it to be adapted to patients' specific needs. Still, there are some patients for whom the intervention is less suitable, e.g., those who lack language or digital skills, those who require specialized care, and those for whom the content is already familiar. The intervention fits well with the role and expertise of GPs and MHWs, but there are some practical barriers for implementation. Most importantly, the low number of patients per practice, as shown in the first trial, limits the opportunities for MHWs to develop expertise and may limit the investments GP practices are willing to make.

REFLECTION ON THE MAIN FINDINGS

We found that FCR is highly prevalent and that while it can fluctuate somewhat (e.g., it can flare up in response to triggers) it does not dissolve over time. Also, almost all respondents with FCR had a need for care. While women and younger people experience somewhat more FCR and report somewhat greater needs for care, FCR and the need for help exist among all groups. Thus, there is no specific group to be targeted. And while informal networks provide an important part of care, the need for professional support remains. Part of this need can be met by doctors, e.g., providing medical check-ups and sharing practical tips on dealing with FCR, but another proportion of this need requires psychological help or coaching.

We developed an effective primary care intervention for FCR. While specialized psycho-oncological care already exists, our intervention has the potential to support a group of patients whose FCR is not so severe or complex that it requires specialized care, but severe enough to limit patients in daily life. In the second trial, we showed that the intervention effectively reduces FCR and improves general mental well-being and that these outcomes remain stable over time. These results were found independent of patient characteristics and individual competences of the MHWs, and also within the group of patients with higher

levels of FCR (≥22). Participants and MHWs were also positive about their experience with the intervention in terms of the content, format, and practical aspects.

Still, in the first trial, we found that the number of patients per GP who accepted the offered intervention was low. This may be partly due to the way they were invited - by letter, not in person by the GP - and the fact that the intervention required participating in research. However, it is likely that there is also a group for whom the impact of FCR on their daily lives does not outweigh the (perceived) time and effort that participating in an intervention requires. Also, some may have negative expectations of therapy[1] or fear being stigmatized.[2] Therefore, in planning the implementation of the intervention, it must be considered that the number of patients per GP practice who seek this type of care may be low.

STRENGTHS AND LIMITATIONS

A strength of this thesis is that it is the first to assess a primary care FCR intervention. Another strength is that we were able to analyze our research topic from various angles: we assessed the prevalence of FCR among cancer survivors and several subgroups and we assessed the need for and provision of support for FCR, including the role of informal support. Also, we assessed the effectiveness of our intervention both in a pragmatic trial that exposed practical barriers and in an RCT with sufficient participants to demonstrate its effect. Finally, we qualitatively interviewed both patients and MHWs to reveal their opinions and experiences regarding the intervention's acceptability and feasibility.

A limitation is that we were unable to recruit enough patients for our pragmatic trial in GP practices to obtain robust results. In our second trial, we offered an online version of the intervention based on self-referral. It is unclear if the intervention would be equally effective if it was offered face-to-face in daily practice and whether this would be feasible. First, while the content would be the same, MHWs would have less focus on this topic and may experience more difficulties in implementing the intervention, which could make it less effective. Although, for the small group that was included in the first trial, the intervention did seem to be effective. Second, the group that was included in the second trial may not have been representative of the general population with FCR since we used self-referral. Our respondents may have been more motivated and more open to online care than the average patient. Third, the fact that this study was done during the COVID-19 pandemic may affect the generalizability of the results. Patients' acceptance of online sessions may have been due to the normality of online meetings at the time of the study because of the COVID-19 pandemic measures that were in place at that time but have now been lifted. On the other hand, given the benefits of online care, fewer patients may be interested if the intervention is offered face-to-face at their GP practice. This is supported by the

low participation rate in the first trial. Therefore, it is important to further investigate the different opportunities to implement this intervention in practice (see implications for clinical practice).

Another limitation, with respect to generalization, might be that this study was designed for the Dutch context. It includes a Dutch online program and was implemented by MHWs working in primary care. Countries in which primary care practices do not employ MHWs will need to look for alternative healthcare professionals to provide this intervention.

IMPLICATIONS FOR CLINICAL PRACTICE

We have shown FCR affects most cancer patients and survivors and needs to be addressed by healthcare providers and policy makers. First, we recommend for healthcare providers to discuss FCR and provide brief psychoeducation to all cancer patients as a standard part of cancer care. A recent feasibility study found lack of FCR awareness and inadequate FCR detection were barriers for patients to obtain care for FCR.[1] Evaluating patients' FCR early in their cancer journey and at transition moments such as the end of active treatment, will normalize FCR and help individuals to seek support when they need it, even if they are no longer undergoing hospital-based treatment or surveillance.[3] Liu et al. (2021) have developed a guide which oncologists can use to discuss FCR.[4] Guassora (2015) recommend including psychosocial matters in discharge letters from hospitals to GPs and arranging a visit to the GP upon hospital discharge to discuss patients' disease and treatment experience.[5] These recommendations support a timely detection of FCR.

Second, some patients can be helped with practical tips and information, for example via existing websites such as kanker.nl. Awareness about where to find this information needs to be increased among doctors and other healthcare professionals so that they can refer their patients to these.

Third, patients expressed a need for additional medical check-ups. However, these check-ups can also trigger FCR. We therefore recommend explaining and discussing surveillance schedules with patients, to increase their understanding and acceptance. If patients know which symptoms are indicative of recurrence and which are not, and why doctors consider the recommended number of check-ups sufficient, they may no longer need additional check-ups to be reassured.[6] Currently, the effect of the personalization of check-up and survivorship care plans on FCR is being evaluated in the NABOR study.[7]

Fourth, for patients who need psychological care, we recommend providing the type and intensity of care that matches their needs and that prevents a larger care need in the future. For many, this could start with our primary care intervention. For some, this intervention will be enough. For others, additional care will be needed, and this can be

built on the foundation of our intervention. Still others will be served best by receiving specialized psycho-oncological care from the start.

Considering the nature of the intervention and the skills required to provide it, our intervention fits well within primary care. However, since the number of patients per practice is low, GPs may not want or be able to invest greatly in this type of care. To overcome these barriers, the online program needs to be easily accessible and widely available to all MHWs. Furthermore, they need to be able to implement it without extensive training. Broadening the topic of the intervention and the training to include other cancer related mental health issues, or fear of recurrence of other illnesses could increase GP practices' interest because of the wider applicability.

A different option for implementation could be for groups of practices that work together, to assign one MHW to serve all their patients with FCR, thus allowing that MHW to gain experience and making it worth the investment to be trained. While there are currently practical and financial barriers for this type of collaboration, it may become more feasible in the future, as there has been a call and trend for increased cooperation between GP practices at a regional level in order to be more effective and efficient.[8] Still another option for implementation could be for nurses or MHWs working in hospitals to provide this intervention. For some cancer types, hospital nurses play a big role in the mental support of patients, and this could fit with that role. In previous studies, nurses have already effectively provided FCR interventions.[9]

Finally, it may be possible to provide the intervention separately from the regular health system, as was done in the second trial. If the intervention is provided online, this will greatly increase the number of patients that can be seen per provider and will offer greater opportunity for the MHW to gain experience and expertise. However, two important preconditions for implementation are financing and fitting in existing healthcare systems and referral pathways.[10] If the intervention is offered by a separate provider, the costs will not (automatically) be covered by insurance and patients will not easily find the care. Therefore, neither precondition will be met, and we currently do not recommend this route, or at least not for the Dutch context.

Overall, we recommend a multilayered approach to implementation: a) include training on cancer survivorship and our intervention in the regular curricula for GPs, MHWs and oncology nurses to increase their knowledge and skills for when they encounter cancer survivors with FCR, b) ensure that the online program is made available in existing e-Health platforms, so that MHWs are regularly reminded of the intervention and can easily implement it when needed, c) provide continuing education programs for MHWs and nurses who want to learn more or specialize in this area, d) create a short online educational module for MHWs and nurses whose focus is not FCR, so that when they do see patients

with FCR, it can help them get started or refresh their memory from previous trainings. Considering that the skills, the level of experience and the educational backgrounds of MHWs vary, this multilayered approach also allows for individual MHWs to seek the level of training they need to be able to support patients with FCR.

RECOMMENDATIONS FOR FUTURE RESEARCH

We have shown a high prevalence of FCR and a correlation with gender and age. However, the explained variance of the factors we investigated was low. Identifying other factors, especially psychosocial factors, that predict the severity of FCR can help to distinguish between different groups of patients with different needs. Also, while existing research has focused on the severity of FCR, the impact and the need for help may not be directly correlated with the severity of FCR. Some patients might be able to manage severe FCR on their own, while others are limited in daily life and need support for relatively mild FCR. More research is needed to uncover what determines the impact and need for help for FCR. This may also result in the selection of different outcome measures for FCR intervention studies that reflect patients' ability to manage their FCR rather than the severity of their FCR.

Furthermore, research is needed to determine which types of patients are served best by which types of care. A pilot study is currently being done in which patients receive different types of care based on the severity of their FCR.[11] However, determining the most suitable care may also include factors such as the impact of FCR, psychiatric comorbidities, individual needs and preferences, and practical aspects such as available time, motivation, and computer skills. Knowing which factors play a role and how these factors work together can help doctors and MHWs distinguish between patients that need to be referred to specialized psycho-oncological care, patients who can be helped by lighter interventions and patients who do not require professional help, at all. This research could also support the design of tools that help doctors and MHWs discuss with patients which care would be most suitable and acceptable for them.

Further research could also help to optimize the use of online treatments by investigating which types of patients are served best online and by identifying specific components of treatment that do and do not work well online.

At a broader level, additional research could help develop strategies to implement and finance psychological interventions for relatively mild complaints that are only needed by small numbers of patients. This could, for example, include a platform on which e-Health programs on these topics are available to patients, and where MHWs and nurses can do brief online trainings to equip them with knowledge and skills to support patients.

CONCLUSION

FCR is experienced by more than half of cancer survivors, most of whom want support. It negatively impacts quality of life and leads to increased healthcare costs. Resource constraints do not permit the provision of specialized mental health care to all survivors with FCR, and for many patients this may also not be the most suitable or preferred option. A primary care intervention combining an online program and sessions with an MHW provides an easily accessible, relatively inexpensive, effective alternative that can potentially replace or precede existing specialized psycho-oncological interventions, especially for patients with moderate FCR. We therefore recommend making it available on all existing e-Health platforms, incorporating it in general education for GPs and MHWs, and ensuring all patients and healthcare providers know that FCR exists, and that care is available.

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SUPPLEMENTARY MATERIALS

The supplementary materials are available in the online version of this thesis.

SUMMARY

The number of cancer survivors is increasing, because cancer is detected earlier due to screening and because treatments have improved over the years. But even after successful cancer treatment, many people experience fear that the cancer will return. This fear is a normal and understandable response, but if the fear starts to dominate daily life and leads to limitations, it can be useful to receive professional guidance to learn new ways to deal with the fear. This thesis is about how many people experience fear of cancer recurrence, what their need for help is, whether it is effective to treat this fear in primary care and whether this is acceptable and feasible according to healthcare providers and patients.

In Chapter 2, we describe how many people experience this fear. In a large international study in which we combined data of 9,311 individual patients, we found that 39.6% experienced moderate fear of recurrence and 19.2% experienced severe fear. Younger people and women experience slightly more fear, but people of all ages, genders, cancer types and continents experience this fear, and regardless of how much time has passed since diagnosis.

In Chapter 3, we analyzed the needs for help of people with this fear, based on a questionnaire that was filled out online by 5,323 respondents. Although many people experience this fear, not everyone needs professional help. Some do not experience enough distress to want support, some do not want to burden healthcare providers with emotional issues, and some view seeking help as a sign of failure or weakness. Nonetheless, we found that 94% of those with this fear need some form of help. Some of this help can be provided by friends and family, for example by talking about the fear or by doing fun activities for distraction. For other needs, such as psychological help, tips and information, professional help is needed. Fortunately, 85% of respondents with a need for help had already received at least one form of support.

For patients who need psychological help, several types of specialized psychological treatments exist. However, given the large number of cancer survivors, and the high prevalence of this fear, it is not possible to provide specialized psycho-oncological care to all. Less intensive forms of care are more scalable and cheaper, and can also be more attractive to patients. As cancer follow-up care is currently shifting from hospital care to primary care, general practitioners (GP) may also play a greater role in providing care for fear of cancer recurrence. Patients often prefer their GP for psychosocial care and GPs consider this a fitting role. Almost all GPs in the Netherlands employ mental health workers (MHW), whose primary task is to provide support to patients with light psychological complaints. Therefore, supporting patients whose fear of recurrence is not so serious or complex that it requires specialized care, but serious enough to limit patients in daily life, fits well with the work of the MHW.

Therefore, we investigated whether treating fear of cancer recurrence in primary care is feasible and (cost-) effective. Therapists and clients of the Helen Dowling Institute developed an e-Health program: Less Fear After Cancer[§]. The program is based on cognitive behavioral therapy (CBT) and includes information, exercises and videos of other patients' experiences. It is available continuously. The program was offered with three to five sessions with a trained MHW. Patients who participated in the study received the treatment in their own general practice. The protocol of this study is described in Chapter 4 and the results are presented in Chapter 5.

Despite the high prevalence of this fear and the great need for help for this fear, only 62 (4.5%) of the invited patients participated in the study. With these low numbers, the effectiveness of the treatment could not be scientifically robustly evaluated, but it had potential with a reduction of 3.5 points on the FCRI questionnaire[¶] in the intervention group and 0.7 points in the control group (according to the per-protocol analysis). Due to the COVID-19 pandemic, it was not possible to recruit additional GP practices for the study. That is why a second study was started, in which the sessions in the GP practice were replaced with video calls and participants were recruited online instead of in the GP practice.

The results of this second study on the effectiveness of the online program Less Fear After Cancer with video calls with an MHW are described in Chapter 6. 173 people participated. The treatment was found to significantly reduce fear of cancer recurrence: 2.7 points (SD=3.9) in the intervention group and 0.6 points (SD=3.6) in the control group, $t(152) = 3.4$, $p < 0.001$ (intention-to-treat analysis). In addition, general anxiety, depression, distress and somatic complaints were also significantly reduced in the intervention group and all these reductions were maintained at the follow-up measurement after 10 months. The treatment was effective for a broad group of patients and independent of the competencies of individual MHWs. Most participants also indicated in a survey that they found the treatment practical and the right approach and were satisfied with the result.

To find out more about the acceptability and feasibility of the treatment, interviews were held with 9 patients and 13 MHWs who had participated in the studies (Chapter 7). These interviews confirmed that the treatment was appreciated by both patients and MHWs. The combination of an online program and conversations with an MHW offered patients the opportunity to be heard and ask questions in the conversations, and to deepen their knowledge and practice what they learned at home. The flexibility of the treatment, including optional modules on different topics, allowed it to be adapted to the specific needs of individual patients. However, there are patients for whom the treatment is less

§ See https://hdi.nl/therapie/minder-angst-na-kanker/

¶ We used the short form of the Dutch version of the Fear of Cancer Recurrence Inventory.

suitable, for example patients with a lack of language or digital skills, patients who require specialized psychological care and patients for whom the content is already familiar.

The treatment fits well with the role and expertise of GPs and MHWs, but there are some practical obstacles to implementation. The most important obstacle is the low number of patients per practice, which limits the opportunities for MHWs to develop expertise and which may also limit the investments that GP practices are willing to make.

Based on the research, we make a number of recommendations for clinical practice: First, to healthcare providers, that they discuss this fear and provide brief psychoeducation to all cancer patients as a standard part of care. Second, to make physicians and other healthcare professionals more aware of where to find information and tips about fear of cancer recurrence so that they can share them with patients. Third, it is recommended to provide matched care to patients who need psychological care for fear of cancer recurrence. For many, this could start with the treatment that was studied. For some, this intervention will be enough. For others, extra psychological care will be required, which can build on our intervention. Still others are probably helped best with a direct referral to specialized psycho-oncological care.

To implement the intervention that was studied, we recommend to a) include information about cancer and this intervention in the regular curricula for GPs, MHWs and oncology nurses, b) ensure that the online program becomes available in existing e-Health platforms to make it easily accessible, c) offer trainings for MHWs and nurses who want to learn more or specialize in this area, and d) create a short online educational module for MHWs and nurses who do not want to specialize in this area, but who do want to know somewhat more to support patients better.

For future research, we recommend identifying more factors, especially psychosocial factors, that predict the severity of fear of cancer recurrence and can help to differentiate between different groups of patients with different needs. Because the impact of the fear does not equal the severity of the fear, we also recommend further research to discover what determines the impact and need for help for this fear and what types of patients can best be helped by what types of care.

SAMENVATTING IN HET NEDERLANDS

Er zijn steeds meer mensen die kanker overleven, omdat het door screening eerder wordt ontdekt en behandelingen in de loop der jaren zijn verbeterd. Ook na een succesvolle kankerbehandeling ervaren veel mensen angst dat de kanker terug kan komen. Deze angst is een normale en invoelbare reactie. Maar, als de angst het dagelijks leven gaat beheersen en leidt tot beperkingen kan het zinvol zijn om met professionele begeleiding nieuwe manieren te leren om hiermee om te gaan. Dit proefschrift gaat over hoe vaak deze angst voorkomt, welke behoefte aan hulp mensen met deze angst hebben, of het mogelijk is om deze angst in de huisartspraktijk te behandelen en of dit wenselijk en haalbaar is volgens hulpverleners en patienten.

In hoofdstuk 2 beschrijven we hoeveel mensen deze angst ervaren. In een groot internationaal onderzoek, waarin we individuele data van 9.311 mensen samenbrachten, ontdekten we dat 39,6% matige angst voor terugkeer ervaart en 19,2% ernstige. Jongere mensen en vrouwen ervaren iets meer angst, maar mensen van alle leeftijden, geslachten, kankertypes en continenten ervaren angst voor terugkeer, en ook ongeacht hoeveel tijd er is verstreken sinds de diagnose.

In Hoofdstuk 3 analyseerden we de hulpbehoeften van mensen met deze angst op basis van een vragenlijst die 5,323 respondenten online invulden. Hoewel veel mensen deze angst ervaren, heeft niet iedereen behoefte aan professionele hulp. Sommigen hebben er niet zodanig last van dat ze hulp willen, sommigen willen zorgverleners niet lastigvallen met emotionele zaken, en sommigen beschouwen het zoeken van hulp als een teken van mislukking of zwakte. Toch ontdekten we dat 94% van degenen met deze angst, behoefte heeft aan een vorm van hulp. Een deel van deze hulp kan worden geboden door vrienden en familie, bijvoorbeeld door te praten over de angst of door leuke activiteiten te doen ter afleiding. Voor andere behoeften, zoals psychologische hulp, tips en informatie, is professionele hulp nodig. Gelukkig had 85% van de respondenten met een behoefte aan hulp al minstens één vorm van ondersteuning gekregen.

Voor de patienten die behoefte aan psychologische hulp hebben, bestaan er gespecialiseerde psychologische behandelingen. Maar, gezien het grote aantal kankeroverlevers, en de hoge prevalentie van deze angst, is het niet mogelijk om iedereen gespecialiseerde psycho-oncologische zorg te bieden. Vanuit een perspectief van passende zorg is dat ook niet nodig of wenselijk. Minder intensieve hulpvormen zijn schaalbaarder en goedkoper, en kunnen ook aantrekkelijker zijn voor patiënten. Aangezien de nazorg bij kanker momenteel verschuift van ziekenhuiszorg naar eerstelijnszorg, kunnen huisartsen ook een grotere rol spelen bij het verlenen van zorg voor angst voor terugkeer van kanker. Patienten geven vaak de voorkeur aan hun huisarts voor psychosociale zorg en huisartsen vinden dit een passende rol. Vrijwel alle huisartsen in Nederland hebben praktijk ondersteuners geeste-

lijke gezondheidszorg (POH-GGZ) in dienst, met als primaire taak om begeleiding en zorg te bieden aan patienten met lichte psychische klachten. Het ondersteunen van patiënten van wie de angst voor terugkeer niet zo ernstig of complex is dat het gespecialiseerde zorg vereist, maar wel ernstig genoeg is om patiënten in het dagelijks leven te beperken, past dus goed bij het werk van de POH-GGZ.

Daarom hebben wij onderzocht of behandeling in de huisartspraktijk voor angst voor terugkeer van kanker haalbaar en effectief is. Therapeuten en cliënten van het Helen Dowling Instituut ontwikkelden een e-Health-programma: Minder Angst na Kanker[**]. Het programma is gebaseerd op cognitieve gedragstherapie (CGT) en bevat informatie, oefeningen en video's van andere patiënten. Het is continu beschikbaar. Het programma werd aangeboden met drie tot vijf gesprekken met een getrainde POH-GGZ. Patienten die deelnamen aan het onderzoek kregen de behandeling in hun eigen huisartspraktijk. Het protocol van deze studie staat beschreven in Hoofdstuk 4 en de resultaten staan in Hoofdstuk 5.

Ondanks de hoge prevalentie van deze angst en de grote behoefte aan hulp voor deze angst, namen slechts 62 (4,5%) van de uitgenodigde patiënten deel aan de studie. Met deze lage aantallen kon de effectiviteit van de behandeling niet wetenschappelijk betrouwbaar worden geëvalueerd, maar er werd wel potentie gezien met een afname van 3,5 punt op de FCRI-vragenlijst[††] in de interventiegroep en 0,7 punten in de controlegroep (per protocolanalyse). Vanwege de COVID-19-pandemie was het niet mogelijk om extra huisartspraktijken te werven voor de studie. Daarom is gekozen voor een vervolgstudie met een andere insteek, waarbij de gesprekken in de huisartspraktijk zijn vervangen door videobelgesprekken, en de deelnemers ook online werden gerecruteerd en niet vanuit de eigen huisartspraktijk.

De resultaten van deze tweede studie over het effect van het online programma Minder Angst na Kanker met videobelgesprekken met een POH-GGZ zijn beschreven in Hoofdstuk 6. 173 mensen deden mee. De behandeling bleek de angst significant te verminderen: 2,7 punten (SD=3,9) in de interventiegroep tegenover 0,6 punten (SD=3,6) in de controlegroep, $t(152) = 3,4$, $p < 0,001$ (intention-to-treat-analyse). Bovendien waren ook algemene angst-, depressie-, distress- en somatische klachten significant verminderd in de interventiegroep en al deze afnames waren nog in stand bij de meting na 10 maanden. De behandeling was effectief voor een brede groep patiënten en onafhankelijk van de competenties van individuele POH-GGZ. Ook gaven de meeste deelnemers in een enquête aan dat ze de behandeling praktisch en de juiste aanpak vonden en tevreden waren met het resultaat.

** Zie https://hdi.nl/therapie/minder-angst-na-kanker/

†† We gebruikten de korte variant van de Nederlandse versie van de Fear of Cancer Recurrence Inventory. Zie https://hdi.nl/meetinstrumenten/ .

Om meer te weten te komen over de wenselijkheid en haalbaarheid van de behandeling zijn interviews gehouden met 9 patiënten en 13 POH-GGZ die deelnamen aan de studies (hoofdstuk 7). Deze interviews bevestigden dat de behandeling werd gewaardeerd door zowel patiënten als POH-GGZ. De combinatie van een online programma en gesprekken met een POH-GGZ bood patiënten de mogelijkheid om gehoord te worden en vragen te stellen in de gesprekken, en thuis hun kennis te verdiepen en te oefenen met wat zij hadden geleerd. Door de flexibiliteit van de behandeling, met o.a. optionele modules over verschillende onderwerpen, kon deze worden aangepast aan de specifieke individuele behoeften van de patiënt. Toch zijn er patiënten voor wie de behandeling minder geschikt is, bijvoorbeeld patiënten met een gebrek aan taal- of digitale vaardigheden, patiënten die gespecialiseerde zorg nodig hebben en patiënten voor wie de inhoud al bekend is.

De behandeling sluit goed aan bij de rol en expertise van huisartsen en POH-GGZ, maar er zijn enkele praktische belemmeringen voor implementatie. De belangrijkste is het lage aantal patiënten per praktijk, waardoor de mogelijkheden voor POH-GGZ om expertise te ontwikkelen beperkt zijn en wat mogelijk ook de bereidheid van huisartspraktijken om investeringen te doen in deze behandeling beperkt.

Op basis van het onderzoek doen we een aantal aanbevelingen voor de klinische praktijk: Ten eerste, aan zorgverleners, om deze angst te bespreken en korte psycho-educatie te geven aan alle kankerpatiënten als standaardonderdeel van de zorg. Ten tweede, om zorgverleners meer bewust te maken over waar informatie en tips over angst voor terugkeer te vinden zijn, zodat zij hun patiënten daar op kunnen wijzen. Ten derde wordt aanbevolen om zorg op maat te bieden aan patiënten die psychologische zorg bij angst voor terugkeer van kanker nodig hebben. Voor velen zou dit kunnen beginnen met de in dit onderzoek onderzochte behandeling. Voor sommigen zal dit voldoende zijn. Voor anderen zal extra zorg nodig zijn, maar die kan dan voortborduren op de onderzochte behandeling. Weer anderen zijn waarschijnlijk het best geholpen met een directe verwijzing naar gespecialiseerde psycho-oncologische zorg.

Om de onderzochte behandeling te implementeren, raden we aan om a) informatie over kanker en over deze behandeling op te nemen in de reguliere curricula voor huisartsen, POH-GGZ en oncologieverpleegkundigen, b) ervoor te zorgen dat het online programma beschikbaar komt in bestaande e-Health-platforms om het gemakkelijk toegankelijk te maken, c) nascholingen aan te bieden voor POH-GGZ en verpleegkundigen die meer willen leren of zich willen specialiseren op dit gebied, en d) een korte online educatieve module te creeeren voor POH-GGZ en verpleegkundigen die zich niet willen specialiseren in deze angst, maar wel voldoende willen weten om begeleiding te kunnen bieden.

We bevelen aan om met verder onderzoek nog beter in kaart te brengen welke factoren, met name psychosociale factoren, de ernst van deze angst voorspellen en hoe dit kan

bijdragen om verschillende groepen patiënten met verschillende zorgbehoeften te onderscheiden. Omdat de impact van de angst niet gelijk is aan de ernst van de angst, raden we ook aan om meer onderzoek te doen om te ontdekken wat de impact en behoefte aan hulp voor deze angst bepaalt en wat bepaalt welke soorten patiënten het beste kunnen worden geholpen door welke soorten zorg.

LIST OF PUBLICATIONS

Chapter 2

Luigjes-Huizer YL, Tauber NM, Humphris G, Kasparian NA, Lam WWT, Lebel S, et al. What is the prevalence of fear of cancer recurrence in cancer survivors and patients? A systematic review and individual participant data meta-analysis. Psychooncology. 2022;(February):1–14.

Chapter 3

Luigjes-Huizer YL, van der Lee ML, Richel C, Masselink RA, de Wit NJ, Helsper CW. Patient-reported needs for coping with worry or fear about cancer recurrence and the extent to which they are being met : a survey study. J Cancer Surviv [Internet]. 2022;Dec 30:1–9.

Chapter 4

Luigjes-Huizer YL, van der Lee ML, de Wit NJ, Helsper CW. Study protocol of the BLANKET trial: A cluster randomised controlled trial on the (cost-) effectiveness of a primary care intervention for fear of cancer recurrence in cancer survivors. Vol. 9, BMJ Open. 2019. p. 1–7.

Chapter 5

Luigjes-Huizer YL, Helsper CW, Gerrits MMJG, de Wit N, van der Lee ML. Need for a primary care–based intervention for fear of cancer recurrence: conclusions from the BLANKET trial. J Psychosoc Oncol Res Pract. 2022;4(4):2–5.

Chapter 6

Luigjes-Huizer YL, Helsper CW, de Wit N, van der Lee ML. Effectiveness of a guided online primary care intervention for fear of cancer recurrence: a randomised controlled trial. *Submitted.*

Chapter 7

YL Luigjes-Huizer YL, Schellekens MPJ, de Wit NJ, Helsper CW, van Dongen SI, van Roozendaal AS, van Woezik RAM, van der Lee ML. A qualitative study on the feasibility and acceptability of a primary care intervention for fear of cancer recurrence. *Submitted.*

DANKWOORD

Aan het einde van vijf prachtige onderzoeksjaren, mag ik nu mijn dankwoord schrijven. En wat is er veel om dankbaar voor te zijn. Ik verwonder me over hoeveel mensen hebben bijgedragen aan dit proefschrift en hoeveel er mogelijk is als mensen zich eensgezind inzetten voor een gezamenlijk doel.

Allereerst wil ik de deelnemers aan het onderzoek bedanken. Zonder jullie konden we niets beginnen. Dank voor jullie vertrouwen en bereidheid om deel te nemen, vragenlijsten in te vullen, geinterviewd te worden en jullie persoonlijke ervaringen te delen.

Ook de POH-GGZ en de huisartsen ben ik veel dank verschuldigd. Jullie nodigden jullie patienten uit, jullie voerden de gesprekken, jullie liepen tegen de obstakels aan en jullie boden de zorg. Heel veel dank hiervoor.

Prof. dr. N.J. de Wit, dr. C.W. Helsper en prof. dr. van der Lee, ik had me geen beter team kunnen wensen. Bij mijn sollicitatie gaf ik aan dat ik graag veel ruimte wilde om mijn werk zelfstandig en op mijn eigen manier te doen, en dat ik van jullie dan graag kaders en ruimte om te sparren zou willen krijgen. Dat heb ik ook gekregen en heeft me heel goed gedaan. Daarnaast was het ook altijd gezellig en plezierig om met jullie samen te werken.

Beste Niek, ik blijf onder de indruk van de zinnige, wijze en vernieuwende adviezen die je elke keer wist te geven tijdens onze overleggen, ookal was dit maar een van de vele zaken waar je mee bezig was. Ook veel dank voor de vriendelijke betrokkenheid en de snelle reacties op mijn stukken.

Beste Charles, dank voor de open en gezellige gesprekken en voor het helpen om de studie in gang te zetten, o.a. in de huisartspraktijken. Met jou besprak ik vaak de meer filosofische of ethische kanten van het onderzoek (en soms ook van het leven), iets wat ik altijd leuk vind om te doen.

Beste Marije, je bent voor mij een inspiratie. Naast natuurlijk je wetenschappelijke inbreng en alles wat je voor patienten bereikt, zet je ons als HDI onderzoeksteam in onze kracht om uit onszelf te halen wat erin zit. Je bent efficient en je houdt honderd ballen in de lucht en toch geef je rust en aandacht aan de persoon die voor je zit. En waar je ook bent, je bent mens en je bent jezelf.

Geachte leden van de beoordelings- en promotiecommissie, Prof. dr. N.H. Chavannes, Prof. dr. A.M. May, Prof. dr. J.B. Prins, Prof. dr. M.J. Schuurmans, Prof. dr. E. van der Wall en Prof. dr. M.Y. Berger, hartelijk dank voor het beoordelen van mijn proefschrift.

Anne, Berend, Laura, Martijn, Melanie, Pascalle, Rosalie, Sophie, Tom en anderen, heel veel dank voor het warme team waarbinnen ik mijn onderzoek mocht doen. Mijn project

was erg zelfstandig, maar ik heb altijd het gevoel gehad dat we allemaal samen de schouders eronder zetten. Prachtig hoe we elkaar helpen, naar elkaar omzien, gedachten delen over van alles en ook heel veel lachen samen. Berend, Rosalie en Anne, jullie wil ik in het bijzonder bedanken voor jullie praktische hulp en optimisme, waarmee jullie me niet alleen enorm veel tijd, maar ook veel energie en veel denkruimte hebben bespaard. Ik had het niet zonder jullie gekund.

Andere HDI-collega's, ook jullie bedankt dat ik onderdeel mocht uitmaken van dit bijzondere instituut. Vergis je niet, jullie zijn stuk voor stuk bijzondere mensen met het hart op de juiste plek en hoe jullie elkaar versterken en wat jullie daardoor samen bieden en aankunnen is uniek en tot grote zegen.

Collega's van het Julius, dank voor het altijd vriendelijke, gezellige en bereidwillige samenwerken. De diversiteit aan onderwerpen en de stevige, scherpende epidemiologische blik vormden een mooie aanvulling op het gefocuste en praktijkgerichte perspectief van het onderzoek bij het Helen Dowling Instituut. Ik heb enorm veel geleerd van de grote en brede verzameling van kennis en expertise die bij het Julius aanwezig is.

Pascalle, Sanne, Paulien en Enne, dank voor de inhoudelijk sterke en leuke trainingen die we mochten geven aan de POH-GGZ. Jullie persoonlijke inbreng was van grote toegevoegde waarde.

To Nina Tauber, the advisory board and all the authors who contributed data to the IPD study, many, many thanks. It was delightful to work together with so many different people from so many different countries and I am very pleased with the result we were able to achieve.

Carol Richel en anderen van NFK, dank voor de warme en productieve samenwerking bij het onderzoek over zorgbehoeften bij angst voor terugkeer van kanker.

Graag wil ik ook alle andere betrokkenen, samenwerkingspartners en co-auteurs bedanken voor hun bijdragen en de prettige samenwerking.

Vrienden en familie, teveel om bij naam te noemen, ook zonder jullie had ik het echt niet kunnen doen. Jullie bieden mij ruimte om mijzelf te zijn. Ruimte om te dromen, om onverwachte plannen aan te gaan en om grote projecten op te pakken en daar vervolgens in op te gaan. Zelfs wanneer ik andere paden dan jullie kies, dan blijven jullie me aanmoedigen en bemoedigen, waarvoor heel veel dank. And Lauren, thank you also for helping me with grammar and word choices in these last few months.

Bob, Rebekka en Elisa, jullie zijn de belangrijkste mensen in mijn leven. Ik ben enorm dankbaar om deel te zijn van onze viereenheid. Bob, bijzonder hoe je oneindig naar mijn gedachten kunt blijven luisteren en me daarmee ook helpt om die te vormen. En heel fijn

hoe je ook vanuit je eigen werk- en PhD-ervaring me kon helpen om dit project te volbrengen en persoonlijke groei door te maken. Rebekka en Elisa, jullie geven me elke dag levenszin en levensvreugde met jullie vrolijkheid en nieuwsgierigheid en gewoon doordat jullie bestaan. Jullie helpen me om diep van binnen te weten wat belangrijk is in het leven.

ABOUT THE AUTHOR

Yvonne Luigjes-Huizer was born on July 28, 1989, in Eindhoven, the Netherlands. She completed the International Baccalaureate program in Newbury Park, California, USA in 2007. Afterwards, she obtained a BSc in Psychology from Utrecht University in 2010 and she completed the MSc program Management, Policy-Analysis and Entrepreneurship in Health and Life Sciences (cum laude) at VU University Amsterdam in 2013.

As part of her MSc program, she worked at mental healthcare institution Altrecht on a project to develop a new intervention for families of people with bipolar disorder. She also did research on infectious disease outbreak management at the National Institute for Health and the Environment (RIVM) during her MSc program. After obtaining her MSc, she worked as a project advisor and monitoring and evaluation specialist for international development organizations for four years, including a year in Burundi.

In every role she takes on, Yvonne aims to improve the health and lives of people and to contribute to the development of better (health) systems. This was also her motivation for starting her PhD project on the prevalence and the burden of fear of cancer recurrence and the role of primary care in treating this fear. She conducted her PhD research at the Helen Dowling Institute and the Julius Center for Health Sciences and Primary Care at the University Medical Center Utrecht. During her PhD project, she obtained a MSc in Epidemiology at Utrecht University.

Yvonne is passionate about improving mental health and mental healthcare in the Netherlands and plans to continue to work in research and implementation to further this cause. Her next step is doing research at 113 Suicide Prevention in Amsterdam.

SUPPLEMENTARY MATERIALS

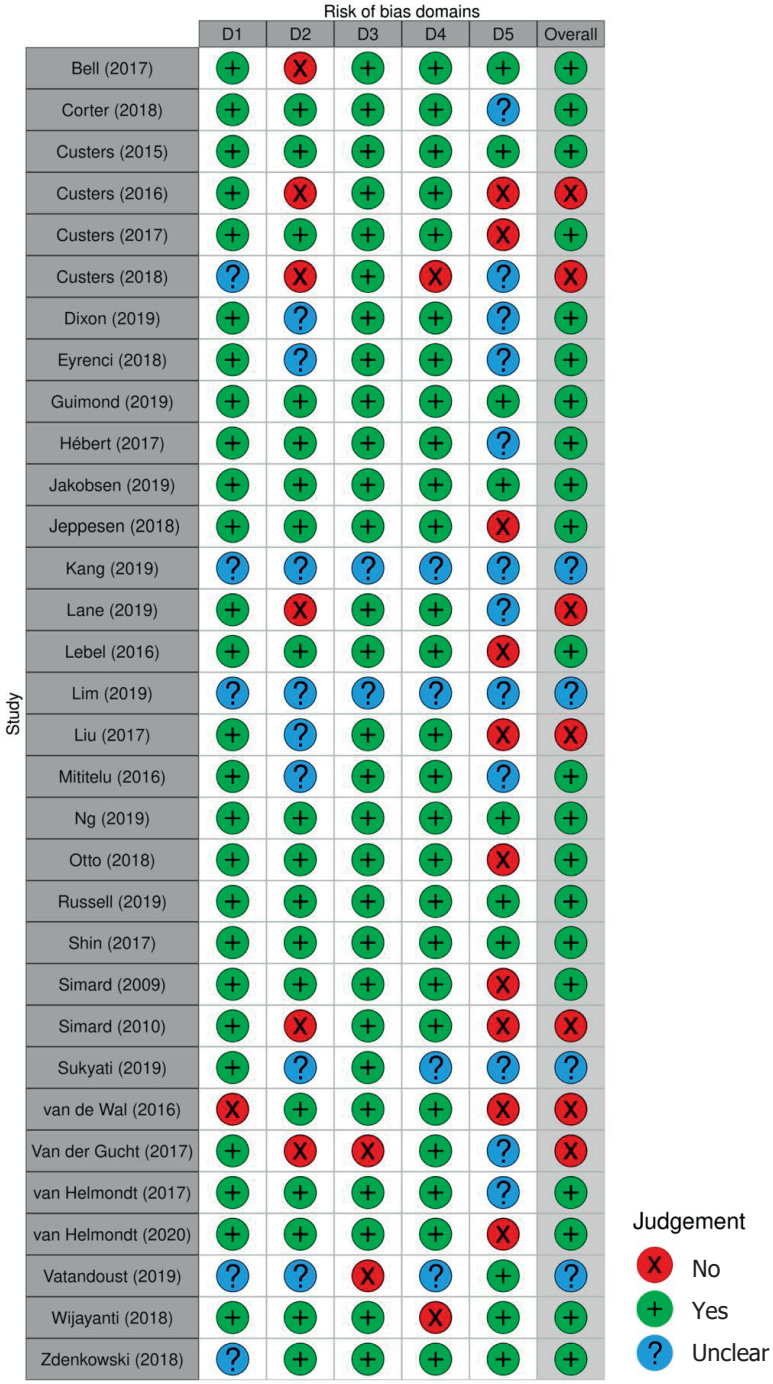
Supplementary Materials 2A: Joanna Briggs Institute Critical Appraisal Checklist for Studies Reporting Prevalence Data

1. Was the sample frame appropriate to address the target population?
2. Were study participants sampled in an appropriate way?
3. Was the sample size adequate?
4. Were the study subjects and the setting described in detail?
5. Was the response rate adequate, and if not, was the low response rate managed appropriately?

We have omitted four questions that were not relevant for this study.

Supplementary Materials 2B: Risk of bias assessment

a)



b)

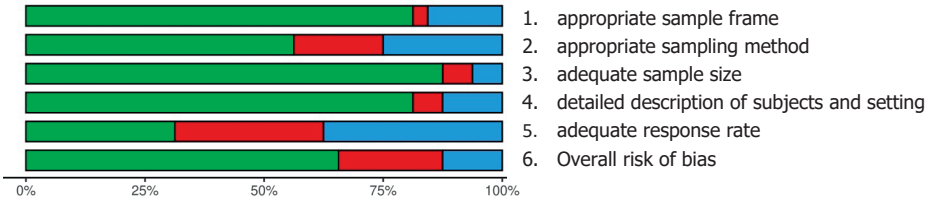
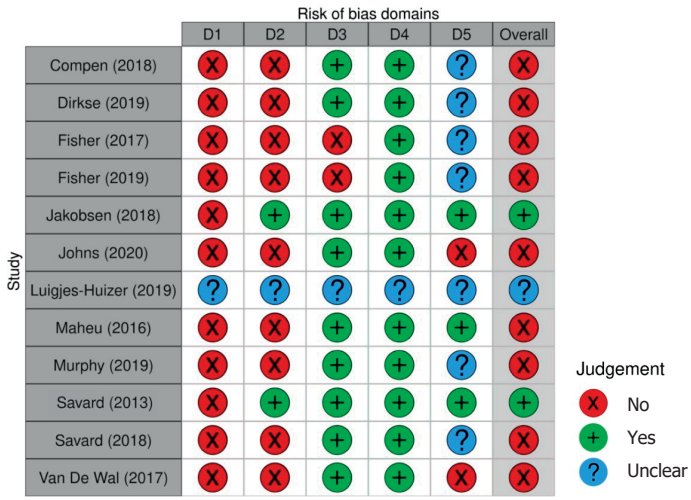


Figure 1. Risk of bias assessment of studies that provided data and did not select on level of FCR, a) shows assessment per study, b) shows a summary of all studies. Figure created using robvis.

a)



b)

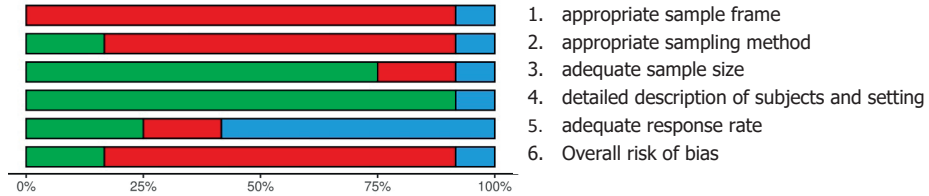


Figure 2. Risk of bias assessment of studies that provided data and selected on level of FCR, a) shows assessment per study, b) shows a summary of all studies. Figure created using robvis.

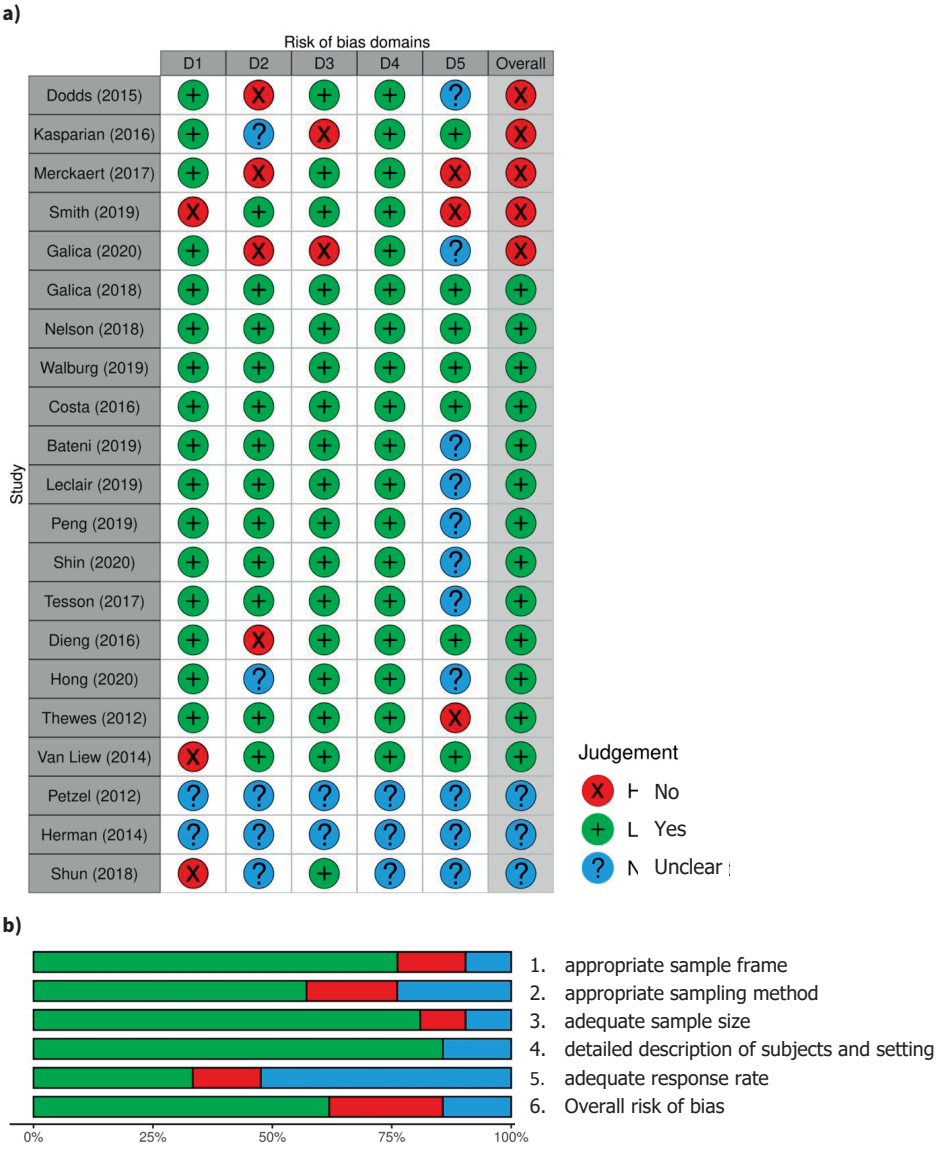


Figure 3. Risk of bias assessment of studies that were included in the aggregate data analysis, a) shows assessment per study, b) shows a summary of all studies. Figure created using robvis (95).

Supplementary Materials 2C: Main characteristics and mean FCR scores per dataset

Table 1. Main characteristics and mean FCR scores for datasets that did not select participants based on their level of fear of cancer recurrence or related factors.

			FCR severity	Mean age			Sex			Patients	Survivors	Mean time since cancer diagnosis
Author	**year**	**n**	**mean (sd)**	**(yrs)**	**Country**	**Language**	***men (n)***	***women (n)***	**Cancer type**	**(n)**	**(n)**	**(yrs)**
Bell	2017	215	15.3 (6.8)	65	Australia	English	137	78	melanoma	0	215	1.3
Corter	2018	125	17.2 (7.6)	56	New Zealand	English	0	125	breast	0	125	0.4
Custers	2015	54	16.9 (7.7)	62	the Netherlands	Dutch	29	25	other	54	0	4.8
Custers	2017	460	16 (6.8)	57	the Netherlands	Dutch	0	460	breast	0	460	2.8
Custers	2016	76	11.6 (7.3)	67	the Netherlands	Dutch	40	36	colorectal	0	76	5.0
Custers	2018	150	13.2 (6.4)	68	the Netherlands	Dutch	97	53	colorectal	150	0	0.0
Dixon	2019	97	24.3 (6.8)	-	USA	English	33	64	breast, lung	0	97	-
Eyrenci	2018	217	15.3 (7.4)	51	Turkey	Turkish	43	174	multiple	0	217	4.5
Galica	*n.p.*	219	17.3 (7.9)	64	Canada	English	40	178	breast, colorectal	0	219	-
Guimond	2019	81	11.5 (5.8)	59	Canada	French	0	81	breast	81	0	0.3
Hebert	2017	38	14.2 (6.6)	69	Canada	French	0	38	endometrial	38	0	-
Jakobsen	2019	141	11.7 (6.3)	66	Denmark	Danish	100	41	colorectal	0	93	1.1
Jeppesen	2018	212	10.4 (7.1)	65	Denmark	Danish	0	212	endometrial	0	212	0.0
Kang	2019	52	12.7 (6.5)	63	Canada	English	52	0	prostate cancer	52	0	1.9
Lane	2019	554	22.8 (7)	34	Canada	English	72	482	multiple	37	301	4.9
Lebel	2016	350	13.8 (7.9)	67	Canada	English	185	165	multiple	2	295	5.9
Lim	2019	125	10.9 (6.7)	59	South Korea	Korean	80	45	colorectal	125	0	-
Liu	2017	405	13.1 (6.7)	56	Singapore	English	81	324	multiple	0	405	-

Table 1. Main characteristics and mean FCR scores for datasets that did not select participants based on their level of fear of cancer recurrence or related factors. (*continued*)

			FCR severity	Mean age			Sex			Patients	Survivors	Mean time since cancer diagnosis
Author	**year**	**n**	**mean (sd)**	**(yrs)**	**Country**	**Language**	***men (n)***	***women (n)***	**Cancer type**	**(n)**	**(n)**	**(yrs)**
Mititelu	2016	32	16.5 (6.5)	-	Canada	English	3	29	multiple	4	13	2.2
Ng	2019	293	10.8 (7.2)	60	Hong Kong	Cantonese	76	217	breast, colorectal	0	293	0.0
Otto	2018	300	15 (7.8)	62	USA	English	0	300	breast	0	300	3.5
Russell	2019	69	16.8 (7.3)	53	Australia	English	32	37	melanoma	0	69	3.9
Shin	2017	239	15.1 (7.2)	50	South Korea	Korean	71	168	multiple	239	0	0.0
Simard	2009	1984	12.9 (6.9)	63	Canada	French	904	1080	multiple	575	1390	4.2
Simard	2010	600	12.9 (6.8)	64	Canada	French	319	281	multiple	451	149	4.7
Sukyati	2019	114	12.2 (7.9)	52	Indonesia	Indonesia	0	114	other	114	0	-
Tauber	*n.p.*	780	15.2 (7.3)	-	Denmark	Danish	0	780	breast	0	780	-
Van de Wal	2016	311	10.7 (7.1)	70	the Netherlands	Dutch	311	0	prostate	0	311	8.3
van der Gucht	2017	11	20.6 (8.1)	21	Belgium	Dutch	6	5	leukemia, lung	0	11	6.0
van Helmondt	2020	454	13.9 (6.9)	58	the Netherlands	Dutch	0	454	breast	0	454	2.6
van Helmondt	2017	290	18.8 (5.1)	52	the Netherlands	Dutch	39	251	-	0	290	-
Vatandoust	2019	51	12.1 (6.6)	64	Australia	English	36	15	colorectal	0	51	4.7
Wijayanti	2018	153	18.9 (5.2)	52	Indonesia	Indonesia	0	153	other	153	0	-
Zdenkowski	2018	59	15.5 (6.1)	52	Australia	English	0	59	breast	0	59	0.0

Table 2. Main characteristics and mean FCR scores for datasets that did select participants based on their level of fear of cancer recurrence or related factors.

			FCR severity	Mean age			Sex			Patients	Survivors	Mean time since cancer diagnosis
Author	year	n	mean (sd)	(yrs)	Country	Language	*men (n)*	*women (n)*	Cancer type	(n)	(n)	(yrs)
Compen	2018	245	21.3 (6.5)	52	the Netherlands	Dutch	35	210	multiple	-	-	3.5
Dirkse	2020	83	21.5 (5)	51	Canada	English	14	69	multiple	0	83	2.1
Fisher	2019	27	25.6 (7.6)	51	United Kingdom	English	3	24	multiple	0	27	-
Fisher	2017	4	30.3 (4.9)	NA	United Kingdom	English	0	4	breast, endometrial	0	4	2.1
Jakobsen	2018	69	12.4 (7)	67	Denmark	Danish	39	30	colorectal	0	31	1.9
Johns	2020	91	19 (5.6)	58	USA	English	0	91	breast	0	91	5.1
Luigjes-Huizer	2019	58	17.6 (7.3)	64	the Netherlands	Dutch	21	26	multiple	0	58	6.9
Maheu	2016	136	23.1 (5.4)	56	Canada	English	0	136	multiple	0	136	2.2
Murphy	2020	114	22.4 (5.7)	53	Australia	English	13	101	multiple	-	-	4.0
Savard	2013	962	14.3 (6.9)	57	Canada	French	343	619	multiple	962	0	0.2
Savard	2018	38	21.4 (5.6)	57	Canada	French	2	36	multiple	9	16	1.1
Van de Wal	2017	88	19.3 (7.2)	59	the Netherlands	Dutch	41	47	multiple	0	88	2.6

Supplementary Materials 2D: Characteristics of FCR severity groups, according to different cutoffs.

For these analyses, 12 additional studies were included, that had selected participants based on the severity of their FCR. The mean FCR severity score for these additional studies was 20.7.

Table 1. Characteristics of FCR severity groups, according to different cutoffs.

	< 13		13-15		16-21		≥22	
	Survivors	Patients	Survivors	Patients	Survivors	Patients	Survivors	Patients
Sex								
Men	1150 (39)	512 (40)	279 (28)	168 (34)	475 (23)	216 (27)	302 (17)	133 (23)
Women	1817 (61)	778 (60)	702 (72)	332 (66)	1581 (77)	575 (73)	1484 (83)	455 (77)
Age groups								
18-29 years	19 (1)	9 (1)	12 (1)	4 (1)	55 (3)	10 (1)	84 (5)	17 (3)
30-44 years	157 (5)	100 (8)	108 (11)	57 (11)	274 (14)	94 (12)	431 (25)	110 (19)
45-59 years	753 (26)	468 (36)	367 (38)	218 (44)	793 (40)	365 (46)	628 (37)	262 (45)
60-74 years	1505 (52)	600 (47)	384 (40)	200 (40)	733 (37)	282 (36)	481 (28)	178 (30)
≥75 years	474 (16)	113 (9)	92 (10)	20 (4)	127 (6)	36 (5)	71 (4)	20 (3)
Cancer type								
Breast cancer	1368 (47)	534 (41)	536 (57)	223 (44)	1148 (60)	385 (49)	1025 (61)	263 (45)
Colon and rectal cancer	373 (13)	235 (18)	102 (11)	56 (11)	171 (9)	112 (14)	133 (8)	61 (11)
Endometrial cancer	123 (4)	59 (5)	25 (3)	32 (6)	38 (2)	33 (4)	33 (2)	28 (5)
Leukemia & non-hodgkin lymphoma	19 (1)	1 (0)	13 (1)	1 (0)	34 (2)	3 (0)	42 (2)	9 (2)
Lung cancer	57 (2)	35 (3)	16 (2)	18 (4)	36 (2)	39 (5)	73 (4)	23 (4)
Melanoma	89 (3)	0 (0)	42 (4)	0 (0)	91 (5)	0 (0)	71 (4)	3 (0)
Prostate cancer	754 (26)	289 (22)	151 (16)	105 (21)	218 (11)	99 (13)	101 (6)	65 (11)
Thyroid cancer	4 (0)	0 (0)	8 (1)	0 (0)	9 (0)	3 (0)	25 (1)	5 (1)
Other cancer types	123 (4)	137 (11)	46 (5)	64 (13)	165 (9)	117 (15)	177 (11)	131 (22)
Time since diagnosis								
0-1 years	779 (33)	764 (69)	262 (35)	290 (67)	514 (35)	440 (65)	486 (37)	304 (60)
2-5 years	1098 (47)	246 (22)	347 (46)	107 (25)	686 (46)	160 (24)	581 (44)	142 (28)
6-10 years	328 (14)	69 (6)	100 (13)	23 (5)	203 (14)	50 (7)	174 (13)	41 (8)
>10 years	153 (6)	26 (2)	40 (5)	12 (3)	83 (6)	26 (4)	76 (6)	16 (3)

A partially imputed dataset was used: the variables FCR severity, age, cancer type and time since cancer diagnosis were not imputed, since the imputation did not converge.

Supplementary Materials 3A: Survey on fear or worry about cancer recurrence (original in Dutch)

General Questions

In order to understand and explain the results of this questionnaire well, we first ask some general questions.

1. Did or do you have cancer?
   - o Yes
   - o No [if so, respondents are disqualified from the survey]

2. How did you find this questionnaire?

<drop down menu>

3. What kind of cancer did or do you have?
   - o acute lymphoblastic leukemia (ALL)
   - o pancreatic cancer
   - o cervical cancer
   - o basal cell carcinoma
   - o breast cancer
   - o bone tumor
   - o chronic myeloid leukemia (CML)
   - o diffuse B-cell lymphoma (DLBCL)
   - o ovarian cancer
   - o essential thrombocytosis
   - o bile duct cancer
   - o glioma
   - o hodgkin lymphoma (HL)
   - o pharyngeal cancer
   - o low-grade B-cell lymphoma
   - o lung cancer
   - o lymphoplasmacytic lymphoma
   - o mantle cell lymphoma (MCL)
   - o multiple myeloma
   - o neuroendocrine carcinoma (NEC)
   - o renal pelvic cancer
   - o non-Hodgkin's lymphoma
   - o ovarian carcinoma
   - o squamous cell carcinoma
   - o acute myeloid leukemia (AML)
   - o anal cancer
   - o uterine cancer
   - o bladder cancer
   - o bone sarcoma
   - o chronic lymphocytic leukemia (CLL)
   - o desmoid tumor
   - o colon cancer
   - o rectal cancer
   - o follicular B-cell lymphoma (FL)
   - o gastrointestinal stromal tumor (GIST)
   - o brain tumor
   - o skin cancer
   - o throat cancer
   - o liver cancer
   - o lymphoblastic lymphoma
   - o stomach cancer
   - o melanoma
   - o mycosis fungoides
   - o neuroendocrine tumor (NET)
   - o kidney cancer
   - o eye melanoma
   - o penile cancer
   - o polycythemia vera

- o prostate cancer
- o rectal cancer
- o thyroid cancer
- o larynx cancer
- o trophoblast tumor of placenta
- o testicular cancer
- o Waldenstrom's disease
- o pseudomyxoma peritonei (PMP)
- o sarcoma
- o esophageal cancer
- o tongue cancer
- o vaginal cancer
- o Kahler's disease

4. Did a hereditary cause play a role in your diagnosis of <cancer name>?
   - o Yes, a proven gene mutation by a clinical geneticist
   - o No, but <cancer name> is common in the family
   - o No (not that I'm aware of)

5. Are you currently receiving treatment for <cancer name>?
   - o Yes
   - o No, I have not yet started the treatment
   - o No, it has been decided to wait and see how it goes
   - o No, the treatment is finished, but I still get check-ups in the hospital
   - o No, the treatment is finished. I no longer get check-ups in the hospital

6. Space to explain:

7. What is the best way to describe your current situation regarding <cancer name>?
   - o (As far as I know) I no longer have cancer
   - o I can (probably) get better
   - o I (probably) cannot get better
   - o I have a chronic form of cancer
   - o I don't know

8. Space to explain:

9. What is your gender?
   - o Man
   - o Woman
   - o Other

10. In what year were you born?

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

- o No education
- o Practically trained
- o Secondary education
- o Higher education
- o I'd rather not say
- o Other, namely:

12. What was your home situation at the time of the <cancer name> diagnosis?
    - o I live with my partner
    - o I live with my partner and child(ren) younger than 16 years
    - o I live with my partner and child(ren) older than 16 years
    - o I live with my partner and children younger and older than 16 years
    - o I live alone
    - o I live with a child(ren) younger than 16 years
    - o I live with a child(ren) older than 16 years
    - o I live with children younger and older than 16 years
    - o I'd rather not say
    - o Other

About the diagnosis

13. In what year was the <cancer name> diagnosis made?

14. In which hospital were you for your <cancer name>?
<drop down menu>

Nature of the worry or fear

15. How would you generally describe yourself before you got cancer? Select a number between 1 and 10, where 1 is 'not at all prone to worry or fearful' and 10 is 'very prone to worry or fearful'.

    If you have (had) cancer, you may be worried or feel fear. This may concern, for example, fear of treatment, fear of cancer returning, worry about your future or worry about loved ones.

16. What applies to you most about <cancer name>?
    - o I have never worried or felt fear [if so, respondents go to question 34]
    - o I used to worry or feel fear, but not now or hardly anymore
    - o I have been worried or fearful since my diagnosis
    - o I worry now or have fear, but before I did not

[If respondents indicated they experienced worry or fear in the past, but not anymore, they were asked to fill out the following questions about how they felt in the past]

17. To what extent are/were you worried or fearful about the topics below regarding <cancer name>? Please rate between 1 and 10. 1 stands for 'no worry or fear. 10 stands for 'a lot of worry or fear'.
    - o Getting cancer again: recurrence in the same 'area'
    - o Getting cancer again: in a different 'area'
    - o Undergoing treatments (again)
    - o Consequences of (treatment of) cancer for myself (e.g. physical, work, social, hobbies, finances / insurance)
    - o Consequences of (treatment of) cancer for my partner
    - o Consequences of (treatment of) cancer for my child(ren)
    - o Consequences of (treatment of) cancer for other relatives (family / friends)
    - o Getting metastatic cancer (and therefore not getting better)
    - o Dying

18. Space to explain:

The level of worry or fear may vary by treatment phase and over time.

19. To what extent were you worried or afraid regarding <cancer name> ... ?
    Please rate between 1 and 10. 1 stands for 'no worry or fear. 10 stands for 'a lot of worry or fear'.
    If a phase does not yet apply, you can also indicate that.
    - Around the diagnosis
    - Between diagnosis and treatment(s)
    - During the treatments
    - Shortly after the end of the treatments (1st year)
    - More than 1 year after the end of the treatment(s)

20. Space to explain:

21. Are there situations that evoke or reinforce the worry or fear regarding <cancer name>?
    Multiple answers possible.
    - o Medical examinations (e.g. check-ups: e.g. blood tests, X-rays/scans)
    - o An appointment with my doctor or other healthcare provider
    - o When I have physical complaints or am sick
    - o When I examine my own body

- o When I hear or see stories about cancer in the media
- o When I hear or see stories about cancer in my environment
- o When I think about the future
- o When I read or talk about chances of cancer recurrence or chances of death
- o No, not in a specific situation
- o Other, describe briefly

22. How much worry or fear have you had because of this/these situation(s)?
    Please rate between 1 and 10. 1 stands for 'no worry or fear. 10 stands for 'a lot of worry or fear'.
    [respondents are shown only the situations they marked in the previous question]

23. Space to explain:

24. What expressions of the worry or fears regarding <cancer name> do you experience?
    Multiple answers possible.
    - o Rumination / not being able to let go
    - o Sleeping poorly
    - o Gloominess
    - o Listlessness
    - o Irritability
    - o Different eating pattern (eating more, less or differently)
    - o Physical complaints such as stomachaches or headaches
    - o Concentration problems
    - o Feeling nervous / restless
    - o Tingling in hands or feet
    - o Increased heart rate
    - o Panic attacks (severe fear of short duration, with e.g. palpitations, sweating, nausea)
    - o Other, namely:

25. In this survey, we have talked about 'worry or fear' regarding <cancer name>.
    How would you describe the feeling you experience? It may also be another word.

26. To what extent do you agree with the statements below?
    If you had worries or fears regarding <cancer name> in the past, but not anymore, think about the consequences at that time.
    Because of worry or fear….
    - o … I have less pleasure in things that I normally enjoy

- o … I do fewer social activities (e.g. meeting friends)
- o … I have relationship problems
- o ... I have difficulty with daily activities (ordinary things such as housework, shopping)
- o … I have trouble with sex or intimacy
- o … there are tensions within the family
- o … I cannot (properly) perform my (volunteer) work
- o ... I cannot (properly) carry out my hobbies
- o … I started to live a less healthy life (e.g. drinking more alcohol)

Answer categories: Strongly disagree, disagree, neutral, agree, strongly agree and not applicable.

27. To what extent do (or did) worries or fears regarding <cancer name> have a negative impact on your quality of life?
    Please rate between 1 and 10. 1 stands for 'no negative impact'. 10 stands for 'a lot of negative impact'

28. Space to explain:

Dealing with worry or fear (support)

For worries or fears there is guidance or (online) support. This can be offered by your social environment, but also, for example, by healthcare professionals or others with experience with cancer. Your social environment is, for example, a partner, friends, family, but can also be colleagues or fellow patients. Healthcare professionals are, for example, your GP, nurses, doctors in the hospital or social workers, company doctors or psychologists.

29. What kind of support or guidance do (or did) you need with regard to worries or fears regarding <cancer name>? *Multiple answers possible.*
    - o Talking about it
    - o Distraction / doing fun things
    - o Explanation or information about cancer worry or fears
    - o Practical tips for myself on dealing with worry or fear
    - o Practical tips for my loved ones on dealing with worry or fear
    - o Mental or psychological help or coaching
    - o Help with lifestyle (e.g. eating healthier, exercising more)
    - o Medication for worry or anxiety (e.g. sleeping pill, tranquilizer, anti-anxiety drug, anti-depressants, homeopathy)
    - o More medical check-ups / physical exams

- o I do not need support or guidance because of worries or fears
- o Other, describe briefly

30. Space to explain:

You have just indicated what kind of support or guidance you need(ed). Support or guidance can be given by several people. People in healthcare such as a general practitioner, treating physician in the hospital, nurse, social worker, company doctor, psychologist or coach. There are also other examples. People close to you, such as family, friends and colleagues can also help.

31. From whom would you like to receive this support or guidance? Describe this briefly. This can also be several caregivers or people from your environment. If you don't know, you can indicate that too.
    [respondents are shown only the types of help they marked in the previous question]

32. You have just indicated what support you need or needed in case of worries or fears regarding <cancer name> and from whom. Can you indicate whether you have also received such support or guidance and if so, whether it has helped?
    [respondents are shown only the types of help they ticked in the previous question]

    Answer categories: no; yes, and this has helped; yes, but this didn't help

33. Space to explain:

34. Did the following persons pay attention to (possible) worries or fears about <name of cancer>? It doesn't matter if you had no, few or many worries or fears.
    - The doctor
    - Healthcare providers in the hospital
    - Your employer
    - Your closest environment

    Answer categories: Yes, a little, no, don't remember, not applicable

35. Space to explain:

Finally

36. Do you have any tips for others regarding cancer worries or fears?

For example, how you dealt with it yourself or what others (relatives or care providers) can do.

Supplementary Materials 3B:

Table 1. Number and percentage of respondents who need the different support types per age group, gender and family situation

	Age				Gender		Family situation					
	20-40	41-55	56-70	70+	Men	Women	With partner	without partner	With children	without children	Alone	Not alone
Talking about FCR	143 (77)	700 (74)	1040 (67)	294 (60)	538 (64)	1646 (71)	1679 (69)	464 (69)	810 (72)	1333 (67)	341 (69)	1802 (69)
Enjoyable activities for distraction	126 (68)	593 (63)	843 (55)	216 (44)	380 (45)	1403 (60)	1363 (56)	391 (58)	682 (61)	1072 (54)	277 (56)	1477 (56)
Psychological help or coaching	119 (64)	495 (53)	569 (37)	97 (20)	231 (27)	1054 (45)	961 (39)	286 (42)	528 (47)	719 (36)	207 (42)	1040 (40)
Practical tips about managing fear for self	84 (45)	406 (43)	524 (34)	125 (25)	251 (30)	892 (38)	852 (35)	259 (38)	434 (39)	677 (34)	199 (40)	912 (35)
Information about FCR	72 (39)	319 (34)	424 (27)	143 (29)	228 (27)	731 (31)	726 (30)	211 (31)	337 (30)	600 (30)	148 (30)	789 (30)
Additional medical check-ups	68 (37)	207 (22)	330 (21)	87 (18)	142 (17)	552 (24)	512 (21)	165 (24)	258 (23)	419 (21)	121 (24)	556 (21)
Practical tips about managing FCR for environment	41 (22)	186 (20)	235 (15)	57 (12)	139 (16)	382 (16)	418 (17)	85 (13)	229 (20)	274 (14)	53 (11)	450 (17)
Lifestyle help	42 (23)	186 (20)	200 (13)	47 (10)	100 (12)	375 (16)	348 (14)	113 (17)	191 (17)	270 (14)	82 (17)	379 (14)
Medication	33 (18)	166 (18)	203 (13)	59 (12)	87 (10)	375 (16)	338 (14)	114 (17)	170 (15)	282 (14)	86 (17)	366 (14)

Table 2. Number and percentage of respondents who need the different support types for different levels of general fearfulness before cancer and treatment phases

	General fearfulness before cancer				Treatment phase*				
	1-3	4-5	6-7	8-10	1	2	3	4	5
Talking about FCR	1471 (68)	315 (72)	234 (67)	165 (69)	105 (66)	30 (64)	716 (69)	1102 (69)	232 (68)
Enjoyable activities for distraction	1192 (55)	260 (59)	184 (53)	149 (63)	82 (52)	23 (49)	646 (62)	871 (55)	163 (48)
Psychological help or coaching	808 (37)	215 (49)	169 (49)	93 (39)	64 (40)	21 (45)	396 (38)	681 (43)	123 (36)
Practical tips about managing FCR for self	736 (34)	164 (38)	157 (45)	87 (37)	59 (37)	15 (32)	368 (35)	592 (37)	110 (32)
Information about FCR	616 (29)	146 (33)	115 (33)	83 (35)	52 (33)	18 (38)	307 (29)	489 (31)	94 (28)
Additional medical check-ups	452 (21)	105 (24)	76 (22)	62 (26)	23 (14)	1 (2)	185 (18)	392 (25)	94 (28)
Practical tips about managing FCR for environment	344 (16)	62 (14)	68 (20)	47 (20)	31 (19)	18 (38)	204 (20)	220 (14)	48 (14)
Lifestyle support	308 (14)	83 (19)	46 (13)	39 (16)	34 (21)	5 (11)	162 (16)	239 (15)	36 (11)
Medication	257 (12)	91 (21)	66 (19)	48 (20)	18 (11)	12 (26)	161 (15)	225 (14)	46 (13)

1 = wait and see, 2 = not yet started, 3 = in treatment, 4 = treatment completed, still check-ups, 5 = treatment completed, no more check-ups

Table 3. Number and percentage of respondents who need the different support types for different FCR expressions

Expressions of FCR	Rumination	Nervousness	Poor sleeping	Sadness	Inability to concentrate	Irritability	Listlessness	Physical complaints	Changed eating pattern	Increased heart rate	Tingling in hands or feet	Panic attacks
Talking about FCR	1556 (73)	1286 (74)	1198 (71)	810 (72)	812 (73)	787 (74)	503 (74)	463 (73)	421 (72)	352 (75)	258 (65)	293 (74)
Enjoyable activities for distraction	1239 (58)	1055 (60)	1003 (60)	663 (59)	681 (62)	641 (61)	391 (58)	404 (64)	359 (61)	298 (63)	223 (56)	219 (55)
Psychological help or coaching	970 (45)	839 (48)	763 (46)	605 (54)	580 (52)	538 (51)	340 (50)	344 (54)	300 (51)	255 (54)	169 (43)	241 (61)
practical tips about managing FCR for self	878 (41)	760 (44)	680 (41)	503 (45)	488 (44)	480 (45)	324 (48)	295 (46)	280 (48)	239 (51)	167 (42)	209 (53)
Information about FCR	715 (34)	604 (35)	559 (33)	380 (34)	374 (34)	380 (36)	238 (35)	258 (41)	204 (35)	182 (39)	135 (34)	149 (38)
Additional medical check-ups	530 (25)	430 (25)	388 (23)	282 (25)	284 (26)	289 (27)	169 (25)	201 (32)	175 (30)	131 (28)	112 (28)	119 (30)
practical tips about managing FCR for environment	370 (17)	329 (19)	316 (19)	203 (18)	228 (21)	241 (23)	149 (22)	139 (22)	117 (20)	116 (25)	76 (19)	100 (25)
Lifestyle support	328 (15)	290 (17)	286 (17)	191 (17)	215 (19)	199 (19)	139 (20)	123 (19)	149 (25)	97 (21)	74 (19)	82 (21)
Medication	361 (17)	305 (17)	342 (20)	240 (21)	222 (20)	182 (17)	151 (22)	145 (23)	129 (22)	116 (25)	76 (19)	126 (32)
No desire for help	92 (4)	74 (4)	65 (4)	41 (4)	49 (4)	37 (3)	29 (4)	17 (3)	21 (4)	15 (3)	22 (6)	8 (2)

Table 4. Number and percentage of respondents who need the different support types for different FCR consequences

Consequences of FCR	Difficulties with sex or intimacy	Less enjoyment of things previously enjoyed	Fewer social activities	Inability to do my (volunteer) work	Difficulties with daily activities	Inability to do my hobbies	Tensions within the family	Relationship problems	Less healthy lifestyle
Talking about FCR	1025 (71)	1113 (71)	995 (71)	777 (72)	876 (69)	862 (70)	454 (73)	334 (72)	205 (68)
Enjoyable activities for distraction	806 (56)	869 (55)	780 (56)	632 (59)	708 (56)	688 (56)	363 (59)	264 (57)	181 (60)
Psychological help or coaching	695 (48)	761 (48)	692 (50)	541 (50)	624 (49)	607 (50)	361 (58)	278 (60)	158 (52)
Practical tips about managing FCR for self	571 (39)	657 (42)	585 (42)	463 (43)	518 (41)	513 (42)	274 (44)	211 (46)	134 (44)
Information about FCR	467 (32)	511 (32)	461 (33)	351 (33)	395 (31)	389 (32)	216 (35)	164 (36)	97 (32)
Additional medical check-ups	341 (24)	384 (24)	333 (24)	259 (24)	297 (23)	293 (24)	148 (24)	103 (22)	86 (28)
Practical tips about managing FCR for environment	279 (19)	285 (18)	261 (19)	230 (21)	255 (20)	250 (20)	153 (25)	111 (24)	47 (16)
Lifestyle support	253 (17)	259 (16)	257 (18)	218 (20)	237 (19)	223 (18)	123 (20)	97 (21)	74 (25)
Medication	242 (17)	303 (19)	266 (19)	218 (20)	246 (19)	248 (20)	118 (19)	102 (22)	65 (22)
No desire for help	71 (5)	68 (4)	60 (4)	45 (4)	55 (4)	53 (4)	20 (3)	14 (3)	13 (4)

Supplementary Materials 4A: Demographic characteristics

The information in table below presents data from the electronic medical records of 44 of the participants. Due to the Covid-19 pandemic, data from the other participants could not be collected and is missing.

Table 1. Demographic characteristics of the participants.

	Intervention group n=25	**Control group n=19**	**Total n=44**
	mean (sd)	**mean (sd)**	**mean (sd)**
Age	64.8 (9.78)	60.6 (13.2)	62.9 (11.6)
Years since diagnosis	7.62 (10.1)	5.85 (4.51)	6.85 (8.13)
Years since end of treatment	4.48 (2.79)	3.85 (2.62)	4.19 (2.70)
number of years registered at GP	17.1 (9.29)	11.5 (6)	14 (7.76)
	n (%)	n (%)	n (%)
Sex			
Male	15 (47)	9 (41)	24 (44)
Female	17 (53)	13 (59)	30 (56)
Cancertype			
Breast	8 (32)	8 (40)	16 (36)
Colorectal	3 (12)	10 (50)	13 (29)
Respiratory system	3 (12)	0 (0)	3 (7)
Digestive system	2 (8)	1 (5)	3 (7)
Gynaecological	2 (8)	1 (5)	3 (7)
Urinary tract	2 (8)	0 (0)	2 (4)
Prostate	1 (4)	0 (0)	1 (2)
Hematological	1 (4)	0 (0)	1 (2)
Endocrine	1 (4)	1 (5)	2 (4)
Head and neck	0 (0)	1 (5)	1 (2)
Other	5 (20)	2 (10)	7 (16)
Highest cancer stage			
1	7 (33)	5 (28)	12 (31)
2	7 (33)	7 (39)	14 (36)
3	6 (29)	5 (28)	11 (28)
4	1 (5)	1 (6)	2 (5)

Table 1. Demographic characteristics of the participants. (*continued*)

	Intervention group n=25 mean (sd)	Control group n=19 mean (sd)	Total n=44 mean (sd)
Cancer treatment			
surgery	22 (88)	19 (95)	41 (91)
radiotherapy	13 (52)	10 (50)	23 (51)
chemotherapy	11 (44)	6 (30)	17 (38)
hormone treatment	9 (36)	5 (25)	14 (31)
other	2 (8)	0 (0)	2 (4)
Medical history			
comorbidities	14 (64)	9 (45)	23 (55)
prior depressive disorder	5 (22)	3 (16)	8 (19)
prior anxiety disorder	2 (9)	2 (9)	4 (10)
prior burnout	3 (13)	2 (10)	5 (12)
prior use of antidepressants	8 (33)	4 (20)	12 (27)
Educational background			
Primary education	2 (6)	0 (0)	2 (4)
Lower vocational education	6 (19)	5 (22)	11 (20)
High school	5 (16)	2 (8)	7 (13)
Intermediate vocational education	6 (19)	3 (13)	9 (16)
Higher vocational education	8 (25)	4 (17)	12 (22)
University	5 (16)	7 (30)	12 (22)
Other	0 (0)	2 (9)	2 (4)
Daily life			
Retired	12 (38)	10 (43)	22 (40)
Employed	11 (34)	9 (39)	20 (36)
Self-employed	3 (9)	2 (9)	5 (9)
Volunteering	2 (6)	1 (4)	3 (5)
Homemaker	2 (6)	0 (0)	2 (4)
Incapacitated for work	2 (6)	0 (0)	2 (4)
Unemployed	0 (0)	1 (4)	1 (2)

Supplementary Materials 5A: Demographic and medical information of the participants

Table 1. Demographic and medical information of the participants

	Primary care FCR intervention n= 85	**Waiting list n= 82**
	mean (SD)	**mean (SD)**
Healthcare use in year before the intervention (number of appointments)		
General practitioner	1.2 (2.0)	1.6 (3.3)
Mental health worker	0.2 (1.0)	0.5 (2.0)
Medical specialist	4.4 (11.2)	3.3 (5.8)
Psychological care	3.7 (4.9)	3.8 (6.4)
Complementary medicine	4.4 (11.0)	5.1 (12.1)
	n (%)	n (%)
Living situation		
Married / registered partnership	40 (50%)	43 (58%)
Living together	17 (21%)	12 (16%)
Widow	6 (8%)	7 (9%)
Divorced	10 (13%)	4 (5%)
Single	7 (9%)	8 (11%)
Cancer type		
Breast cancer	38 (45%)	33 (43%)
Colon cancer / digestive system	16 (19%)	17 (22%)
Uterine and gynaecological cancers	8 (10%)	11 (14%)
Skin cancer	10 (13%)	8 (11%)
Haematological cancers	9 (11%)	8 (11%)
Prostate cancer	2 (3%)	2 (3%)
Head and neck	1 (1%)	2 (3%)
Endocrine cancer	0 (0%)	2 (3%)
Lung cancer / respiratory system	1 (1%)	1 (1%)
Cancer of the urinary tract	1 (1%)	0 (0%)
Other	11 (14%)	11 (14%)

Table 1. Demographic and medical information of the participants (*continued*)

	Primary care FCR intervention n= 85 mean (SD)	Waiting list n= 82 mean (SD)
Cancer treatment		
Chemotherapy	45 (53%)	49 (58%)
Radiotherapy	39 (46%)	35 (42%)
Surgery	68 (80%)	63 (75%)
Immunotherapy	13 (25%)	17 (20%)
Hormone therapy	20 (24%)	16 (19%)
Other	9 (11%)	8 (10%)

Supplementary Materials 5B: Analysis of subgroups

Table 1. β-values, 95% confidence intervals, standard errors, t-values and p-values for the different subgroups.

	β	CI	Std. error	t-value	p-value
(Intercept)	3.32	-4.65 - 11.27	4.48	0.74	0.46
Group	2.07	-9.14 - 13.16	6.28	0.33	0.74
Time (months)	-0.08	-0.37 - 0.21	0.15	-0.56	0.58
Age	0.00	-0.07 - 0.07	0.04	-0.03	0.98
Sex	-0.82	-2.73 - 1.1	1.08	-0.76	0.45
Practical education	0.88	-5.39 - 7.19	3.55	0.25	0.80
Secondary education	1.55	-4.83 - 7.99	3.62	0.43	0.67
Higher education	0.80	-5.26 - 6.86	3.42	0.24	0.81
Other	6.02	-1.47 - 13.35	4.17	1.44	0.15
FCR severity baseline	0.72	0.55 - 0.9	0.10	7.42	0.00
FCR distress baseline	-0.14	-0.4 - 0.12	0.15	-0.96	0.34
4DSQ depression baseline	-0.08	-0.42 - 0.27	0.19	-0.39	0.69
4DSQ distress baseline	0.09	-0.1 - 0.27	0.10	0.83	0.41
4DSQ anxiety baseline	-0.14	-0.56 - 0.25	0.23	-0.64	0.52
4DSQ somatization baseline	0.02	-0.13 - 0.18	0.09	0.27	0.79
Age*Group	0.00	-0.11 - 0.1	0.06	-0.07	0.95
Sex*Group	-0.61	-3.38 - 2.17	1.56	-0.39	0.70
Practical education*Group	2.06	-5.05 - 9.2	4.02	0.51	0.61
Secondary education*Group	0.25	-7.54 - 8.01	4.39	0.06	0.95
Higher education*Group	1.71	-5.11 - 8.54	3.85	0.44	0.66
Other*Group	-0.42	-10.59 - 9.96	5.78	-0.07	0.94
FCR severity baseline*Group	-0.03	-0.28 - 0.23	0.14	-0.20	0.84
FCR distress baseline*Group	0.35	-0.05 - 0.74	0.22	1.56	0.12
4DSQ depression baseline*Group	0.10	-0.37 - 0.58	0.27	0.37	0.71
4DSQ distress baseline*Group	-0.17	-0.42 - 0.07	0.14	-1.27	0.21
4DSQ anxiety baseline*Group	0.32	-0.14 - 0.79	0.26	1.23	0.22
4DSQ somatization baseline*Group	-0.11	-0.32 - 0.11	0.12	-0.87	0.38

NB The significant p-values of FCR severity baseline indicate that those starting with higher scores also end with higher scores. Since there is no significant interaction effect of baseline FCR and Group, intervention effectiveness is not related to FCR severity baseline scores.

Table 2. β-values, 95% confidence intervals, standard errors, t-values and p-values comparing the intervention outcome for different MHWs.

	β	CI	Std. error	t-value	p-value
(Intercept)	4.27	0.94 - 7.6	1.74	2.46	0.01
FCR severity baseline	0.75	0.65 - 0.85	0.05	14.25	0.00
Time (months)	-0.13	-0.41 - 0.15	0.14	-0.89	0.37
MHW 2	-0.29	-2.46 - 1.89	1.14	-0.25	0.80
MHW 3	1.04	-1.44 - 3.51	1.29	0.80	0.42
MHW 4	0.37	-2.8 - 3.56	1.66	0.22	0.82
MHW 5	1.30	-0.88 - 3.49	1.15	1.14	0.26
MHW 6	-3.15	-6.92 - 0.64	1.98	-1.59	0.11
MHW 7	-0.22	-2.85 - 2.42	1.38	-0.16	0.87
MHW 8	-1.08	-3.69 - 1.54	1.37	-0.79	0.43

Table 3. β-values, 95% confidence intervals, standard errors, t-values and p-values for educational backgrounds and years of work experience of the MHWs.

	β	CI	Std. error	t-value	p-value
(Intercept)	4.04	1.12 - 6.97	1.51	2.68	0.01
FCR severity baseline	0.74	0.64 - 0.84	0.05	14.17	0.00
Time (months)	-0.14	-0.43 - 0.14	0.15	-0.98	0.33
Work experience MHW (years)	0.06	-0.11 - 0.22	0.09	0.67	0.51
MHW background 2	-1.42	-5.58 - 2.77	2.15	-0.66	0.51
MHW background 3	0.01	-4.69 - 4.76	2.43	0.00	1.00
MHW background 4	0.39	-3.05 - 3.85	1.78	0.22	0.83

Table 4. β-values, 95% confidence intervals, standard errors, t-values and p-values for healthcare use.

	β	CI	Std. error	t-value	p-value
(Intercept)	4.42	1.81 - 7.01	1.37	3.23	0.00
FCR severity baseline	0.70	0.61 - 0.8	0.05	13.86	0.00
Group	2.74	1.16 - 4.34	0.85	3.24	0.00
Time (months)	-0.10	-0.37 - 0.19	0.14	-0.67	0.50
number of appointments complementary medicine T0-T1	0.18	-0.92 - 1.28	0.58	0.31	0.75
number of appointments psychological care T0-T1	-0.94	-2.36 - 0.49	0.76	-1.24	0.21
number of appointments GP T0-T1	-2.09	-5.17 - 1.03	1.64	-1.27	0.20
number of appointments specialist T0-T1	0.72	-0.32 - 1.75	0.55	1.31	0.19
number of appointments MHW T0-T1	1.32	-1.44 - 4.07	1.46	0.90	0.37
number of appointments complementary medicine T0-T1*Group	-0.37	-1.67 - 0.93	0.69	-0.54	0.59
number of appointments psychological care T0-T1*Group	0.76	-1.33 - 2.83	1.11	0.68	0.49
number of appointments GP T0-T1*Group	0.84	-2.49 - 4.14	1.76	0.48	0.63
number of appointments specialist T0-T1*Group	-0.77	-2.66 - 1.11	1.00	-0.77	0.44
number of appointments MHW T0-T1*Group	-0.43	-3.74 - 2.89	1.76	-0.24	0.81

Table 5. β-values, 95% confidence intervals, standard errors, t-values and p-values comparing the intervention outcome for first being waitlisted or not.

	β	CI	Std. error	t-value	p-value
(Intercept)	5.15	2.26-8.04	1.48	3.48	0.00
FCR severity baseline	0.67	0.55-0.79	0.06	11.16	0.00
Waitlist	-0.66	-1.84-0.52	0.60	-1.09	0.28
Time (months)	-0.06	-0.16-0.04	0.05	-1.14	0.26

Supplementary Materials 5C: Participant experience

The responses of the intervention group to the quantitative questions in the survey on feasiblity and acceptability are presented in Table 1. In the open-ended questions, when asked what helped the most, 41% mentioned conversations with the MHW. Others mentioned part of the program, such as the exercises, the videos and the modules on CBT, rumination, and relaxation. Notably, these same parts were also mentioned by others when asked what helped the least.

Table 1. Mean scores and percentages scoring 3-5 for the survey on participant experiences with the intervention.

Item	Mean score (1-5)* (SD)	% scoring 3-5
Experienced burden of FCR before the intervention	3.3 (1.1)	57 (76%)
Contentment with the outcome	3.7 (1.0)	67 (91%)
To what extent do you consider this to be the right approach?	3.6 (0.9)	64 (89%)
Practicality of the intervention	3.7 (0.9)	64 (90%)
Sufficiency of the information before the intervention	3.8 (0.8)	67 (94%)
Satisfaction with the way the intervention ended	3.8 (1.0)	65 (93%)
To what extent do you consider this intervention to be burdensome?	1.6 (0.7)	8 (11%)
Would you recommend this intervention?	3.9 (1.0)	64 (90%)
Do you consider the general practice the right place for this intervention?	3.0 (1.2)	51 (72%)
Did you appreciate the intervention being completely online?	3.2 (1.1)	56 (79%)

*1 = not at all, 2 = slightly, 3 = moderately, 4 = very, 5 = extremely

While most would recommend the intervention, some people emphasised it would not be the right fit for everyone and suggested first having an intake to check what people are looking for, whether they are independent and self-disciplined enough to participate in such a program on their own and whether they have already completed a similar program. About offering the program at GP practices, some respondents stressed that professionals needed to have expertise in psycho-oncology and that this was not always available at GP practices. Some mentioned that since patients are at a hospital for their cancer treatment it might be logical to offer this intervention there as well.

Regarding the intervention being offered online, about two thirds mentioned the benefit of saving time, some appreciated being able to have the sessions in their own environment and some appreciated being able to plan the sessions in between other activities. However, some others mentioned that travel time can also help to prepare for the conversation and to unwind afterwards and that a home environment can also be distracting. Also, over one

third of respondents stated they preferred having face-to-face sessions, due to non-verbal communication and finding it easier to have deep, personal conversations face-to-face, and to build a connection. In addition, a quarter mentioned sometimes having technical or connection issues. Respondents were also asked if they minded not knowing the MHW beforehand. For most this was not a problem.

Supplementary Materials 6A: Interviewguides on the feasibility and acceptability of a primary care intervention for fear of cancer recurrence

INTERVIEWGUIDE FOR PATIENTS

Complaints

1. Before we talk about the support you received: Can you tell us something about the complaints you had when you decided to participate in the study?
   - Anxiety/worries about cancer recurrence, ruminating
   - Sleep problems, physical complaints, tension
   - Work, social contacts, going out, family, household

Needs

2. Can you tell us something about the expectations you had of the guidance you would receive?
   - Positive expectations
   - Doubt

Experiences

3. Can you briefly describe the intervention you received?
   - Mental health worker/general practitioner/referral
   - Online program

4. What was it like for you to receive the intervention?
   - Positive experiences, explanation
   - Negative experiences, explanation
   - Make sure that it remains clear whether it concerns the general practitioner / MHW / online programme

5. What do you think helped and why?
   - Which aspects? and how/why? what helped the most?

6. What didn't help and why?
   - Intervention components that had no effect
   - Missing parts
   - Not the right intensity/setting
   - Right timing

7. Can you tell us something about how you experienced the contact with the GP (in the context of this intervention)?
   - How was the contact?
   - How is the contact in general?

8. Can you tell us something about how you experienced your contact with the MHW (in the context of this intervention)?
   - How was the contact?
   - Had you had contact before?

9. If applicable, what was it like to do the online program?
   - Which parts had added value and why? (show overview of components)
   - Which parts had no added value and why?
   - Did everything work, or did something sometimes not work?
   - What did you think about the online platform?
   - What made it convenient or inconvenient to use?

10. What did you think of the exercises?
    - Did the exercises help you? With what and how? (ask for examples)
    - What have you learned?
    - Are you still doing the exercises? When? Which?

11. Was the care you received useful to you? Why or why not?
    - Travel time and costs
    - Time and location of care
    - Availability/speed of feedback
    - Clarity of agreements made (appointments etc)

12. Do you feel that the intervention has helped? How do you notice that?
    - Fear
    - Sleep problems, physical complaints, tension
    - Work, social contacts, going out, family, household

13. Did you receive any other forms of support during the same period that made a difference to you? Which kinds? How was it helpful?
    - Care from family/friends
    - Books
    - Religious/spiritual support

Ending the interview

14. Can you briefly indicate to what extent this intervention is appealing and what the added value is according to you?

15. Is there anything else you would like to share?

16. What was it like for you to participate in the study?

Appendix 1

Overview of modules of the online program

Two basic modules

1. Psycho-education: recognizing fear
2. Basic principles of CBT (part 1 and 2)

Five optional modules

1. Rumination
2. Avoidance
3. Undertaking enjoyable activities
4. Learning to relax
5. Reassurance

Overview of exercises

Recognizing signals of fear
Recognizing situations that cause fear
Charting feelings, thoughts and responses to situations that cause fear
Recognizing unhelpful thoughts, challenging these thoughts and thinking of helpful thoughts

Thoughts-stop technique
Rumination fifteen minutes
Rumination elastic
Not thinking but doing (something else)

Charting situations that you avoid and breaking through avoidance

Undertaking enjoyable activities

Learning to relax

Reassurance strategies

INTERVIEWGUIDE FOR MHWS

Questions about the training

1. What was it like to participate in the training?
   - What was of added value? What was not? Why?
   - What points for improvement do you see? Why?
   - New things learned
   - Duration
   - Right aspects: knowledge, self-efficacy, practicing with actor
   - Is it a topic that has priority for you?

Questions about the guidance

2. Has your way of treating patients changed since you participated in the training?
   - Example / explanation

3. Can you briefly describe the treatment you provided to your patients?
   - Number of sessions, topics
   - Online program

4. What was it like for you to provide the treatment?
   - Positive experiences
   - Negative experiences

5. When you think about your patients who have received treatment, do you feel that the treatment has had an effect? Do you notice a difference compared to before the treatment?
   - Fear
   - Sleep, physical complaints, tension
   - Work, social contacts, family, household

6. In what way and through which aspects did the treatment have added value in your opinion?
   - Which aspects? and how/why?
   - Psycho-education, normalization, self-management
   - Show a list of parts and exercises and ask what worked and what did not

7. In what way did the treatment not help?
   - Intervention components that had no effect
   - Missing parts

- Not the right intensity/setting

8. Was the care you provided practical for you and your patient?
   - Time investment
   - Appropriate intensity of contact
   - Clarity of agreements
   - For people who had five sessions: could it have been less for those patients? For those who had less sessions: was five too much?

9. What is your opinion of the online program offered?
   - Complete? Better than alternatives?
   - What did you think of the online platform?
   - Was it convenient to use?

10. Do you think that this type of care and this issue is appropriate for the general practitioner and the MHW (either online or face-to-face)?
    - Does it fit with the relationship patients usually have with their GP? (in your experience)
    - Is the subject too vulnerable?
    - Did you feel sufficiently equipped? Would you have felt equipped without the training?

11. *For part B only*: How did you feel about offering this treatment online, to patients you do not know?
    - Is it appropriate for the subject?

Ending the interview

12. In summary, do you think this form of care by the MHW (either online or face-to-face) is appealing and has added value?
    - Follow-up question: Are there groups for whom it is not appealing or of added value? Why?
    - For which people do you think this works especially well? Why?
    - Which people would you not offer this? Why?
    - Do you see any points for improvement for this type of care?

13. What possibilities do you see for offering this type of care in daily practice?

14. Is there anything else you would like to share?

15. What was it like for you to participate in the study? Why did you choose to participate?